Online ISSN: 3007 – 0244
Print ISSN: 2410 – 4280
www.newjournal.ssmu.kz

ҚАЗАҚСТАН РЕСПУБЛИКАСЫ ПРЕЗИДЕНТІНІҢ ЖАНЫНДАҒЫ
ҰЛТТЫҚ ҒЫЛЫМ АКАДЕМИЯСЫ

Science & Healthcare

PEER-REVIEWED MEDICAL SCIENTIFIC JOURNAL

РЕЦЕНЗИРУЕМЫЙ МЕДИЦИНСКИЙ НАУЧНО-ПРАКТИЧЕСКИЙ ЖУРНАЛ

# Наука и Здравоохранение

# Ғылым және Денсаулық Сақтау

РЕЦЕНЗИЯЛАНАТЫН МЕДИЦИНАЛЫҚ ҒЫЛЫМИ-ПРАКТИКАЛЫҚ ЖУРНАЛ

Volume 27
Issue 3
2025

**Министерство здравоохранения Республики Казахстан**
**Учредитель: НАО «Медицинский университет Семей»**
**Основан в 1999 году**.

Журнал зарегистрирован в Министерстве информации и коммуникаций Республики Казахстан Комитете информации **№ 17773-Ж.**

Входит в Перечень изданий, рекомендуемых Комитетом по обеспечению качества в сфере науки и высшего образования МНиВО Республики Казахстан для публикации основных результатов научной деятельности **(Приказ №603 от 12.07.2024г.)**

Включен в **Ulrich's Periodicals Directory**, **Global Health, CAB Abstracts, InfoBase Index, Directory of Research Journals Indexing, Российский индекс научного цитирования (РИНЦ), E-library.ru, Cyberleninka.ru, Norwegian register for scientific journals (NSD), Всесоюзный институт научной и технической информации Российской академии наук (ВИНИТИ РАН), Ассоциацию CONEM, РАЦС, DataBase Indexing, ICI World of Journals, Crossref.**

**Подписной индекс 74611**
**в каталоге «Казпочта»**
Цена свободная

**Сайт** http://newjournal.ssmu.kz
**e-mail:** selnura@mail.ru

**Адрес редакции:**
071400, г. Семей
ул. Абая Кунанбаева, 103
контактный телефон:
(7222) 56-42-09 (вн. № 1054)
факс: (7222) 56-97-55

**Выпускающий редактор:**
Э.Ф. Сапаргалиева
**Переводчики:**
С.А. Жаукенова, Н.А. Шумский

This work is licensed under a **Creative Commons Attribution 4.0 International License**

**При цитировании материалов ссылка на журнал обязательна.**

Отпечатано в типографии Медицинского университета Семей
*Подписано в печать: 30.06.2025г.*
Формат 60x90/8.
Печать цифровая. Усл.п.л 36,0
Тираж 500 экз., зак.188

**Online ISSN: 3007 – 0244**
**Print ISSN: 2410 – 4280**

# НАУКА И ЗДРАВООХРАНЕНИЕ

## РЕЦЕНЗИРУЕМЫЙ МЕДИЦИНСКИЙ НАУЧНО-ПРАКТИЧЕСКИЙ ЖУРНАЛ

**Том 27 №3, 2025**

Журнал «Наука и Здравоохранение» - рецензируемый медицинский научно-практический журнал, который публикует результаты оригинальных исследований, обзоры литературы, клинические случаи, краткие сообщения и отчеты о конференциях по широкому кругу вопросов, связанных с клинической медициной и общественным здоровьем. Основной читательской аудиторией журнала является медицинское научное сообщество, практикующие врачи, докторанты и магистранты в области медицины и общественного здоровья.

**Главный редактор:** **А.А. Дюсупов**
доктор медицинских наук, профессор

**Зам. главного редактора:** **Д.М. Шабдарбаева**
доктор медицинских наук, профессор

**Редакционный совет:**
Абдрахманов А.С. (Нур-Султан, Казахстан)
Акильжанова А.Р. (Нур-Султан, Казахстан)
Акшулаков С.К. (Нур-Султан, Казахстан)
Баймаханов Б.Б. (Алматы, Казахстан)
Брузати Лука Джиованни Карло (Удин, Италия)
Виджай Кумар Чатту (Торонто, Канада)
Гржибовский А.М. (Архангельск, Российская Федерация)
Гюрель Фазыл Сердар (Анкара, Турция)
Даутов Т.Б. (Нур-Султан, Казахстан)
Джерзи Крупински Белецки (Барселона, Испания)
Жумадилов Ж.Ш. (Нур-Султан, Казахстан)
Кавальчи Чемиль (Анкара, Турция)
Карпенко А.А. (Новосибирск, Российская Федерация)
Ковальчук В.В. (Санкт-Петербург, Российская Федерация)
Лесовой В.Н. (Харьков, Украина)
Лукьянов С.А. (Москва, Российская Федерация)
Мутиг К. (Шарите, Германия)
Носо Й. (Шимане, Япония)
Раманкулов Е.М. (Нур-Султан, Казахстан)
Степаненко В.Ф. (Обнинск, Российская Федерация)
Тапбергенов С.О. (Семей, Казахстан)
Тринчеро Элизабетта Флора Ольга (Милан, Италия)
Хоссейни Хенгаме (Скрантон, Соединенные Штаты Америки)
Хоши М. (Хиросима, Япония)
Шейнин А. (Тель-Авив, Израиль)

**The Ministry of Healthcare of the Republic of Kazakhstan**

**Publisher: NCJSC «Semey Medical University»**

**Established in 1999**

Journal is registered in Ministry of Information and Communication of the Republic of Kazakhstan in the Committee of Information. Certificate of registration of a periodical printed publication **№ 17773-Ж.**

The journal is included in the List of publications recommended by the Committee for Quality Assurance in the Field of Science and Higher Education of the Ministry of Science and Higher Education of the Republic of Kazakhstan for the publication of the main results of scientific activity **(Order from 12.07.2024 №603)**

The journal is indexed in **Ulrich's Periodicals Directory**, **Global Health, CAB Abstracts, InfoBase Index, Directory of Research Journals Indexing, Russian Science Citation Index, Scientific electronic library E-library.ru, Cyberleninka.ru, NSD (Norwegian register for scientific journals), VINITI RAN, CONEM, RASS, DataBase Indexing, ICI World of Journals, Crossref.**

**Subscription index in catalogue of "Kazpost" 74611**

Open price.

**Website** http://newjournal.ssmu.kz

**e-mail:** selnura@mail.ru

**Address of editor office and publisher:**
071400, Semey, Abay st. 103,
Tel. (7222) 56-42-09 (in1054)
Fax: (7222) 56-97-55

**Publishing editor:**
E.F. Sapargaliyeva
**Translators:**
S.A. Zhaukenova,
N.A. Shumskiy

This work is licensed under a **Creative Commons Attribution 4.0 International License**

**In case of citation of materials, a link on the journal is required.**

Printed by printing office of Semey medical university
**Signed in press** on 30 June 2025
Format 60x90/8. 36,0 Digital printing.
Circulation 500 copies, ord. 188

**Online ISSN: 3007 – 0244**
**Print ISSN: 2410 – 4280**

# SCIENCE & HEALTHCARE

**PEER-REVIEWED SCIENTIFIC-PRACTICAL MEDICAL JOURNAL**

**Volume 27 №3, 2025**

«Science & Healthcare» is a peer-reviewed scientific-practical medical journal, which publishes original articles, literature reviews, clinical case, short communications and conference reports covering all areas of clinical medicine and public health. The primary audience of the journal includes medical scientific community, practicing physicians, doctoral- and master - students in the fields of medicine and public health.

**Chief editor:** **A.A. Dyussupov**
Doctor of medical science, Professor

**Deputy Editor in Chief:** **D.M. Shabdarbayeva**
Doctor of medical science, Professor

**Editorial board:**
Abdrakhmanov A.S. (Nur-Sultan, Kazakhstan)
Akilzhanova A.R. (Nur-Sultan, Kazakhstan)
Akshulakov S.K. (Nur-Sultan, Kazakhstan)
Baimakhanov B.B. (Almaty, Kazakhstan)
Brusati Luca G. (Udine, Italy)
Vijai Kumar Chattu (Toronto, Canada)
Grjibovski A.M. (Arkhangelsk, Russian Federation)
Gurel Fazil Serdar (Ankara, Turkey)
Jerzy Krupinski Bielecki (Barselona, Spain)
Dautov T.B. (Nur-Sultan, Kazakhstan)
Zhumadilov Zh.Sh. (Nur-Sultan, Kazakhstan)
Karpenko A.A. (Novosibirsk, Russian Federation)
Kavalci Cemil (Ankara, Turkey)
Kovalchuk V.V. (St. Petersburg, Russian Federation)
Lesovoy V.N. (Kharkiv, Ukraine)
Luk'yanov S.A. (Moscow, Russian Federation)
Mutig K. (Sharite, Germany)
Noso Y. (Shimane, Japan)
Ramankulov Ye.M. (Nur-Sultan, Kazakhstan)
Stepanenko V.F. (Obninsk, Russian Federation)
Tapbergenov S.O. (Semey, Kazakhstan)
Trinchero Elisabetta Flora Olga (Millan, Italy)
Hosseini Hengameh (Scranton, United States of America)
Hoshi M. (Hiroshima, Japan)
Sheinin Anton (Tel-Aviv, Israel)

**Қазақстан Республикасы денсаулық сақтау министрлігі**

**Құрылтайшы: КеАҚ «Семей медицина университеті» 1999 негізі салынды**

Журнал Қазақстан Республикасы ақпарат және комуникациялар министрлігі, Ақпарат комитетінде тіркелген. Мерзімді баспасөз басылымын есепке қою туралы куәлігі **№ 17773-Ж**

**Журнал Ғылыми еңбектің негізгі нәтижелерін жариялау үшін Қазақстан Республикасы Ғылым және жоғары білім министрлігінің Ғылым және жоғары білім саласында сапаны қамтамасыз ету комитеті ұсынатын ғылыми басылымдар** Тізбесіне кіреді (Бұйрық №603 12.07.2024ж.)

**Ulrich's Periodicals Directory, Global Health, CAB Abstracts, InfoBase Index, Directory of Research Journals Indexing, Ғылыми дәйектеу Ресейлік индекс (РИНЦ), E-library.ru. - Ғылыми электронды кітапханаға, Cyberleninka.ru, NSD (Norwegian register for scientific journals), ВИНИТИ РАН, CONEM, РАЦС, DataBase Indexing, ICI World of Journals, Crossref** енгізілді.

**Каталогтағы жазылу индексі «Казпочта» 74611**

Бағасы еркін
**Сайт** http://newjournal.ssmu.kz
**e-mail:** selnura@mail.ru

**Баспаның және баспагердің мекен-жайы:**
071400, Семей қаласы,
Абай көшесі, 103.
тел. (87222) 56-42-09 (ішкі 1054);
факс: (7222) 56-97-55

**Баспа редакторы:**
Э.Ф. Сапаргалиева
**Аудармашылар**:
С.А. Жаукенова, Н.А. Шумский

This work is licensed under a Creative Commons Attribution 4.0 International License

**Материалдарды дәйектеу кезінде журналға сілтеме жасау міндетті.**

Семей медицина университетінің баспаханасында басылған

Баспаға қол қойылды30.06.2025.
Формат 60х90/8. Баспа сандық.
Шартты-баспа парағы 36,0
Таралуы 500 дана. Зак.188

**Online ISSN: 3007 – 0244**
**Print ISSN: 2410 – 4280**

# ҒЫЛЫМ ЖӘНЕ ДЕНСАУЛЫҚ САҚТАУ

## РЕЦЕНЗИЯЛАНАТЫН МЕДИЦИНАЛЫҚ ҒЫЛЫМИ-ПРАКТИКАЛЫҚ ЖУРНАЛ

**Том 27 №3, 2025**

«Ғылым және денсаулық сақтау» журналы - рецензияланатын медициналық ғылыми-практикалық журнал, клиникалық медицина мен қоғамдық денсаулықпен байланысты бірегей зерттеулер нәтижелерін, әдеби шолуларды, кең шеңберлі сұрақтар бойынша конференциялар туралы қысқа мәлімдемелер мен есептерді жариялайды. Медициналық ғылыми қоғамдастық, тәжірибелік дәрігерлер, медицина мен қоғамдық денсаулық саласындағы докторанттар мен магистранттар журналдың негізгі оқырман аудиториясы болып табылады.

**Бас редактор**: **А.А. Дюсупов**
медицина ғылымдарының докторы, профессор

**Бас редактордың орынбасары: Д.М. Шабдарбаева,**
медицина ғылымдарының докторы, профессор

**Редакциялық кеңес:**
Абдрахманов А.С. (Нұр-Сұлтан, Қазақстан)
Ақылжанова А.Р. (Нұр-Сұлтан, Қазақстан)
Акшулаков С.К. (Нұр-Сұлтан, Қазақстан)
Баймаханов Б.Б. (Алматы, Қазақстан)
Брузати Лука Джиованни Карло (Удин, Италия)
Виджай Кумар Чатту (Торонто, Канада)
Гржибовский А.М. (Архангельск, Российская Федерация)
Гюрель Фазыл Сердар (Анкара, Түркия)
Джерзи Крупински Белецки (Барселона, Испания)
Даутов Т.Б. (Нұр-Сұлтан, Казақстан)
Жумадилов Ж.Ш. (Нұр-Сұлтан, Қазақстан)
Кавальчи Чемиль (Анкара, Түркия)
Карпенко А.А. (Новосибирск, Ресей Федерациясы)
Ковальчук В.В. (Санкт-Петербург, Ресей Федерациясы)
Лесовой В.Н. (Харьков, Украина)
Лукьянов С.А. (Москва, Ресей Федерациясы)
Мутиг К. (Шарите, Германия)
Носо Й. (Шимане, Жапония)
Раманқұлов Е.М. (Нұр-Сұлтан, Қазақстан)
Степаненко В.Ф. (Обнинск, Ресей Федерациясы)
Тапбергенов С.О. (Семей, Қазақстан)
Тринчеро Элизабетта Флора Ольга (Милан, Италия)
Хоссейни Хенгаме (Скрантон, Америка Құрама Штаттары)
Хоши М. (Хиросима, Жапония)
Шейнин А. (Тель-Авив, Израиль)

## Содержание

### *ОРИГИНАЛЬНЫЕ ИССЛЕДОВАНИЯ*

**Bekbossynova M.S., Sailybaeva A.I., Kabduyeva G.A., Jetybayeva S.K., Tauekelova A.T., Novikova S.P., Myrzakhmetova G.Sh., Duisenbina Zh.S., Sakhipova A., Akzholova K.T., Kushugulova A.R.** 7-15
Epidemiology, Resource Distribution, and Management Challenges of Chronic Heart Failure in Kazakhstan: A National Retrospective Analysis

**Murtazaliyeva A.V., Berezina G.M., Svyatova G.S., Yesset M.S. Burabayeva A.T.** 16-26
Prevalence of polymorphisms in warfarin metabolism-related genes among the Kazakh population

**Antikeev D.A., Orazkhan A.A., Temirbulatova L.B., Beisimbayeva D.Zh., Abiltayev A.M., Tashtemirova O.G., Shukimbayeva A.M., Makhmutova A.M.** 27-35
Neurological complications in extracorporeal membrane oxygenation: risk factors for the development of acute cerebrovascular events

**Zhautikova S.B., Urazalina N.M., Tolubayeva D.B.** 36-41
The effect of repaglinide and metformin on external respiratory function in patients with diabetes and ischemic heart disease associated with obesity

**Uruzbayeva G.A., Bulegenov T.A., Mussakhanova A.K., Dzhusupov K., Ibekenov O.T., Smailova Zh.K., Baibussinova A.Zh., Imanbayev M.N., Zharykbassova F.Zh., Kussainova A.S., Armankyzy A.** 42-52
Retrospective analysis of patients with obliterating atherosclerosis of the lower extremity arteries in the Abai region of the Republic of Kazakhstan

**Khangeldi A.Ye., Khamidullina Z.G., Shanazarov N.A., Afanasyev M.S., Grishache T.G., Akkazhieva N.N., Tanysheva G.A.** 53-63
Эффективность фотодинамической терапии в лечении предраковых состояний шейки матки, вызванных вирусом папилломы человека

**Kyrykbayeva S.S., Oshibaeva A.E., Nuskabayeva G.O., Goremykina M.V., Urazalina N.M.** 64-69
Domestic Violence as a Public Health Challenge: Results of a Mass Sociological Study in Turkistan Region

**Bayzullina A.O., Zhamaliyeva L.M., Ermagambetova A.P.** 70-78
Assessment of depression, fatigue, and psychological well-being in patients after stroke: results of a cross-sectional study using the BECK, FAS, and MHC-SF scales

**Duisekova S., Gaisina M., Akhmetova K., Uazhanov M., Sekenova R.K., Dauletova G.Sh.** 79-87
Social Determinants of Health Among Unemployed Youth in Kazakhstan: How Economic Disparity Affects Quality of Life

**Adilzhanov A.B., Adilgozhin M.S., Ibrayeva Zh.B., Urazalina N.M., Mukanova D.A., Zemlyanskaya N.S., Aitenova E.R., Shamshudinov T.M., Kassym L.T., Kussainova A.A.** 88-97
Analysis of socio-demographic determinants and risk factors of tuberculosis in the Abai region during the period 2014–2022

## Table Of Contents

### *ORIGINAL ARTICLES*

**Бекбосынова М.С., Сайлыбаева А.И., Кабдуева Г.А., Жетибаева С.К., Тауекелова А.Т., Новикова С.П., Мырзахметова Г.Ш., Дуйсенбина Ж.С., Сахипова А., Акжолова К.Т., Кушугулова А.Р.**
Проблемы эпидемиологии, распределения ресурсов и управления хронической сердечной недостаточностью в Казахстане: Национальный ретроспективный анализ

**Муртазалиева А.В., Березина Г.М., Святова Г.С., Есет М.С., Бурабаева А.Т.**
Распространенность полиморфизмов генов, связанных с метаболизмом варфарина, в казахской популяции

**Антикеев Д.А., Оразхан Ә.А., Темирбулатова Л.Б., Бейсимбаева Д.Ж., Абильтаев А.М., Таштемирова О.Г., Шукимбаева А.М., Махмутова А.М.**
Неврологические осложнения при экстракорпоральной мембранной оксигенации: факторы риска развития острого нарушения мозгового кровообращения

**Жаутикова С.Б., Уразалина Н.М., Толубаева Д.Б.**
Влияние Репаглинида и Метформина на функцию внешнего дыхания у пациентов с сахарным диабетом и ишемической болезнью сердца, ассоциированной с ожирением

**Урузбаева Г.А., Булегенов Т.А., Мусаханова А.К., Джусупов К., Ибекенов О.Т., Смаилова Ж.К., Байбусинова А.Ж., Иманбаев М.Н., Жарыкбасова Ф.Ж., Кусаинова А.С., Арманкызы А.**
Ретроспективный анализ больных облитерирующим атеросклерозом артерий нижних конечностей в Абайском районе Республики Казахстан

**Хангелді А.Е., Хамидуллина З.Г., Шаназаров Н.А., Афанасьев М.С., Гришачева Т.Г., Аккажиева Н.Н., Танышева Г.А.**
Эффективность фотодинамической терапии в лечении предраковых состояний шейки матки, вызванных вирусом папилломы человека

**Кырыкбаева С.С., Ошибаева А.Е., Нускабаева Г.О., Горемыкина М.В., Уразалина Н.М.**
Домашнее насилие как вызов общественному здравоохранению: результаты массового социологического исследования в Туркестанской области

**Байзуллина А.О., Жамалиева Л.М., Ермагамбетова А.П.**
Оценка выраженности депрессии, усталости и уровня психологического благополучия у пациентов после инсульта: результаты поперечного исследования с применением шкал BECK, FAS и MHC-SF

**Дуйсекова С., Гайсина М., Ахметова К., Уажанов М., Секенова Р.К., Даулетова Г.Ш.**
Социальные детерминанты здоровья безработной молодежи в Казахстане: как экономическое неравенство влияет на качество жизни

**Адилжанов А.Б., Адильгожин М.С., Ибраева Ж.Б., Уразалина Н.М., Муканова Д.А., Землянская Н.С., Айтенова Э.Р., Шамшудинов Т.М., Касым Л.Т., Кусаинова А.А.**
Анализ социально-демографических детерминант и факторов риска туберкулёза в области Абай за 2014–2022 гг.

**Mukasheva G.D., Maukayeva S.B., Kudaibergenova N.K., Shabdarbayeva D.M., Smailova Zh.K., Tokayeva A.Z., Smail Y.M., Nuralinova G.I., Issabekova Zh.B., Karimova S.S., Kozubayeva D.B., Goremykina M.V., Urazalina N.M.**
Analysis of antibiotic susceptibility and resistance of Klebsiella pneumoniae in various biological materials
**98-107 Мукашева Г.Д., Маукаева С.Б., Кудайбергенова Н.К., Шабдарбаева Д.М., Смаилова Ж.К., Токаева А.З., Смаил Е.М., Нуралинова Г.И., Исабекова Ж.Б., Каримова С.С., Козубаева Д.Б., Горемыкина М.В., Уразалина Н.М.**
Анализ чувствительности и устойчивости Klebsiella Pneumoniae к антибиотикам в различных биоматериалах

**Aldabekova G.U., Musina A.A., Kamalbekova G.M., Khamidullina Z.G, Danbayeva Zh.S. Abdrashidova S.B., Zhumabayeva E.M., Kokisheva G.A., Tanysheva G.A.**
Infection control in the maternity care system: assessment of resource availability, human capacity and professional development
**108-116 Алдабекова Г.У., Мусина А.А., Камалбекова Г.М., Хамидуллина З.Г., Данбаева Ж.С., Абдрашидова С.Б., Жумабаева Э.М., Кокишева Г.А., Танышева Г.А.**
Инфекционная безопасность в системе родовспоможения: оценка обеспеченности ресурсами, кадрового потенциала и профессионального развития

**Furlan A.,Mukasheva G.D., Maukayeva S.B., Kudaibergenova N.K., Shabdarbayeva D.M., Smailova Zh.K., Turakhanova B.S., Kozubayeva D.B., Goremykina M.V., Issabekova Zh.B., Karimova S.S., Urazalina N.M.**
Clinical and immunological characteristics of bronchial asthma in children and adolescents in the Abay region
**117-124 Фурлан А., Мукашева Г.Д., Маукаева С.Б., Кудайбергенова Н.К., Шабдарбаева Д.М., Смаилова Ж.К., Тураханова Б.С., Козубаева Д.Б., Горемыкина М.В., Исабекова Ж.Б., Каримова С.С., Уразалина Н.М.**
Клинико-иммунологическая характеристика бронхиальной астмы у детей и подростков в Абайской области

**Yerdalieva L.K., Gainutdin A.E., Nersesov A.V., Raisova A.M., Suleimenova D.S., Ashimova N.A., Madenova S.S., Shamshidinova M.A., Abdullaeva G.U., Zhakipova A.A., Seitkabilova Z.S., Baiduisenova G.A., Yerengaiyp B.S., Nurbekova F.N.**
Experience using capsule endoscopy
**125-134 Ердалиева Л.К., Гайнутдин А.Е., Нерсесов А.В., Раисова А.М., Сулейменова Д.С., Ашимова Н.А., Маденова С.С., Шамшидинова М.А., Абдуллаева Г.У., Жакипова А.А., Сейткабилова З.С., Байдуйсенова Г.А., Еренгайып Б.С., Нурбекова Ф.Н.**
Опыт использования капсульной эндоскопии

**Tuktiyeva N.A., Dossanov B.A., Zhunussov Ye.T. Abdulvakhabov G.M.**
Surgical treatment of Legg-Calve-Perthes disease in children
**135-142 Tuktiyeva N.A., Dossanov B.A., Zhunussov Ye.T. Abdulvakhabov G.M.**
Surgical treatment of Legg-Calve-Perthes disease in children

**Ibekenov O.T., Baymakhanov A.N.. Berkinbay A.B.. Zheldibaev Y.M., Duisebekov M.K.. Esenbekov N.B., Iskakov S.K., Abdykadyrov M.K., Tulebaev E.S., Myrzash D.D.**
Analysis of treatment outcomes for bleeding from esophageal and gastric varices
**143-150 Ибекенов О.Т., Баймаханов А.Н., Беркинбай А.Б., Желдибаев Е.М., Дуйсебеков М.К., Есенбеко Н.Б., Искаков С.И., Абдыкадыров М.К., Тулебаев Е.С., Мырзаш Д.Д.**
Анализ результатов лечения кровотечений из варикозно-расширенных вен пищевода и желудка

**Valiyeva S.R., Glushkova N.E., Buribayeva Zh.K., Izekenova A.K.**
Evaluation of the effectiveness of molecular allergy diagnostic methods in the personalized management of patients with allergic rhinitis
**151-156 Сабина В.Р., Наталья Г.Е., Жанар Б.К., Изекенова А.К.**
Оценка эффективности методов молекулярной аллергодиагностики в персонализированном ведении пациентов с аллергическим ринитом

## *АКТУАЛЬНАЯ ТЕМА - COVID-19*

## *COVID-19 - TOPICAL SUBJECT*

**Janzakova A.K., Buribaeva J.K., Kamhen V.B., Janzakov B.B., Izekenova A.K., Doskojaeva S.T., Kurmanova G.K., Shin A.L.**
Analysis of Clinical and Epidemiological Features of Herpesvirus Reactivation in Individuals with a History of COVID-19
**157-164 Джанзакова А.К., Бурибаева Ж.К., Камхен В.Б., Джанзаков Б.Б., Изекенова А.К., Доскожаева С.Т., Курманова Г.М., Шин А.Л.,**
Анализ клинико-эпидемиологических признаков реактивации герпесвирусов у лиц, перенёсших COVID-19

## *ОБЗОР ЛИТЕРАТУРЫ*

## *REVIEWS*

**Dyussupov A., Chaizhunussova N., Baibussinova A., Massabayeva M., Abenova M., Pivina L., Orekhov A., Smailova Zh., Mukanova D., Lepesbayev M., Kissina R., Akhmadiyeva T., Alibayeva G., Apbassova S., Abdildinova G., Izdenov A., Dosmagambetova R., Shabdarbayeva D.**
Radiation Exposure in the Semipalatinsk Region: Transgenerational Risks and Dosimetry Approaches
**165-174 Дюсупов А., Чайжунусова Н., Байбусинова А., Масабаева М., Абенова М., Пивина Л., Орехов А., Смаилова Ж., Муканова Д., Лепесбаев М., Кисина Р., Ахмадиева Т., Алибаева Г., Апбасова С., Абдильдинова Г., Изденов А., Досмагамбетова Р., Шабдарбаева Д.**
Радиационное воздействие в Семипалатинском регионе: трансгенерационные риски и дозиметрические подходы

**Orazayeva B.B., Iskakova N.S., Serikova-Esengeldina D.S., Urazalina N.M., Atabayeva A.K., Khismetova Z.A.**
Trends and patterns of male reproductive system diseases in the context of medical and demographic indicators. Literature review
**Isakhanov R.B., Zhanbyrbekuly U., Akkaliev M.N., Nogayeva M.G., Novikova E.G.**
Infectious complications of urological interventions for urolithiasis. Literature review
**Samarova U.S., Kalbagaeva Zh.Ye., Zgotova N.S., Yegizbayeva G.S., Nogayeva M.G., Tazhibayeva K.N., Ibrayeva T.B., Iskakova A.M.,**
The prevalence of chronic obstructive pulmonary disease as a global health problem
**Kalbagayeva Zh.Ye., Khismetova Z.A., Iskakova N.S., Atabayeva A.K., Serikova-Esengeldina D.S. Razakova N.G., Zheksebergenova A.B.**
The quality of life of patients with COPD. Literature review
**Kozhabayeva A.D., Mansurova J.A., Zhunuspekova A.S., Orekhov A.Yu., Kassymova A.A., Ashirov B.A., Smailova Zh.K., Kapakova M.A., Urazalina N.M., Karazhanova L.K.**
The SST2 biomarker as a predictor of adverse clinical outcomes in heart failure. Literature review

**Petrova Y.V., Goremykina M.V., Ivanova R.L., Kozhakhmetova D.K., Botabayeva A.S., Razvodova A.A.**
Capabilities of Artificial Intelligence in Modern Rheumatology. Literature review
**Kapanova A.A., Alimbaeva A.R., Dairbekov Y.E., Abylgazinova A.Zh., Bektar Zh.S., Kovylina R.G., Masalov A.Ye., Terdykbayeva Z.S.**
Cognitive component in the rehabilitation of preschool children with congenital heart defects. Literature review
**Iskakova A.M., Algazina T.O., Touir G.Z., Batpenova G.R., Kotlyarova T.V., Samarova U.S., Bengu N.-A., Ibrayeva T.B.**
Advanced Approaches to Psoriasis Treatment. Literature review
**Rakhmetova V.S., Sarkulova S.M., Derbissalina G.A., Bedelbaeva G.G., Amirkhanova L.M., Smailova D.S.**
Mediterranean-style diet for nonalcoholic fatty liver disease. Literature review

## *КЛИНИЧЕСКИЙ СЛУЧАЙ*

**Goremykina M.V., Vento S.**
Extrapulmonary tuberculosis in a kazakh patient with mixed connective tissue disease. Clinical case
**Rymbayeva T.Kh., Kanapiyanova G.B., Madiyeva M.R., Kaskabayeva A.Sh., Bersimbekova G.B., Goremykina M.**
The effect of steroid therapy on bone tissue in rheumatic diseases (description of a clinical case)

**175-188 Оразаева Б.Б., Искакова Н.С., Серикова-Есенгелдина Д.С., Уразалина Н.М., Атабаева А.К., Хисметова З.А.**
Тенденции и закономерности заболеваний репродуктивной системы мужчин в контексте медико-демографических показателей. Обзор литературы
**189-199 Исаханов Р.Б., Жаңбырбекұлы У., Аккалиев М.Н., Ногаева М.Г., Новикова Е.Г.**
Инфекционные осложнения урологических вмешательств по поводу мочекаменной болезни. Обзор литературы
**200-214 Самарова У.С., Калбагаева Ж.Е., Зготова Н.С., Егизбаева Г.С., Ногаева М.Г., Тажибаева К.Н., Ибраева Т.Б., Искакова А.М.**
Распространенность хронической обструктивной болезни легких как глобальная проблема здравоохранения
**215-226 Калбагаева Ж.Е., Хисметова З.А., Искакова Н.С., Атабаева А.К., Серикова-Есенгелдина Д.С., Разакова Н.Г., Жаксебергенова А.Б.**
Качество жизни пациентов с ХОБЛ (обзор литературы)
**227-235 Кожабаева А.Д., Мансурова Ж.А., Жунуспекова А.С., Орехов А.Ю., Касымова А.А., Аширов Б.А., Смаилова Ж.К., Капакова М.А., Уразалина Н.М., Каражанова Л.К.**
Биомаркер SST2 как предиктор неблагоприятных клинических исходов при сердечной недостаточности. Обзор литературы
**236-244 Петрова Ю.В., Горемыкина М.В., Иванова Р.Л., Кожахметова Д.К., Ботабаева А.С., Разводова А.А.**
Возможности искусственного интеллекта в современной ревматологии. Обзор литературы
**245-254 Қапанова А.А., Алимбаева А.Р., Даирбеков Е.Е., Абылгазинова А.Ж., Бектар Ж.С., Ковылина Р.Г., Масалов А.Е., Тердыкбаева З.С.**
Когнитивный компонент в реабилитации дошкольников с врожденными пороками сердца. Обзор литературы
**255-266 Искакова А.М., Алгазина Т.О., Туир Г.З., Батпенова Г.Р., Котлярова Т.В., Самарова У.С., Бенгу Н.-А., Ибраева Т.Б.**
Передовые подходы к лечению псориаза. Обзор литературы
**267-274 Рахметова В.С., Саркулова С.М., Дербисалина Г.А., Бедельбаева Г.Г., Амирханова Л.М., Смаилова Д.С.**
Средиземноморская диета при неалкогольной жировой болезни печени. Обзор литературы

## *CLINICAL CASE*

**275-279 Горемыкина М.В., Венто С.**
Внелегочный туберкулез у казахского пациента со смешанным заболеванием соединительной ткани. Клинический случай
**280-284 Рымбаева Т.Х., Канапиянова Г.Б., Мадиева М.Р., Каскабаева А.Ш., Берсимбекова Г.Б., Горемыкина М.В.**
Влияние стероидной терапии ревматических заболеваний на состояние костной ткани (описание клинического случая)

Received: 16 January 2025 / Accepted: 14 May 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2025.27.3.001***

***UDC 616.1-036.22(574)***

This work is licensed under a Creative Commons Attribution 4.0 International License

# EPIDEMIOLOGY, RESOURCE DISTRIBUTION, AND MANAGEMENT CHALLENGES OF CHRONIC HEART FAILURE IN KAZAKHSTAN: A NATIONAL RETROSPECTIVE ANALYSIS

**Makhabbat S. Bekbossynova[1], https://orcid.org/0000-0003-2834-617X**
**Aliya I. Sailybaeva[1], https://orcid.org/0000-0002-1489-3837**
**Gulden A. Kabduyeva[1], https://orcid.org/0009-0007-1435-1177**
**Saltanat K. Jetybayeva[1], https://orcid.org/0000-0003-3442-3223**
**Ainur T. Tauekelova[1], https://orcid.org/0000-0002-4237-9835**
**Svetlana P. Novikova[1], https://orcid.org/0000-0001-8161 -7712**
**Gulzhan Sh. Myrzakhmetova[1], https://orcid.org/0000-0001-8325-1267**
**Zhadyra S. Duisenbina[1], https://orcid.org/0009-0006-1801-009X**
**Aiym Sakhipova[1], https://orcid.org/0000-0002-0507-6704**
**Kamila T. Akzholova*[2], https://orcid.org/0009-0000-2527-8947**
**Almagul R. Kushugulova[1], https://orcid.org/0000-0001-9479-0899**

**[1] University Medical Center" Corporate Fund, Astana, Republic of Kazakhstan;**
**[2] Nazarbayev University School of Medicine, Astana, Republic of Kazakhstan.**

**Abstract**

**Background**. Chronic heart failure is a growing global health challenge, particularly in Kazakhstan, where demographic changes and rising numbers of comorbidities are worsening the burden. However, data on CHF prevalence, diagnosis and healthcare resource distribution in the regions remain limited.

This study **aims** to assess and compare the epidemiological trends, regional disparities and healthcare system capacity of CHF in Kazakhstan based on recent national data.

**Materials and methods**. A retrospective analysis was conducted using national healthcare records from 2023–2024, including chronic heart failure prevalence, new diagnoses, stage distribution, regional healthcare resources and surgical interventions of patients. The Gini index was used to evaluate regional disparities, along with other statistical analyses.

**Results**. In 2024, 87,260 patients were examined, with a 19% increase from 2023. Of 12,874 new cases, 75.6% were identified in early stages (A and B), suggesting progress in early detection. However, regional disparities were severe, with Gini indices for ProBNP testing and echocardiography at 0.556 and 0.480, respectively. High-resource areas like Almaty contrasted sharply with under-resourced regions such as Mangystau and Kyzylorda wtih heart transplants being declined, while LVAD usage increasing which reflects evolving treatment patterns amid limited donor availability.

**Conclusion**. Chronic heart failure is increasing in Kazakhstan amid significant regional and systemic inequalities in care. Targeted interventions with improved diagnostic access, equitable resource allocation, and national policy reform are urgently needed to manage the growing burden and improve outcomes of patients across the country.

***Key words:*** *chronic heart failure, epidemiology, health resource distribution, healthcare inequality*.

***For citation:***

*Bekbossynova M.S., Sailybaeva A.I., Kabduyeva G.A., Jetybayeva S.K., Tauekelova A.T., Novikova S.P., Myrzakhmetova G.Sh., Duisenbina Zh.S., Sakhipova A., Akzholova K.T., Kushugulova A.R.* Epidemiology, Resource Distribution, and Management Challenges of Chronic Heart Failure in Kazakhstan: A National Retrospective Analysis // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 7-15. doi 10.34689/SH.2025.27.3.001

**Резюме**

# ПРОБЛЕМЫ ЭПИДЕМИОЛОГИИ, РАСПРЕДЕЛЕНИЯ РЕСУРСОВ И УПРАВЛЕНИЯ ХРОНИЧЕСКОЙ СЕРДЕЧНОЙ НЕДОСТАТОЧНОСТЬЮ В КАЗАХСТАНЕ: НАЦИОНАЛЬНЫЙ РЕТРОСПЕКТИВНЫЙ АНАЛИЗ

**Махаббат С. Бекбосынова[1], https://orcid.org/0000-0003-2834-617X**
**Алия И. Сайлыбаева[1], https://orcid.org/0000-0002-1489-3837**
**Гулден А. Кабдуева[1], https://orcid.org/0009-0007-1435-1177**
**Салтанат К. Жетибаева[1], https://orcid.org/0000-0003-3442-3223**
**Айнур Т. Тауекелова[1], https://orcid.org/0000-0002-4237-9835**

**Светлана П. Новикова[1] https://orcid.org/0000-0001-8161 -7712**
**Гульжан Ш. Мырзахметова[1], https://orcid.org/0000-0001-8325-1267**
**Жадыра С. Дуйсенбина[1], https://orcid.org/0009-0006-1801-009X**
**Айым Сахипова[1], https://orcid.org/0000-0002-0507-6704**
**Камила Т. Акжолова*[2], https://orcid.org/0009-0000-2527-8947**
**Алмагуль Р. Кушугулова[1], https://orcid.org/0000-0001-9479-0899**

**[1] Корпоративный фонд «University Medical Center», г. Астана, Республика Казахстан;**
**[2] Назарбаев Университет, г. Астана, Республика Казахстан.**

**Введение**. Хроническая сердечная недостаточность становится растущей проблемой общественного здравоохранения во всем мире, особенно в Казахстане, где демографические изменения и рост сопутствующих заболеваний усугубляют бремя. Однако данные о распространенности ХСН, диагностике и распределении ресурсов здравоохранения в регионе остаются ограниченными.

**Цель.** Оценка эпидемиологических тенденций, географических различий и возможностей системы здравоохранения, связанных с ХСН в Казахстане, на основе последних национальных данных.

**Материалы и методы.** Ретроспективный анализ проводился с использованием национальных записей здравоохранения за 2023–2024 годы. Данные включали распространенность ХСН, новые диагнозы, распределение стадий, региональные ресурсы здравоохранения и хирургические вмешательства. Для оценки региональных различий использовались показатели неравенства, такие как индекс Джини.

**Результаты.** В 2024 году было обследовано 87 260 пациентов с ХСН, что на 19% больше, чем в 2023 году. Из 12 874 новых случаев 75,6% были выявлены на ранних стадиях (A и B), что свидетельствует о прогрессе в раннем выявлении. Однако региональные различия в лечении были резкими: индексы Джини для тестирования ProBNP и эхокардиографии составили 0,556 и 0,480 соответственно. Регионы с высоким уровнем ресурсов, такие как Алматы, резко контрастировали с регионами с низким уровнем ресурсов, такими как Мангистауская и Кызылординская области. Количество трансплантаций сердца сократилось, в то время как использование LVAD увеличилось, что отражает меняющиеся модели лечения на фоне ограниченного количества доноров.

**Заключение.** ХСН растет в Казахстане на фоне значительного регионального и системного неравенства в лечении. Целевые вмешательства — улучшение диагностического доступа, справедливое распределение ресурсов и реформа национальной политики — срочно необходимы для управления растущим бременем и улучшения результатов по всей стране.

***Ключевые слова**: хроническая сердечная недостаточность, эпидемиология, распределение ресурсов здравоохранения, неравенство в здравоохранении.*

***Для цитирования:***

*Бекбосынова М.С., Сайлыбаева А.И., Кабдуева Г.А., Жетибаева С.К., Тауекелова А.Т., Новикова С.П., Мырзахметова Г.Ш., Дуйсенбина Ж.С., Сахипова А., Акжолова К.Т., Кушугулова А.Р.* Проблемы эпидемиологии, распределения ресурсов и управления хронической сердечной недостаточностью в Казахстане: национальный ретроспективный анализ // Наука и Здравоохранение. 2025. Т.27 (3), С. 7-15. doi: 10.34689/SH.2025.27.3.001

**Түйіндеме**

# ҚАЗАҚСТАНДАҒЫ СОЗЫЛМАЛЫ ЖҮРЕК ЖЕТКІЛІКСІЗДІГІНІҢ ЭПИДЕМИОЛОГИЯСЫ, РЕСУРСТАРЫН БӨЛУ ЖӘНЕ БАСҚАРУ МӘСЕЛЕЛЕРІ: ҰЛТТЫҚ РЕТРОСПЕКТИВТІ ТАЛДАУ

**Махаббат С. Бекбосынова[1], https://orcid.org/0000-0003-2834-617X**
**Алия И. Сайлыбаева[1], https://orcid.org/0000-0002-1489-3837**
**Гулден А. Кабдуева[1], https://orcid.org/0009-0007-1435-1177**
**Салтанат К. Жетибаева[1], https://orcid.org/0000-0003-3442-3223**
**Айнур Т. Тауекелова[1], https://orcid.org/0000-0002-4237-9835**
**Светлана П. Новикова[1], https://orcid.org/0000-0001-8161 -7712**
**Гульжан Ш. Мырзахметова[1], https://orcid.org/0000-0001-8325-1267**
**Жадыра С. Дуйсенбина[1], https://orcid.org/0009-0006-1801-009X**
**Айым Сахипова[1], https://orcid.org/0000-0002-0507-6704**
**Камила Т. Акжолова*[2], https://orcid.org/0009-0000-2527-8947**
**Алмагуль Р. Кушугулова[1], https://orcid.org/0000-0001-9479-0899**

**[1] "University Medical Center" корпоративтік қоры, Астана қ., Қазақстан Республикасы;**
**[2] Назарбаев Университеті, Астана қ., Қазақстан Республикасы**

**Кіріспе.** Созылмалы жүрек жеткіліксіздігі бүкіл әлемде, әсіресе демографиялық өзгерістер мен қатар жүретін аурулардың өсуі ауыртпалықты күшейтетін Қазақстанда қоғамдық денсаулықты алаңдатып отыр. Дегенмен, аймақта аурудың таралуы, диагностикасы және денсаулық сақтау ресурстарын бөлу туралы деректер шектеулі болып қала береді.

**Мақсаты.** Бұл зерттеу соңғы ұлттық деректер негізінде Қазақстандағы жүрек жеткіліксіздігіне байланысты эпидемиологиялық үрдістерді, географиялық теңсіздіктерді және денсаулық сақтау жүйесінің әлеуетін бағалауға бағытталған.

**Материалдар мен әдістері.** 2023-2024 жылдар аралығындағы ұлттық денсаулық сақтау жазбалары арқылы ретроспективті талдау жүргізілді. Деректер жүрек жеткіліксіздігінің таралуын, жаңа диагноздарды, кезеңді бөлуді, аймақтық денсаулық сақтау ресурстарын және хирургиялық араласуды қамтиды. Аймақтық теңсіздіктерді бағалау үшін Джини индексі сияқты теңсіздік көрсеткіштері пайдаланылды.

**Нәтижелер.** 2024 жылы жүрек жеткіліксіздікпен ауыратын 87 260 науқас бағаланды, бұл 2023 жылмен салыстырғанда 19%-ға өсті. 12 874 жаңа жағдайдың 75,6%-ы ерте кезеңдерінде (A және B) анықталды, бұл ерте анықтаудағы прогресті көрсетеді. Дегенмен, күтімдегі аймақтық диспропорциялар қатты болды, ProBNP сынағы мен эхокардиографияға арналған Джини индекстері сәйкесінше 0,556 және 0,480 болды. Алматы сияқты ресурстары жоғары аудандар Маңғыстау және Қызылорда сияқты ресурстары аз аймақтармен күрт қарама-қайшы болды. Жүректі трансплантациялау азайды, ал LVAD қолдану өсті, бұл донорлардың шектеулі қолжетімділігі жағдайында дамып келе жатқан емдеу үлгілерін көрсетеді.

**Қорытынды.** Созылмалы жүрек жеткіліксіздігі Қазақстанда медициналық көмек көрсетудегі елеулі аймақтық және жүйелік теңсіздік жағдайында өсуде. Мақсатты араласулар — диагностикалық қолжетімділікті жақсарту, ресурстарды тең бөлу және ұлттық саясатты реформалау — өсіп келе жатқан ауыртпалықты басқару және бүкіл ел бойынша нәтижелерді жақсарту үшін шұғыл қажет.

***Түйінді сөздер**: созылмалы жүрек жеткіліксіздігі, эпидемиология, денсаулық сақтау ресурстарын бөлу, денсаулық сақтау саласындағы теңсіздік*

***Дәйексөз үшін:***

*Бекбосынова М.С., Сайлыбаева А.И., Кабдуева Г.А., Жетибаева С.К., Тауекелова А.Т., Новикова С.П., Мырзахметова Г.Ш., Дуйсенбина Ж.С., Сахипова А., Акжолова К.Т., Кушугулова А.Р.* Қазақстандағы созылмалы жүрек жеткіліксіздігінің эпидемиологиясы, ресурстарын бөлу және басқару мәселелері: ұлттық ретроспективті талдау // Ғылым және Денсаулық. 2025. Т.27 (3), Б. 7–15. doi: 10.34689/SH.2025.27.3.001

**Introduction**

Chronic heart failure (CHF) is a multifaceted clinical syndrome characterized by the heart's inability to meet the body's circulatory demands [8]. Its heterogeneity in etiology and presentation complicates accurate epidemiological assessment and healthcare planning [5]. The disease being a significant cause of morbidity and mortality both in Kazakhstan and worldwide, CHF represents a critical public health issue and poses unique challenges in Kazakhstan due to its demographic and healthcare dynamics.

In Kazakhstan, as in other countries globally, the burden of CHF is rising due to an aging population, increasing prevalence of cardiovascular risk factors such as hypertension, diabetes, and obesity and the growing transition to more sedentary lifestyles [4, 13]. Recent global estimates indicate a CHF prevalence of 1–2% among the general adult population, increasing sharply to 11.8% among those aged 65 years and older [6, 7]. These numbers likely reflect similar trends in Kazakhstan, where the growing burden of multimorbidity worsens healthcare challenges.

Accurate data on CHF patients in Kazakhstan remains limited, mirroring the broader gap in disease epidemiological insights across Central Asia countries. However, global studies suggest that populations in lower- and middle-income countries, including Kazakhstan, may face unique risks due to the double burden of non-communicable diseases (NCDs) and infectious diseases which is of particular interest to further investigation [19]. The socioeconomic disparities prevalent in the country is further being impacted with individuals from less affluent backgrounds experiencing earlier onset and higher comorbidity burdens.

Kazakhstan has experienced a notable increase in the prevalence of CHF, with 4.7% of the population, approximately 320,000 people, diagnosed with this condition [18]. Between 2014 and 2021, the total number of patients diagnosed with CHF had risen to 501,663. Also, there was a significant increase in prevalence from 4,393 to 22,088 per million population [20]. The burden is further highlighted by the increaing mortality rates, which escalated from 367 to 721 per million during the same time period. Regional data indicate the highest cardiovascular disease incidence in Almaty, accounting for 4% of cases [1].

According to the statistical collection "Health of the population of the Republic of Kazakhstan and the activities of healthcare organizations in 2022-2023", the mortality burden of the different diseases associated with cardiovascular systems account for 128.92 and 126.50 people for 100 000 people in 2022 and 2023 respectively [14]. The statistical data shows the significant difference in mortality rates, compared to malignant and benign tumors, diseases of the digestive system, lungs, infectious or parasitic diseases, traumas and poisoning with the cardiovascular diseases illustrating the highest mortality rate in Kazakhstan. Contributing factors to the mortality rate of CHF include mainly arterial hypertension, coronary heart disease, chronic kidney disease and other comorbidities. However, one more contributing factor is the disparity in CHF coding and classification, as well as the challenge in recognizing CHF as

a primary cause of mortality which further complicates accurate data representation. This growing challenge emphasizes the need for enhanced cardiac care and preventive measures across the country, as well as improved diagnostics.

In addition to the existing challenges faced by patients with chronic heart failure, barriers to effective self-management represent a significant obstacle. Common issues include a lack of understanding about the named disease and its treatment, psychological distress such as anxiety or depression, and difficulties practicing the complex dietary and medication regimens. Physical limitations of patients and their conditions, as well as general limited access to rehabilitation further compound these challenges. Addressing them requires targeted interventions, such as patient educational programs to enhance disease awareness. Also, it is possible to implement structured support systems for managing dietary, medication compliance and accessible mental health counseling. Furthermore, personalized exercise and rehabilitation programs can encourage patients with CHF to maintain physical activity levels appropriate to their condition. By identifying and mitigating these obstacles, healthcare providers can improve patients' ability to manage CHF effectively, thereby enhancing their quality of life and reducing hospital readmissions [11].

Heart transplantation remains the gold-standard treatment for end-stage heart failure that is opposite to medical therapy. However, it is accessible to only a limited number of patients globally, including in Kazakhstan, due to various challenges such as the remoteness of specialized cardiac surgery centers, a persistently growing number of patients awaiting transplants, a low supply of donor hearts and a lack of motivation within the population to participate in organ donation. Consequently, patients often have to wait for suitable donors, further complicating their worsening condition. The urgent need for alternative treatment strategies and improved organ donation policies in future is required [2, 16].

Furthermore, CHF subtypes such as heart failure with preserved ejection fraction (HFpEF) are showing clearer prominence due to their association with aging and obesity-related conditions which are both rising in Kazakhstan [14, 15].

This study provides insights into the CHF's prevalence, risk factors and demographic disparities. By focusing on Kazakhstan, this research emphasizes the need to implement public health strategies tailored to the region's unique epidemiology and diagnostic tools which will contribute to more effective healthcare interventions and policy planning.

**Materials and methods**

This study is a retrospective epidemiological research to evaluate the burden, trends, and healthcare resource distribution data related to chronic heart failure in Kazakhstan. The research focuses on estimating CHF prevalence, incidence, disease progression, regional distribution, healthcare infrastructure and treatment patterns based on national healthcare system data collected over a 12-month period in 2024 which includes data from 2023 for comparison purposes. Diagnostic and treatment comparisons in the paper analyze variations in echocardiograms, NT-proBNP testing, and advanced interventions (LVAD, ICD, CRT-D, transplantation). The study also evaluates healthcare system capacities which includes in itself the distribution of CHF-specialized facilities and specialists.

For 2024, a total of 326 offices of chronic heart failure management are functioning within different regional and city cardiology centers, multidisciplinary hospitals and outpatient clinics across the whole Kazakhstan. These offices offer specialized care for patients with CHF, diagnostic tools, condition monitoring and treatment selection. In CHF offices, patients receive care from cardiologists, therapists, and general practitioners. Over the course of 2024, a total of 87 260 patients with chronic heart failure were examined on an outpatient basis, compared to 73,082 in 2023. Among these, 12 874 cases were newly diagnosed (12,393 in 2023). The distribution of newly identified cases by stage is as follows:

- Stage A (CHF risk) – 3 943 cases
- Stage B – 5 800 cases
- Stage C (symptomatic CHF) – 2 875 cases
- Stage D (progressive CHF) – 256 cases.

*Statistical analysis*

Descriptive statistics were used to assess and compare CHF prevalence and regional distributions of patients. Inequality in healthcare resource allocation was evaluated and statistically analyzed using Gini, Theil and concentration indices. Lorenz curves illustrated disparities in diagnostic access of the disease across cabinets in Kazakhstan. A generalized linear model with negative binomial regression was applied to identify factors associated with new CHF diagnoses, if possible. Multicollinearity was assessed using VIF and overdispersion was confirmed prior to model selection.

*Ethical approval*

This study is based on de-identified and anonymous, aggregated healthcare data and does not involve direct patient interactions or their personal information. Ethical approval (2023/01-009) was obtained from institutional review board and all the analyses were conducted in compliance with national data protection regulations.

**Results**

***Prevalence and Incidence of CHF***

In 2024, a total of 87,260 patients with CHF were examined on an outpatient basis across Kazakhstan, marking an increase from 73,082 in 2023. Among these, 12,874 new cases of CHF were diagnosed in 2024, compared to 12,393 in 2023 as illustrated in Figure 1. The distribution of these newly diagnosed cases by stage is as follows: 3,943 in Stage A (CHF risk), 5,800 in Stage B, 2,875 in Stage C (symptomatic CHF), and 256 in Stage D (progressive CHF).

*Regional Distribution of CHF Cases*

The distribution of CHF cases by stage across different regions of Kazakhstan reveals notable regional disparities as shown in Table 1. The highest number of outpatients was recorded in Almaty (21,046), followed by Pavlodar (12,473) and Shymkent city (6,212). The proportion of patients diagnosed with Stage A and Stage B CHF was more significant in regions with larger urban populations, such as Almaty and Shymkent, indicating a higher prevalence in metropolitan areas. Conversely, rural regions like Mangystau and Kyzylorda exhibited lower numbers of cases and fewer cases in advanced stages of CHF.

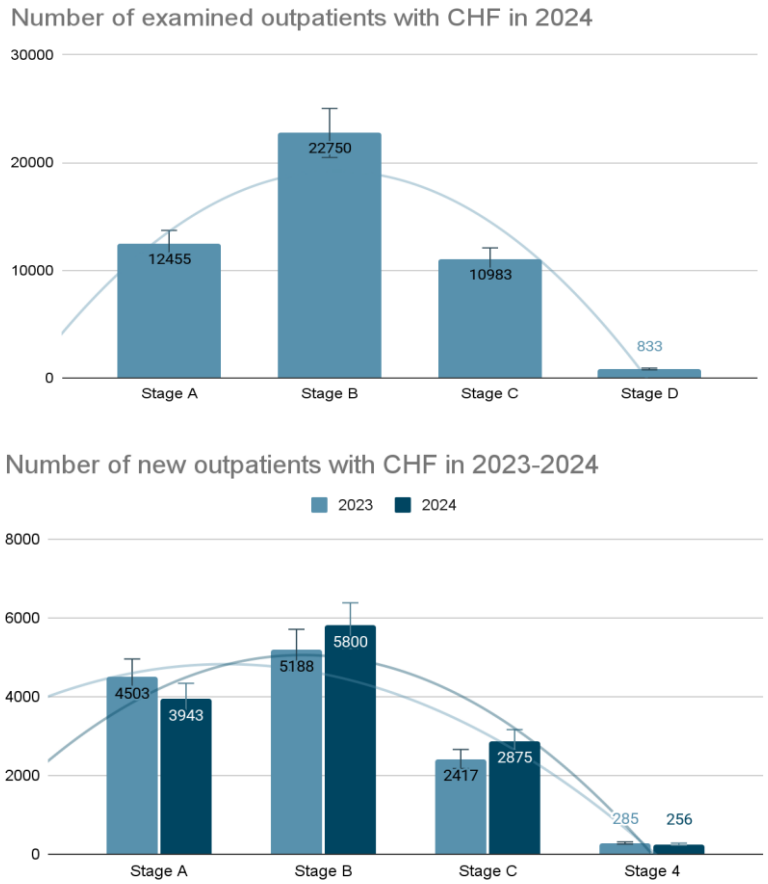



**Figure 1. A: Number of examined outpatients with CHF in 2024.**
**B: Number of new outpatients with CHF in 2023-2024.**

*Table 1.*

**Distribution of outpatients in different regions of the Kazakhstan.**

| Region | Stage A | Stage B | Stage C | Stage D | Total number of examined outpatients |
|---|---|---|---|---|---|
| Abay | 205 | 322 | 137 | 11 | 1107 |
| Akmola | 84 | 150 | 83 | 12 | 931 |
| Aktobe | 147 | 516 | 184 | 3 | 1615 |
| Jetisu | 313 | 417 | 290 | 9 | 1443 |
| Almaty | 564 | 1637 | 303 | 7 | 3430 |
| Atyrau | 69 | 677 | 1124 | **151** | 3195 |
| East Kazakhstan | 243 | 1649 | 406 | 4 | 3239 |
| Zhambyl | **2032** | 1196 | 530 | 50 | 6788 |
| West Kazakhstan | 177 | 1009 | 621 | 97 | 3661 |
| Karagandy | 333 | 868 | 401 | 13 | 6032 |
| Kostanay | 1041 | 761 | 963 | 63 | 3151 |
| Kyzylorda | 108 | 451 | 229 | 9 | 2191 |
| Mangystau | 38 | 105 | 162 | 19 | 502 |
| Pavlodar | 1023 | 4012 | **1136** | 93 | **12473** |
| North Kazakhstan | 659 | **2792** | 603 | 42 | 6414 |
| Turkestan | 72 | 228 | 350 | 23 | 1656 |
| Shymkent city | 2278 | 1570 | 678 | 130 | 6212 |
| Almaty city | *2957* | 3882 | 2526 | 79 | *21046* |
| Astana city | 112 | 508 | 257 | 18 | 1904 |

***Surgical Interventions for CHF***

Surgical treatments for CHF, including heart transplantation, Left Ventricular Assist Devices (LVAD), and implantable devices, have increased in recent years. In 2024, there was a notable rise in the number of patients receiving LVADs (27 in 2024 vs. 13 in 2023), while the number of heart transplants decreased (8 in 2024 vs. 21 in 2023) as stated in Table 2. The increase in LVADs reflects advancements in treatment options for end-stage heart failure, whereas the decline in heart transplants could be attributed to the limited availability of suitable donor organs.

*Table 2.*

**Number of patients, referred for surgical treatment of CHF.**

| Surgical treatment | 2023 | 2024 |
|---|---|---|
| Heart transplantation | 21 | 8 |
| LVAD | 13 | 27 |
| Implantable cardioverter-defibrillator | 380 | 406 |
| CRTD | 92 | 140 |

*Regional Inequalities in CHF Resources*

The distribution of healthcare resources related to CHF, such as CHF-specialized cabinets, cardiologists, and diagnostic tests (e.g., ProBNP tests, echocardiograms) shows significant regional inequality. The Gini index values for CHF cabinets (0.283), cardiologists (0.315), and total specialists (0.317) suggest moderate levels of inequality in resource distribution across Kazakhstan. Diagnostic resources exhibit even more significant disparities, with the Gini index for ProBNP tests reaching 0.556 and for echocardiograms 0.480 as shown in Figure 2. This highlights the unequal availability of diagnostic capabilities, impacting the quality of care in less resource-rich regions.

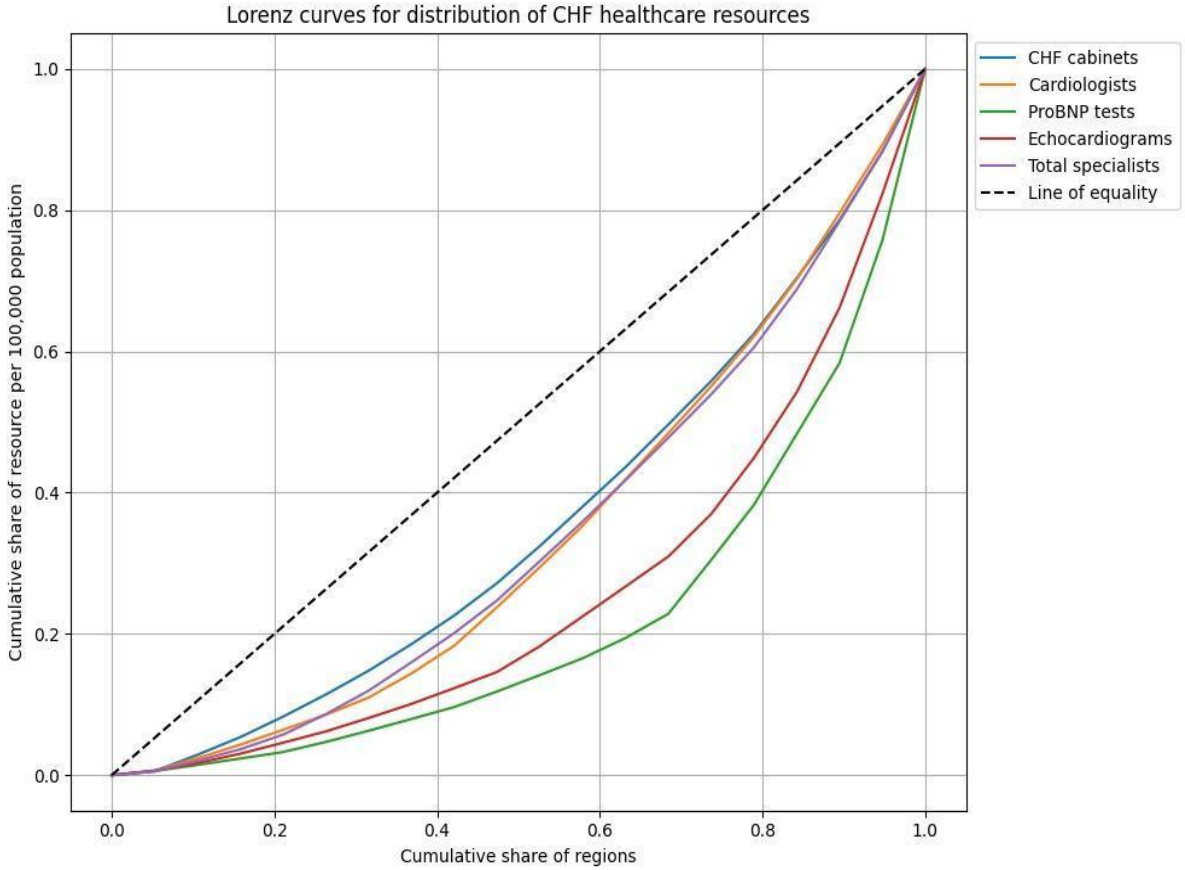



**Figure 2. Lorenz curves for CHF resources (per 100,000 adult population).**

*Table 3.*

**Summary table of inequality metrics (normalized per 100,000 people).**

| Metric | Gini Index | Theil Index | Concentration index |
|---|---|---|---|
| CHF cabinets | 0.283223 | 0.133656 | -1.108772 |
| Total specialists | 0.316630 | 0.167422 | -1.192982 |
| Cardiologists | 0.314568 | 0.165891 | -1.108772 |
| ProBNP tests | 0.555502 | 0.541351 | -1.389474 |
| Echocardiograms | 0.479690 | 0.382255 | -1.463158 |

***Contribution of Regions to Inequality in CHF Resources***

Analysis of regional contributions to resource inequality reveals that regions with both an excess and a deficit of CHF-related resources contribute to overall inequality. For example, regions such as West Kazakhstan and Pavlodar show an overconcentration of resources, whereas Astana and East Kazakhstan region experience significant shortages. These imbalances indicate the need for targeted redistribution of resources to ensure more equitable access to CHF care across the country (Figure 3).

***Factors Associated with CHF Diagnosis***

A generalized linear regression model was applied to assess factors associated with new CHF diagnoses across regions. The results suggest a weak but positive relationship between the number of CHF-specialized cabinets and the number of new CHF cases, though this association was not statistically significant ($p = 0.250$). A marginally significant positive correlation was observed between the number of echocardiograms performed and the detection of new CHF cases (OR = 0.0017, $p = 0.068$), suggesting that greater availability of echocardiography could lead to higher rates of diagnosis (Table 4).

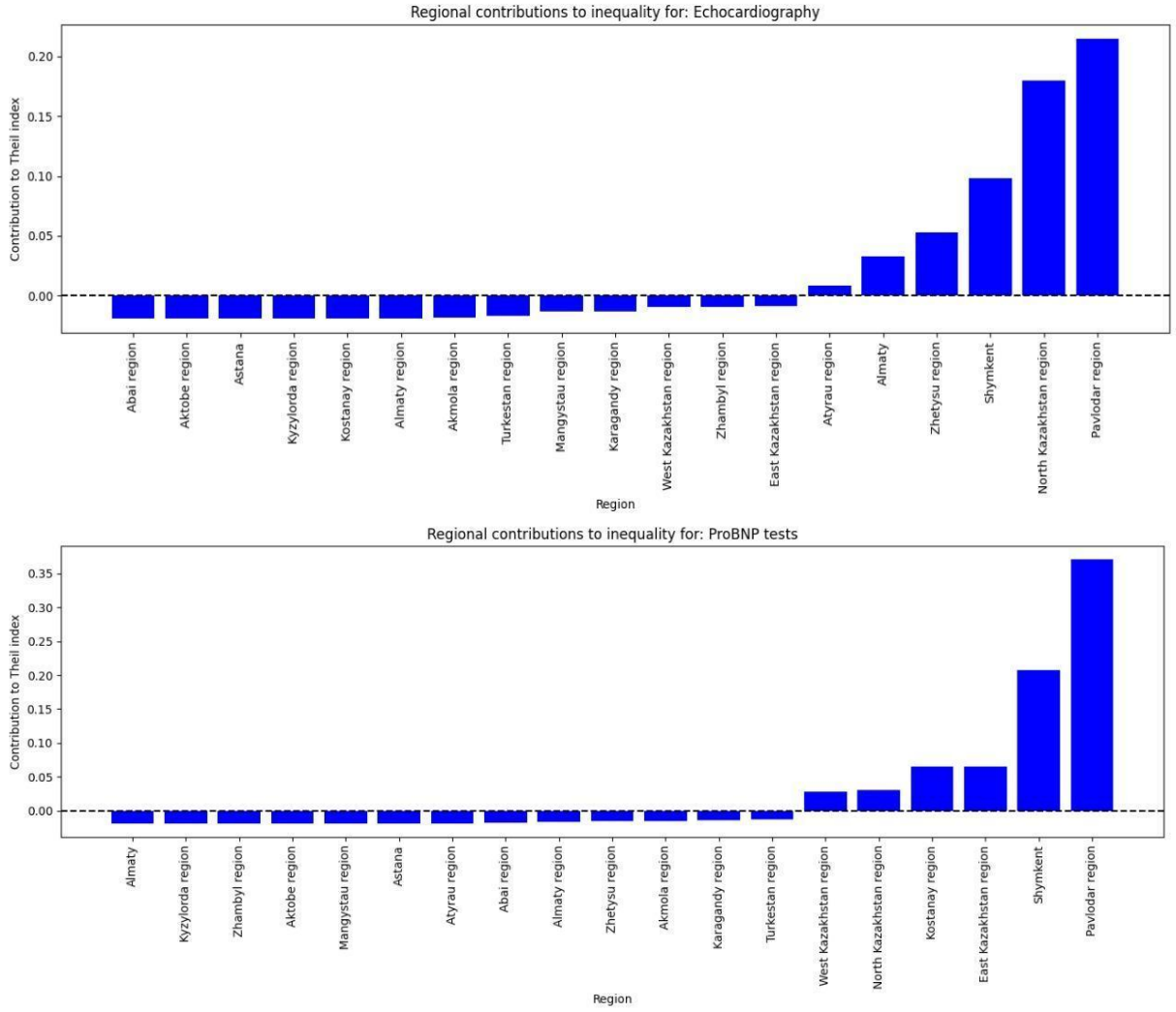



**Figure 3. Inequality graphs of echocardiography and ProBNP tests.**

*Table 4.*

**Generalized linear regression model.**

| Characteristics | OR [CI 95%] | p value |
|---|---|---|
| Intercept | -8.3566 [-9.962; -6.751] | 0.000 |
| CHF cabinets (per 100 000) | 0.2763 [-0.195; 0.747] | 0.250 |
| Cardiologist (per cabinet) | 0.0958 [-1.217; 1.409] | 0.886 |
| ProBNP tests (per 100 000) | -0.0008 [-0.0006; 0.0005] | 0.764 |
| Echocardiogram (per 100 000) | 0.0017 [-0.0000; 0.0004] | 0.068 |

**Discussion**

Driven by an aging population, increasing rates of hypertension, diabetes and poor lifestyles, chronic heart failure is becoming a more serious health problem in Kazakhstan. Though advances in cardiac care have been made, the number of CHF cases has grown dramatically in recent years, stressing the healthcare system and underdiagnosing CHF, particularly in rural areas with restricted access to specialists and diagnostic tools. Many patients have several diseases as well, which complicates therapy.

Though access stays inconsistent, advanced treatments such torasemide and cardiac resynchronization therapy have shown encouraging outcomes. Public knowledge is poor; rehabilitation services and preventive care are insufficient. Kazakhstan has to plan concentrating on early detection, improved access to treatment, enhanced patient education, and funding of digital and community-based health solutions in order to meet these difficulties.

The results of this study confirm the increasing load of CHF in Kazakhstan, therefore highlighting epidemiological patterns and systematic deficiencies. The year-on-year rise in the number of examined CHF outpatients—from 73,082 in 2023 to 87,260 in 2024—along with a growing incidence rate, suggests an intensifying public health issue. The growing prevalence might indicate a real rise in disease incidence as well as better detection efforts, probably motivated by demographic changes, lifestyle choices, and the growing load of comorbid diseases like hypertension, diabetes, and chronic kidney disease linked to higher death rates.

The stage-wise distribution of newly diagnosed cases with a significant proportion falling into Stage A (30.6%) and Stage B (45.0%) may suggest some effectiveness in early identification. However, the persistence of symptomatic and

progressive stages (Stages C and D totaling over 24%) highlights the need for more proactive screening and patient follow-up procedures.

Significant regional differences in the number of CHF cases—most notably in Almaty, Pavlodar, and Shymkent—showcase potential inequalities in diagnostic capacity as well as urban-centric healthcare access. In contrast, areas like Mangystau and Kyzylorda reported much fewer cases, which might be due more to a lack of adequate healthcare facilities than to a real decline in the disease challenge. Moderate inequality (Gini indices of 0.283 and 0.315, respectively) is also evident in the distribution of cardiologists and cabinets with expertise in CHF. This result supports policy-level initiatives to decentralize cardiac care and is in line with past research showing Kazakhstan's healthcare system is highly centralized. It should be noted that the first CHF room was opened in 2014 at the National Cardiac Surgery Research Center in Astana in connection with the introduction of LVAD technologies, but in the regions, CHF rooms began operating in 2022, 119 rooms immediately began operating in the regions in connection with the implementation of the roadmap of the Ministry of Health of the Republic of Kazakhstan; as of 2025, 326 rooms were already functioning. This time gap further highlights the inequality in resource distribution in the organization of CHF care. In general, inequality in health resource distribution has been identified as a global public health priority, but geographic variations and temporal trends in distribution and inequality in Kazakhstan remain unclear.

The imbalance is more pronounced with regard to diagnostic testing. The high Gini index values for ProBNP tests (0.556) and echocardiography (0.480) illustrate unequal access to essential diagnostic tools which are critical for confirming CHF diagnoses and guiding treatment. Importantly, this diagnostic inequality likely contributes to delayed or missed diagnoses, further worsening disease progression and increasing the burden on tertiary care facilities.

Surgical and device-based treatments for CHF, such as LVAD implantation and CRT-D therapy, have shown incremental increases. However, the sharp decline in heart transplants—from 21 in 2023 to only 8 in 2024 - raises concern. This trend may be attributed to systemic limitations in donor availability, logistic barriers in organ allocation, or insufficient public engagement in organ donation. The observed growth in LVAD usage suggests a gradual shift towards mechanical circulatory support as a more accessible treatment. These data highlight the evolving therapeutic landscape and the necessity for continued investment in high-complexity cardiac interventions.

The generalized linear regression analysis exploring factors associated with new CHF diagnosis revealed a weak, statistically non-significant correlation between the number of CHF-specialized cabinets and newly diagnosed cases ($p = 0.250$). While not conclusive, this may suggest that merely increasing physical infrastructure without enhancing care quality, staffing, and diagnostic reach may not translate into improved case identification. The modest association between echocardiography rates and new diagnoses ($p = 0.068$) was closer to significance, supporting the notion that greater diagnostic capacity can contribute to earlier detection. However, this signal remains tentative and warrants cautious interpretation.

The limitations of this research study are firstly, the fairly low significance levels probably indicate unmeasured confounding variables such provider experience, patient education, and local healthcare-seeking behaviors. Second, aggregated regional data could hide intra-regional differences. These constraints imply that although infrastructure and diagnostics are important, tackling CHF in Kazakhstan calls for a more integrated approach including community-based care, public education, and workforce training.

All things considered, the findings point to a thorough, equitable national plan. It is crucial to strengthen early diagnostic networks, guarantee fair distribution of cardiology resources, increase advanced treatments, and broaden public awareness campaigns. Furthermore, regional CHF registries' growth and use of digital health tools could improve monitoring and guide tailored interventions.

**Conclusion**

This study is the first to describe temporal and geographic differences in resource allocation in organizational care for the diagnosis and treatment of CHF, despite sample limitations. The effectiveness of diagnostic and treatment services is impacted by disparities in financial and organizational strategies, as well as temporal and geographic variations, which lead to unequal resource allocation. To effectively reduce inequalities and allocate resources, it is crucial to draw in administrative support, investment, and the appropriate strategy.

***Disclosure:*** *All authors have no conflict of interest.*

***Acknowledgments:*** *none.*

***Funding:*** *This study was funded by the Science Committee of the Ministry of Science and Higher Education of the Republic of Kazakhstan (PTF #BR21882152). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.*

***Literature:***

1. *Bashirov Ansar.* Chronic Heart Failure Epidemiology In Kazakhstan And Other Countries. Ulyanovsk Medico-biological Journal, 2024. 17–27. DOI: 10.34014/2227-1848-2024-3-17-27

2. *Bekbossynov S., Medressova A., Murzagaliyev M., Salov R., Dzhetybayeva S., Andossova S., Bekbossynova M., Pya Y.* Surgical heart failure treatment program – the experience of Kazakhstan. Giornale Italiano di Cardiologia, 2014. 15(3).

3. *Benjamin E.J., Muntner P., Alonso A.* et al. Heart Disease and Stroke Statistics - 2019 Update: A Report From the American Heart Association. Circulation, 2019. 139(10). DOI: 10.1161/CIR.0000000000000659

4. *Cho J.H.* Sudden Death and Ventricular Arrhythmias in Heart Failure With Preserved Ejection Fraction. Korean Circ J, 2022. 52(4), 251. DOI: 10.4070/kcj.2021.0420

5. *Conrad Nathalie* et al. Temporal trends and patterns in heart failure incidence: a population-based study of 4 million individuals. The Lancet, 2018. 391(10120), 572–580.

6. *Curtis L.H., Whellan D.J., Hammill B.G., Hernandez A.F., Anstrom K.J., Shea A.M., Schulman K.A.* Incidence and prevalence of heart failure in elderly persons, 1994–2003. Arch Intern Med, 2008. 168, 418–424.

7. Global Burden of Disease Study 2015 (GBD 2015) results. Seattle, WA: Institute for Health Metrics and Evaluation (IHME), University of Washington; 2016.

8. *Groenewegen A., Rutten F.H., Mosterd A., & Hoes, A.W.*. Epidemiology of heart failure. Eur J Heart Fail, 2020. 22, 1342–1356. https://doi.org/10.1002/ejhf.1858

9. *Haydock P.M., Flett A.S.* Management of heart failure with reduced ejection fraction. Heart, 2022. 108(19), 1571–1579. DOI: 10.1136/heartjnl-2020-318811

10. *Inamdar A.A., & Inamdar A.C.* Heart failure: Diagnosis, management and utilization. J Clin Med, 2016. 5(7). DOI: 10.3390/jcm5070062

11. National Scientific Cardiac Surgery Center. Chronic heart failure: Methodological recommendations. Astana: National Scientific Cardiac Surgery Center. 2022.

12. Norhammar - Bodegard J., Vanderheyden M. et al. Prevalence, outcomes and costs of a contemporary, multinational population with heart failure. Heart. Published online February 13, 2023. DOI: 10.1136/heartjnl-2022-321702

13. *Pfeffer M.A., Shah A.M., Borlaug B.A.* Heart failure with preserved ejection fraction in perspective. Circ Res 2019., 124, 1598–1617.

14. *Pieske B., Tschöpe C., De Boer R.A.* et al. How to diagnose heart failure with preserved ejection fraction: the HFA-PEFF diagnostic algorithm. Eur Heart J., 2019. 40, 3297–3317.

15. *Ponikowski P., Voors A.A., Anker S.D.* et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur J Heart Fail, 2016. 18, 891–975.

16. *Semenova Y., Shaisultanova S., Beyembetova A.* et al. Examining a 12-year experience within Kazakhstan's national heart transplantation program. Scientific Reports, 2024.14(10291). https://doi.org/10.1038/s41598-024-61131-1

17. Statistical collection "Health of the population of the Republic of Kazakhstan and the activities of healthcare organizations in 2022–2023"

18. *Tazhieva A.E., Khabizhanova V.B. Tuleutayeva S.A., Erlepesova A.T.* Течение хронической сердечной недостаточности на фоне COVID-19, обзорный анализ. Pharmaceutical Kazakhstan, 2024. 22(45), 118–122. https://doi.org/10.53511/pharmkaz.2024.22.45.014

19. *Townsend N., Bhatnagar P., Wilkins E., Wickramasinghe K., Rayner M.* Cardiovascular disease statistics. London: British Heart Foundation, 2015.

20. *Zhakhina G., Gusmanov A., Sakko Y., Yerdessov, S., Mussina K., Gaipov A.* Burden of heart failure in Kazakhstan: data from the unified national healthcare system 2014–2021. European Journal of Public Health, 2023. 33. https://doi.org/10.1093/eurpub/ckad160.1274

**Author Information**

**Makhabbat S. Bekbossynova** - Associated Professor, Deputy Chairman of the Management Board, cardiologist, "University Medical Center" Corporate Fund, Astana, Kazakhstan, Turan avenue, 38, cardiacsurgeryres@gmail.com, https://orcid.org/0000-0003-2834-617X ; 8 (7172) 70 31 00

**Aliya I. Sailybaeva** - Chief of Research Department, "University Medical Center" Corporate Fund, Astana, Kazakhstan, Turan avenue, 38, s.aliya@umc.org.kz, https://orcid.org/0000-0002-1489-3837 ; +7 701 795 17 76

**Gulden A. Kabduyeva** - Manager in Research Department, "University Medical Center" Corporate Fund, Astana, Kazakhstan, Turan avenue, 38, cardiacsurgeryres@gmail.com, https://orcid.org/0009-0007-1435-1177 +7 778 000 13 06

**Saltanat K. Jetybayeva** - Cardiologist,"University Medical Center" Corporate Fund, Astana, Kazakhstan, Turan avenue, 38, cardiacsurgeryres@gmail.com, https://orcid.org/0000-0003-3442-3223

**Ainur T. Tauekelova** - Cardiologist, "University Medical Center" Corporate Fund, Astana, Kazakhstan, Turan avenue, 38, a.tauekelova@umc.org.kz,https://orcid.org/0000-0002-4237-9835

Svetlana P. Novikova - Cardiac surgeon, "University Medical Center" Corporate Fund, Astana, Kazakhstan, Turan avenue, 38, cardiacsurgeryres@gmail.com, https://orcid.org/0000-0001-8161 -7712

**Gulzhan Sh. Myrzakhmetova** - Chief of Cardiology Department 2, "University Medical Center" Corporate Fund, Astana, Kazakhstan, Turan avenue, 38, mgsh2000@mail.ru, https://orcid.org/0000-0001-8325-1267

**Zhadyra S. Duisenbina** - Doctor, "University Medical Center" Corporate Fund, Astana, Kazakhstan, Turan avenue, 38, cardiacsurgeryres@gmail.com, https://orcid.org/0009-0006-1801-009X

**Aiym Sakhipova** - Neuropathist, "University Medical Center" Corporate Fund, Astana, Kazakhstan, Turan avenue, 38, cardiacsurgeryres@gmail.com, https://orcid.org/0000-0002-0507-6704

**Kamila T. Akzholova** - Doctor of Medicine program student, Nazarbayev University, School of Medicine, kamila.akzholova@nu.edu.kz, https://orcid.org/0009-0000-2527-8947 ; +7 707 489 84 78

**Almagul R. Kushugulova** - Head of the Microbiome Laboratory at the Center for Life Sciences of the C.U. National Laboratory Astana, akushugulova@nu.edu.kz https://orcid.org/0000-0001-9479-0899

***Corresponding author:**

**Kamila T. Akzholova** - Doctor of Medicine program student, Nazarbayev University, School of Medicine, Astana, Kazakhstan, https://orcid.org/0009-0000-2527-8947

**Post address:** Turan avenue, 38, Astana, 010000, Republic of Kazakhstan;

**E-mail:** kamila.akzholova@nu.edu.kz

**Phone:** +7 707 489 84 78

Received: 16 February 2025 / Accepted: 14 May 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2025.27.3.002***

***UDC 575.17+615.03***

This work is licensed under a Creative Commons Attribution 4.0 International License

# PREVALENCE OF POLYMORPHISMS IN WARFARIN METABOLISM-RELATED GENES AMONG THE KAZAKH POPULATION

**Alexandra V. Murtazaliyeva[1],** http://orcid.org/0000-0001-9156-5944

**Galina M. Berezina[2],** http://orcid.org/0000-0002-5442-4461

**Gulnara S. Svyatova[1],** http://orcid.org/0000-0001-5092-3143

**Meruyert S. Yesset[2],** http://orcid.org/0000-0003-2906-5636

**Asem T. Burabayeva[2],** http://orcid.org/0009-0005-4527-7729

**[1] LLP "Center for Molecular Medicine", Almaty, Republic of Kazakhstan;**
**[2] JSC "Scientific Center for Obstetrics, Gynecology, and Perinatology", Almaty, Republic of Kazakhstan.**

**Abstract**

**Objective:** The study aims to perform a comparative analysis of population frequencies of minor alleles of polymorphisms in the genes CYP2C9 *2 (rs1799853), *3 (rs1057910), *5 (rs28371686), and *6 (rs9332131); CYP2C19 (rs3814637), VKORC1 (rs9934438), CYP4F2 (rs2108622), GGCX (rs11676382), as well as GWAS-associated variants related to resistance to vitamin K antagonists in an ethnically homogeneous Kazakh population, and to assess the distribution and perform a comparative analysis of metabolic phenotypes ("metabolizer types") in comparison with previously studied global populations.

**Materials and Methods:** The research was based on genomic analysis data from 1,900 conditionally healthy individuals of Kazakh ethnicity, obtained within the framework of the 7th Framework Programme of the European Union under Grant Agreement No. 282540.

**Results:** A high frequency of the minor allele of the "Asian" variant rs11676382 in the GGCX gene was identified in the Kazakh population (14.4%) compared to European, East Asian, and South Asian groups. It may indicate a potentially more pronounced impact of this polymorphism on individual warfarin dosing requirements in individuals of Kazakh ethnicity.

In the studied Kazakh group, the identified phenotypes and frequencies of metabolizers for CYP2C9 *2 (rs1799853) and *3 (rs1057910) alleles were as follows: 1/1 (80.1%), 1/3 (13.0%), 3/3 (0.25%), 1/2 (6.0%), 2/3 (0.40%), and 2/2 (0.25%). Normal metabolizers (*2 and *3 alleles) comprised 80.1%, intermediate metabolizers - 19.0%, and slow metabolizers - 0.9%.

For CYP2C9 *5 (rs28371686) and *6 (rs9332131) alleles, the phenotypes and metabolizer frequencies were: 1/1 (90.0%), 1/6 (6.7%), 1/5 (2.9%), 5/6 (0.3%), and 5/5 (0.1%). Normal metabolizers for *5 and *6 alleles accounted for 90.0%, intermediate - 9.6%, and slow - 0.4%.

**Conclusion.** The results provide additional pharmacogenetic database information for Central Asia, facilitating a better understanding of warfarin pharmacokinetics and pharmacodynamics for individualized warfarin dosing in patients undergoing heart surgery in Kazakhstan.

***Keywords:*** *Population frequencies, gene polymorphisms, metabolizers, minor allele, warfarin pharmacogenetics.*

***For citation:***

Murtazaliyeva A.V., Berezina G.M., Svyatova G.S., Yesset M.S., Burabayeva A.T. Prevalence of polymorphisms in warfarin metabolism-related genes among the Kazakh population // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 16-26. doi 10.34689/SH.2025.27.3.002

**Резюме**

# РАСПРОСТРАНЕННОСТЬ ПОЛИМОРФИЗМОВ ГЕНОВ, СВЯЗАННЫХ С МЕТАБОЛИЗМОМ ВАРФАРИНА, В КАЗАХСКОЙ ПОПУЛЯЦИИ

**Александра В. Муртазалиева[1],** http://orcid.org/0000-0001-9156-5944

**Галина М. Березина[2],** http://orcid.org/0000-0002-5442-4461

**Гульнара С. Святова[1],** http://orcid.org/0000-0001-5092-3143

**Меруерт С. Есет[2],** http://orcid.org/0000-0003-2906-5636

**Асем Т. Бурабаева[2],** http://orcid.org/0009-0005-4527-7729

**[1] Центр молекулярной медицины, г. Алматы, Республика Казахстан;**
**[2] АО «Научный центр акушерства, гинекологии и перинатологии», г. Алматы, Республика Казахстан.**

**Введение.** В настоящее время приоритетным направлением персонализированной медицины является фармакогенетическое тестирование, в том числе определение типа метаболизаторов лекарственных препаратов.

**Цель исследования:** Определить удельный вес «типов метаболизаторов» в казахской популяции и провести сравнительный анализ популяционных частот минорных аллелей полиморфизмов генов CYP2C9*2 (rs1799853), *3 (rs1057910), *5 (rs28371686) и *6 (rs9332131); CYP2C19 (rs3814637), VKORC1 (rs9934438), CYP4F2 (rs2108622), GGCX (rs11676382), GWAS ассоциированных с резистентностью к антикоагулянтам группы антагонистов витамина К, в этнически однородной популяции казахов с ранее изученными популяциями мира.

**Материалы и методы.** В данном исследовании использована геномная база данных 1900 условно здоровых казахов, полученная в рамках выполнения проекта «Генетические исследования преэклампсии в популяциях Центральной Азии и Европы» (InterPregGen).

**Результаты.** В исследуемой группе казахов определены фенотипы и частоты метаболизаторов по аллелям *2 (rs1799853) и *3 (*rs1057910) *гена CYP2C9* - 1/1, 1/3, 3/3, 1/2, 2/3, 2/2 которые составили: 80,1%, 13,0%, 0,25%, 6,0%, 0,40%, 0,25%, соответственно. Нормальные метаболизаторы по аллелям *2 и *3 имеют частоту 80,1%, промежуточные – 19,0% и медленные – 0,9%.

Определены фенотипы и частоты метаболизаторов аллелей *5 (rs28371686) и *6 (rs9332131) гена *CYP2C9* - 1/1, 1/6, 1/5, 5/6, 5/5 в популяционной выборке казахов составили: 90,0%, 6,7%, 2,9%, 0,3%, 0,1%, соответственно. Частоты нормальных метаболизаторов по аллелям *5, и *6 составили 90,0%, промежуточных - 9,6% и медленных - 0,4%.

Сравнительный анализ популяционных частот изученных полиморфизмов генов показал их промежуточное положение по сравнению с изученными Европейскими, Восточно Азиатскими и Южно Азиатскими популяциями.

**Выводы.** Полученные результаты по популяционным частотам изученных полиморфизмов генов у казахов являются дополнительной информацией для фармакогенетических баз данных по Центральной Азии и будут использованы для понимания фармакогенетики варфарина при дифференцированном подходе к назначению дозы варфарина пациентам с оперированным сердцем в Казахстане.

***Ключевые слова:*** *Популяционные частоты, полиморфизмы генов, метаболизаторы, минорный аллель, фармакогенетика варфарина.*

***Для цитирования:***

*Муртазалиева А.В., Березина Г.М., Святова Г.С., Есет М.С., Бурабаева А.Т.* Распространенность полиморфизмов генов, связанных с метаболизмом варфарина, в казахской популяции // Наука и Здравоохранение. 2025. Т.27 (3), С. 16-26. doi: 10.34689/SH.2025.27.3.002

**Түйіндеме**

# ҚАЗАҚ ПОПУЛЯЦИЯСЫНДА ВАРФАРИН АЛМАСУЫМЕН БАЙЛАНЫСТЫ ГЕНДІК ПОЛИМОРФИЗМДЕРДІҢ ТАРАЛУЫ

**Александра В. Муртазалиева[1], http://orcid.org/0000-0001-9156-5944**

**Галина М. Березина[2], http://orcid.org/0000-0002-5442-4461**

**Гульнара С. Святова[1], http://orcid.org/0000-0001-5092-3143**

**Меруерт С. Есет[2], http://orcid.org/0000-0003-2906-5636**

**Асем Т. Бурабаева[2], http://orcid.org/0009-0005-4527-7729**

**[1] Молекулярлық медицина орталығы, Алматы қ., Қазақстан Республикасы;**
**[2] «Акушерлік, гинекология және перинатология ғылыми орталығы» АҚ, Алматы қ., Қазақстан Республикасы.**

**Кіріспе.** Қазіргі уақытта дербестендірілген медицинаның басым бағыты — дәрілік заттардың метаболизатор түрін анықтауды қоса алғанда, фармакогенетикалық тестілеу болып табылады.

**Зерттеу мақсаты:** Қазақ популяциясындағы «метаболизатор түрлерінің» үлестік салмағын анықтап, CYP2C9*2 (rs1799853), *3 (rs1057910), *5 (rs28371686), *6 (rs9332131); CYP2C19 (rs3814637), VKORC1 (rs9934438), CYP4F2 (rs2108622), GGCX (rs11676382) гендер полиморфизмдерінің, сондай-ақ К витаминінің антагонистері тобына жататын антикоагулянттарға төзімділікпен байланысты GWAS маркерлерінің аз жиілікті аллельдерінің популяциялық жиіліктерін бұрын зерттелген әлем популяцияларымен салыстыра отырып талдау жүргізу.

**Материалдар мен әдістері.** Бұл зерттеуде Орталық Азия мен Еуропа популяцияларында преэклампсияны генетикалық зерттеу жобасы (InterPregGen) аясында алынған 1900 шартты түрде сау қазақтың геномдық деректер базасы пайдаланылды.

**Нәтижелер.** Зерттелген қазақ тобы арасында CYP2C9 генінің *2 (rs1799853) және *3 (rs1057910) аллельдері бойынша келесі фенотиптер мен жиіліктер анықталды: 1/1 – 80,1%, 1/3 – 13,0%, 3/3 – 0,25%, 1/2 – 6,0%, 2/3 – 0,40%, 2/2 – 0,25%. *2 және *3 аллельдері бойынша қалыпты метаболизаторлардың жиілігі – 80,1%, аралық – 19,0%, баяу – 0,9%.

Сондай-ақ CYP2C9 генінің *5 (rs28371686) және *6 (rs9332131) аллельдері бойынша фенотиптер мен жиіліктер анықталды: 1/1 – 90,0%, 1/6 – 6,7%, 1/5 – 2,9%, 5/6 – 0,3%, 5/5 – 0,1%. *5 және *6 аллельдері бойынша қалыпты метаболизаторлар – 90,0%, аралық – 9,6%, баяу – 0,4%.

Зерттелген ген полиморфизмдерінің популяциялық жиіліктерін салыстырмалы талдау олардың Еуропа, Шығыс Азия және Оңтүстік Азия популяцияларымен салыстырғанда аралық позицияда екенін көрсетті.

**Қорытындылар.** Қазақ популяциясында зерттелген ген полиморфизмдерінің жиіліктері бойынша алынған нәтижелер Орталық Азияға арналған фармакогенетикалық деректер базасына қосымша ақпарат болып табылады және Қазақстанда жүрекке ота жасалған пациенттерге варфариннің дозасын даралап тағайындау кезінде варфариннің фармакогенетикасын түсіну үшін қолданылатын болады.

***Түйінді сөздер:*** *Популяциялық жиіліктері, гендердің полиморфизмдері, метаболизаторлары, кіші аллельдері, варфариннің фармакогенетикасы.*

***Дәйексөз үшін:***

*Муртазалиева А.В., Березина Г.М., Святова Г.С., Есет М.С., Бурабаева А.Т.* Қазақ популяциясында варфарин алмасуымен байланысты гендік полиморфизмдердің таралуы // Ғылым және Денсаулық. 2025. Т.27 (3), Б. 16-26. doi: 10.34689/SH.2025.27.3.002

**Introduction**

Cardiovascular diseases (CVD) are the leading cause of mortality worldwide and remain a significant public health concern both in Kazakhstan and globally. In most developed European countries, the mortality rate from CVD reaches up to 40% [30]. Currently, around two million people in Kazakhstan are registered as suffering from CVD, which accounts for 12% of the economically active population. The incidence rate of diagnosed circulatory system diseases is 3856.4 per 100,000 population [1].

Patients with CVD with a history of heart valve replacement surgery, cardiac arrhythmias, or venous thromboembolic complications are forced to take long-term anticoagulant therapy to prevent potential complications. Warfarin is the primary oral anticoagulant used in the Republic of Kazakhstan, and it is included in the Kazakhstan National Drug Formulary (Anatomical Therapeutic Chemical Classification B01AA03, 2023).

Modern approaches in personalized medicine aim to improve the effectiveness of long-term anticoagulant therapy through pharmacogenetic testing. The main goal is to identify genetic markers that determine warfarin metabolism in each patient, thereby optimizing individualized treatment and minimizing the risk of side effects. However, significant challenges arise when attempting to adapt existing international personalized medicine protocols to the Kazakhstani population due to genetic differences among ethnic groups. Genetic predisposition to warfarin metabolism can vary from 0% to 50%, depending on ethnicity. It highlights the need for dedicated scientific research that takes into account the genetic characteristics of specific ethnic groups in order to achieve optimal treatment outcomes [2,3,4,6,9,28,34].

Central Asian populations are underrepresented in the scientific literature regarding the frequency of gene polymorphisms associated with warfarin pharmacogenetics. Several pharmacogenetic studies of the Kazakh population are known. For example, in the study by Zholdybayeva E. et al. (2014), allele frequencies of several polymorphisms in the Kazakh population were presented, along with promising directions for pharmacogenomic research in Kazakhstan [33]. In the study by Iskakova A. et al. (2016), gene polymorphisms affecting the metabolism of drugs concerning several multifactorial diseases (cardiovascular diseases, diabetes) in Kazakhs were investigated [12].

This study aims to determine the distribution of types of metabolizers in the Kazakh population and conduct a comparative analysis of the frequencies of minor alleles of polymorphisms of the CYP2C9 genes (* 2,* 3,* 5,* 6), CYP2C19, VKORC1, CYP4F2, and GGCX, which GWAS are associated with resistance to anticoagulants (vitamin K antagonists) compared with previously studied populations worldwide.

**Materials and methods.** The scientific research on warfarin pharmacogenetics in the Kazakh population was approved by the Local Ethics Committee of the "National Scientific Center of Surgery named after A.N. Syzganov" (Protocol No. 3 dated August 25, 2023).

*Type of study:* fundamental research.

The study used the genomic database of a control group of 1,900 conditionally healthy Kazakhs. The inclusion criteria for the control group were Kazakh ethnicity, reproductive age, and the ability to conceive. All participants provided informed consent and understood the study's purpose.

The genomic database was obtained through the InterPregGen project, with molecular genetic studies conducted at the Decode Genetics Center (Iceland) using IlluminaOmniChip 2.5 arrays. Quality control measures included the exclusion of SNPs based on statistical analysis of minor allele frequency (MAF < 0.05). Quality control measures excluded SNPs based on statistical analysis of minor allele frequency (MAF < 0.05). The PLINK software performed allele frequency statistics and non-parametric $\chi^2$ (chi-square) tests.[21].

**Results**

The most well-known clinically significant biomarkers for drug dosing are genes encoding cytochrome P450 enzymes (CYP450). Polymorphisms in the CYP450 family (particularly CYP2C9 and CYP2C19) are highly polymorphic, exhibit ethnographic variation, and display specific patterns of metabolizer phenotypes. Other important genetic determinants of warfarin dosage include polymorphisms in the VKORC1, CYP4F2, and GGCX genes [6,9, 10, 32, 34].

Table 1 presents the genetic characteristics of the gene polymorphisms, including the SNP identifier, reference number, chromosomal location, actual base pair position, and the full gene name.

The metabolic capacity of the enzyme systems encoded by the examined gene polymorphisms varies between individuals and ethnic groups. These interindividual and interethnic differences affect drug metabolism processes within the population. As a result, the metabolic conversion and drug elimination rates can range from extremely slow to ultra-rapid among different individuals. Through the screening of genetic variants, it is possible to characterize an individual's drug metabolism phenotype [9,23,34,35].

*Table 1.*

**Genetic characteristics of significant gene polymorphisms associated with sensitivity to warfarin.**

| N | Gene | | Chromosome | rs | Position | A1 | A2 |
|---|---|---|---|---|---|---|---|
| 1 | CYP2C9*2 | Cytochrome P450 Family 2 Subfamily C Member 9 | 10q23.33 | rs1799853 | 94942290 | C | T |
| 2 | CYP2C9*3 | | | rs1057910 | 94981296 | A | C |
| 3 | CYP2C9*5 | | | rs28371686 | 94981301 | C | G |
| 4 | CYP2C9*6 | | | rs9332131 | 94949282 | A | del |
| 5 | CYP2C19 | Cytochrome P450 Family 2 Subfamily C Member 19 | 10q23.33 | rs3814637 | 94761288 | C | T |
| 6 | VKORC1 (-1639G>A) | Vitamin K Epoxide Reductase Complex Subunit 1 | 16p11.2 | rs9923231 | 31096368 | C | T |
| 7 | CYP4F2 | Cytochrome P450 Family 4 Subfamily F Member 2 | 19p13.12 | rs2108622 | 15879621 | C | T |
| 8 | GGCX | Gamma-Glutamyl Carboxylase | 2p11.2 | rs11676382 | 85550510 | C | G |
| *Note: A1 – wild-type allele, A2 – minor allele* | | | | | | | |

The main metabolizer phenotypes are distinguished for several drugs, including warfarin. Normal or fast metabolizers (NM/FM) are defined by the presence of two functional alleles of gene polymorphisms. Carriers of one normal and one non-functional minor allele are classified as intermediate metabolizers (IM), while individuals with two non-functional alleles are considered slow metabolizers (SM). People with duplicated copies of normal alleles in their haplotype are categorized as ultra-rapid metabolizers (UM) [8,9].

In recent years, studies on the genetic basis of adverse drug reactions, therapy effectiveness, and dosage variations have increased [19,35]. Therefore, data on the variability of gene polymorphisms associated with sensitivity to anticoagulants from the vitamin K antagonist group are of great importance for optimizing genotyping in the pharmacotherapy of medications for each ethnic group within a specific population.

The allele and genotype distribution frequencies of significant gene polymorphisms were analyzed in the Kazakh population to determine the metabolic phenotype and population-specific frequencies of gene polymorphisms and to perform a comparative analysis with other global populations: CYP2C9*2 (rs1799853), *3 (rs1057910), *5 (rs28371686), *6 (rs9332131); CYP2C19 (rs3814637), VKORC1 (rs9934438), CYP4F2 (rs2108622), GGCX (rs11676382), based on GWAS data associated with sensitivity to anticoagulants from the vitamin K antagonist group.

Ethnicity is an important factor determining both warfarin's sensitivity and maintenance dose. It has been observed that Asians are highly sensitive, whereas African Americans are less sensitive. According to previous publications, the variability in the warfarin dosage from 2% to 40% depends on the genotypes that affect its metabolism. In populations from Iran, European countries, and the Americas, the CYP2C9*2/*3 variants have shown the greatest influence on CYP2C9 enzyme activity [3,5,13,23,28].

*Razavi F. et al.* (2017) describe SNPs determining CYP2C9 activity (allele *2 rs1799853 and allele *3 rs1057910). Data from 120 individuals of the Iranian population are presented regarding the frequency of CYP2C9 metabolic phenotypes 1/1, 1/2, 2/2, 3/1, 3/2, and 3/3, which were 64.1%, 15.8%, 0%, 17.5%, 2.5%, and 0%, respectively [23].

If an individual is homozygous for the wild-type alleles *2 and *3 of the CYP2C9 gene, the normal genotype CYP2C9 1/1 is defined. The combination of homozygous wild-type *3 and heterozygous *2 corresponds to the CYP2C9 1/2 genotype. The CYP2C9 2/2 genotype is defined by the presence of homozygous wild-type *3 and homozygous minor allele *2. Individuals who are homozygous for the wild-type *2 allele and heterozygous for *3 have the CYP2C9 1/3 genotype. Heterozygosity for both *2 and *3 alleles defines the CYP2C9 2/3 genotype. The CYP2C9 3/3 genotype is defined by homozygosity for the frequent allele *2 and homozygosity for the rare allele *3 [23].

As shown in Table 2, the frequencies of metabolizer phenotypes based on the two CYP2C9 alleles (*2, *3) for the Kazakh ethnic group were determined as follows: 1/1 – 80.1%, 1/3 – 13.0%, 3/3 – 0.25%, 1/2 – 6.0%, 2/3 – 0.40%, and 2/2 – 0.25%. Normal metabolizers accounted for 80.1%, intermediate metabolizers - 19.0%, and poor metabolizers - 0.9%.

The frequencies of metabolizer phenotypes based on two other CYP2C9 alleles (*5, *6) — 1/1, 1/6, 1/5, 5/6, and 5/5 - were 90.0%, 6.7%, 2.9%, 0.3%, and 0.1%, respectively, as shown in Table 2. The frequency of normal metabolizers was 90.0%, intermediate metabolizers – 9.6%, and poor metabolizers – 0.4%.

Globally, the prevalence of drug metabolizer types via CYP2C9 varies. In Southern Europe, the frequency of CYP2C9 metabolites ranges from 3-4%. The east coast of the Mediterranean Sea, Asia, and Africa show less than 1% poor metabolizers, except for the United Arab Emirates (UAE), where the incidence of CYP2C9 *3 and *5 is 11.1%. Intermediate metabolizers of CYP2C9 are most common in the UAE (48.7%), Croatia (41.2%), and Iran (40.3%) [35]. Most studies have shown that carriers of the “slow” allelic variants *2 and *3 of the CYP2C9 gene exhibit reduced rates of warfarin biotransformation and higher plasma concentrations of the drug. As a result, warfarin remains in circulation longer, and lower doses are required to achieve the desired anticoagulant effect [4,8,10,27].

Table 3 presents a comparative analysis of minor allele frequencies of gene polymorphisms associated with sensitivity to vitamin K antagonists in the Kazakh population based on GWAS data, compared with previously studied populations worldwide.

*Table 2.*

**Frequencies of CYP2C9 metabolic phenotypes based on *2 and *3, *5 and *6 polymorphisms in the Kazakh population control group.**

| Gene | Polymorphisms, Genotypes | | Frequency | | Metabolic Phenotype | |
|---|---|---|---|---|---|---|
| | *2 | *3 | в % | n | | |
| | CC | AA | 80,09 | 1593 | 1/1 | NM |
| | CC | CA | 12,97 | 258 | 1/3 | IM |
| | CC | CC | 0,25 | 5 | 3/3 | PM |
| | TC | AA | 6,03 | 120 | 1/2 | IM |
| | TC | CA | 0,40 | 8 | 2/3 | PM |
| | TT | AA | 0,25 | 5 | 2/2 | PM |
| | | | Всего | N=1989 | | |
| CYP2C9 | *5 | *6 | в % | n | Метаболический фенотип | |
| | CC | AA | 90,04 | 1790 | 1/1 | NM |
| | CC | delA | 6,69 | 133 | 1/6 | IM |
| | GC | AA | 2,87 | 57 | 1/5 | IM |
| | GC | delA | 0,15 | 3 | 5/6 | PM |
| | GG | AA | 0,10 | 2 | 5/5 | PM |
| | GG | delA | 0,05 | 1 | 5/6 | PM |
| | GG | deldel | 0,10 | 2 | 5/6 | PM |
| | | | Всего | N=1988 | | |

*Note: NM – normal metabolizer; IM – intermediate metabolizer; PM – poor metabolizer*

The superfamily of proteins known as cytochrome P450 (CYP) enzymes is involved in synthesizing and metabolizing various endogenous and exogenous cellular components. The CYP2C9 gene (Cytochrome P450 Family 2 Subfamily C Member 9) encodes an isoform of the endoplasmic reticulum enzyme that is involved in the metabolism of steroid hormones and fatty acids and plays a key role in the breakdown of the drug warfarin.

It has been reported that CYP2C9 *2 reduces warfarin metabolism by 30%, and the CYP2C9 *3 allele reduces it by 90% [17]. It has been established that carriers of the *2 or *3 alleles metabolize warfarin more slowly, leading to a prolonged drug elimination from the bloodstream. As a result, lower doses are required to achieve adequate anticoagulant effects and prevent complications. [2,8,9]. Thus, patients carrying one or two copies of the *2 or *3 allele are at a higher risk of bleeding during initiation of warfarin therapy at standard doses [2,8,9,10,27,11,17].

Several CYP2C9 alleles (*6, *15, *25, and *35) are associated with a complete loss of hydroxylation activity, whereas most other variants (*2, *3, *5, *11) are associated with reduced enzymatic activity [6,8].

Scientific studies conducted in 70 populations worldwide have demonstrated that the CYP2C9*2 allele is more commonly found in European populations, with an average frequency of 14%, including 15.0% in France, the Middle East (Iran – 18.1%), Brazil (10.7%), Croatia (16.5%), and Lebanon (15.4%). Intermediate frequencies are observed in Mexico (3.7%) and Peru (3.8%). In comparison, the lowest frequencies are found in Africans (0.46%), except North Africa (about 12%), as well as in Asians (0.56%), Ecuador (0.5%), and Native Americans (1.25%). The CYP2C9*2 allele is not found in East Asian populations; low frequencies (approximately 5%) were registered in South Asian populations. [35].

Populations of the Middle East and Europe have a high frequency of the allele *3 of CYP2C9 (average 7.8%), including Spain (10.1%) and Turkey (9.8%). Frequencies in South America have also been reported: Uruguay (7.6%), Colombia (6.8%), and Brazil (6.0%). As opposed to the *2 allele, the *3 allele is prevalent in South Asia, with frequencies of 9.9% in Pakistan, 11.6% in Bangladesh, and up to 13.1% in India. A very high frequency of the *3 allele has been identified in the United Arab Emirates (21.3%) and among Indigenous Malaysians (36.0%) [6,8,35]. The combination of *2 and *3 variants within a single genotype is rare (<2%) and occurs more often in individuals of African or Asian descent [35].

According to the literature, the CYP2C9 *5 and *6 alleles are rare, and their ethnographic distribution is poorly studied. However, they have been detected in the United Arab Emirates (7.8%) and Sudan (2%). CYP2C9 *5 occurs among African Americans at a frequency of 1.56%, while CYP2C9 *6 is more common among Black Africans, with a frequency of 2.70% [35].

Table 3 shows that the frequency of the minor T allele of the CYP2C9*2 polymorphism (rs1799853) in the Kazakh ethnic sample is 3.5%, which is significantly higher ($p < 0.05$) compared to the corresponding frequency in East Asian populations (e.g., 0.5% in China; virtually absent in Japan and Vietnam), but significantly lower than the population frequency in Europe (England – 8.8%, Spain – 14.0%, Italy – 15.4%) ($p<0.001$). No statistically significant differences were found compared to previously studied South Asian populations (Bangladesh – 1.7%, India – 4.9%, Pakistan – 5.2%) ($p>0.05$).

The minor C allele frequency of CYP2C9 *3 (rs1057910) in Kazakhs was 6.9%, which is comparable to its frequency in European populations (England – 7.1%, Spain and Italy – 8.4%) and in some Asian populations (China – 4.8%, Vietnam – 3.5%, Pakistan – 9.9%) ($p>0.05$). However, it was significantly higher than the corresponding frequency in specific Southeast Asian populations (Bangladesh – 1.2%, India – 1.3%, Japan – 1.9%) ($p<0.05$).

For the CYP2C9 *5 (rs28371686) and CYP2C96* (rs9332131) alleles, the minor allele frequency in the Kazakh ethnic group was 1.8% and 3.6%, respectively. For the population samples from Europe, South Asia, and East Asia presented in Table 3, the corresponding frequencies were 0, indicating their infrequent occurrence in those populations.

*Table 3.*

**Comparative analysis of population frequencies of minor alleles of gene polymorphisms associated with warfarin sensitivity in Kazakhs and global populations.**

| Population | N | MAF | χ2 | p |
|---|---|---|---|---|
| CYP2C9*2 (rs1799853) | | | | |
| Kazakhs | 1995 | 0,03534 | 3849 | 141 |
| Europe: | | | | |
| England** | 91 | 0,088 | 13,284* | <0,001 |
| Spain** | 107 | 0,14 | 57,220* | <0,001 |
| Italy** | 107 | 0,154 | 72,330* | <0,001 |
| East Asia: | | | | |
| China** | 105 | 0,005 | 5,710* | 0,017 |
| Japan** | 104 | 0 | 7,606* | 0,006 |
| Vietnam** | 99 | 0 | 7,241* | 0,008 |
| South Asia: | | | | |
| Bangladesh** | 86 | 0,017 | 1,581 | 0,209 |
| India** | 103 | 0,049 | 0,985 | 0,322 |
| Pakistan** | 96 | 0,052 | 1,476 | 0,225 |
| CYP2C9*3 (rs1057910) | | | | |
| Kazakhs | 1996 | 0,06914 | 3709 | 283 |
| Europe: | | | | |
| England** | 91 | 0,071 | 0,001 | 0,978 |
| Spain** | 107 | 0,084 | 0,534 | 0,465 |
| Italy** | 107 | 0,084 | 0,534 | 0,465 |
| East Asia: | | | | |
| China** | 105 | 0,048 | 1,666 | 0,197 |
| Japan** | 104 | 0,019 | 8,288* | 0,004 |
| Vietnam** | 99 | 0,035 | 3,698 | 0,055 |
| South Asia: | | | | |
| Bangladesh** | 86 | 0,116 | 5,034* | 0,025 |
| India** | 103 | 0,131 | 10,372* | 0,002 |
| Pakistan** | 96 | 0,099 | 2,155 | 0,143 |
| CYP2C9*5 (rs28371686) | | | | |
| Kazakhs | 1991 | 0,01808 | 3910 | 72 |
| Europe: | | | | |
| England** | 91 | 0 | 3,349 | 0,068 |
| Spain** | 107 | 0 | 3,937* | 0,048 |
| Italy** | 107 | 0 | 3,937* | 0,048 |
| East Asia: | | | | |
| China** | 105 | 0 | 3,863* | 0,050 |
| Japan** | 104 | 0 | 3,827 | 0,051 |
| Vietnam** | 99 | 0 | 3,643 | 0,057 |
| South Asia: | | | | |
| Bangladesh** | 86 | 0 | 3,165 | 0,076 |
| India** | 103 | 0 | 3,790 | 0,052 |
| Pakistan** | 96 | 0 | 3,533 | 0,061 |
| CYP2C9*6 (rs9332131) | | | | |
| Kazakhs | 1995 | 0,03609 | 3846 | 144 |
| Europe: | | | | |
| England** | 91 | 0 | 0,662 | 0,416 |
| Spain** | 107 | 0 | 0,779 | 0,378 |
| Italy** | 107 | 0 | 0,779 | 0,378 |
| East Asia: | | | | |
| China** | 105 | 0 | 0,764 | 0,382 |
| Japan** | 104 | 0 | 0,757 | 0,385 |
| Vietnam** | 99 | 0 | 0,721 | 0,396 |
| South Asia: | | | | |
| Bangladesh** | 86 | 0 | 0,626 | 0,429 |
| India** | 103 | 0 | 0,750 | 0,387 |
| Pakistan** | 96 | 0 | 0,699 | 0,404 |

*Continuation of Table 3.*

| | | | | |
|---|---|---|---|---|
| CYP2C19 (rs3814637) | | | | |
| Kazakhs | 1984 | 0,04637 | 3784 | 184 |
| Europe: | | | | |
| England** | 91 | 0,066 | 1,480 | 0,224 |
| Spain** | 107 | 0,079 | 4,853* | 0,028 |
| Italy** | 107 | 0,084 | 6,292* | 0,013 |
| East Asia: | | | | |
| China** | 105 | 0,09 | 8,393* | 0,004 |
| Japan** | 104 | 0,12 | 22,654* | <0,001 |
| Vietnam** | 99 | 0,076 | 3,580 | 0,059 |
| South Asia: | | | | |
| Bangladesh** | 86 | 0,14 | 29,986* | <0,001 |
| India** | 103 | 0,136 | 32,575* | <0,001 |
| Pakistan** | 96 | 0,12 | 20,879* | <0,001 |
| VKORC1 (rs9923231) | | | | |
| Kazakhs | 1988 | 0,288 | 2831 | 1145 |
| Europe: | | | | |
| England** | 91 | 0,357 | 4,035* | 0,045 |
| Spain** | 107 | 0,36 | 5,072* | 0,025 |
| Italy** | 107 | 0,477 | 34,575* | <0,001 |
| East Asia: | | | | |
| China** | 105 | 0,89 | 333,748* | <0,001 |
| Japan** | 104 | 0,9 | 345,342* | <0,001 |
| Vietnam** | 99 | 0,843 | 269,998* | <0,001 |
| South Asia: | | | | |
| Bangladesh** | 86 | 0,157 | 13,957* | <0,001 |
| India** | 103 | 0,175 | 12,389* | <0,001 |
| Pakistan** | 96 | 0,198 | 7,308* | 0,007 |
| CYP4F2 (rs2108622) | | | | |
| Kazakhs | 1992 | 0,3303 | 2668 | 1316 |
| Europe: | | | | |
| England** | 91 | 0,286 | 1,570 | 0,211 |
| Spain** | 107 | 0,355 | 0,564 | 0,453 |
| Italy** | 107 | 0,336 | 0,034 | 0,853 |
| East Asia: | | | | |
| China** | 105 | 0,2 | 15,474* | <0,001 |
| Japan** | 104 | 0,231 | 8,925* | 0,003 |
| Vietnam** | 99 | 0,222 | 10,044* | 0,002 |
| South Asia: | | | | |
| Bangladesh** | 86 | 0,413 | 5,043* | 0,025 |
| India** | 103 | 0,437 | 9,978* | 0,002 |
| Pakistan** | 96 | 0,391 | 2,999 | 0,084 |
| GGCX (rs11676382) | | | | |
| Kazakhs | 1991 | 0,1444 | 3407 | 575 |
| Europe: | | | | |
| England** | 91 | 0,159 | 0,313 | 0,576 |
| Spain** | 107 | 0,093 | 4,331* | 0,038 |
| Italy** | 107 | 0,042 | 17,755* | <0,001 |
| East Asia: | | | | |
| China** | 105 | 0 | 35,145* | <0,001 |
| Japan** | 104 | 0 | 34,813* | <0,001 |
| Vietnam** | 99 | 0 | 33,151* | <0,001 |
| South Asia: | | | | |
| Bangladesh** | 86 | 0,023 | 20,172* | <0,001 |
| India** | 103 | 0,01 | 29,912* | <0,001 |
| Pakistan** | 96 | 0,021 | 23,409* | <0,001 |

*Note: N – number of DNA samples; MAF – minor allele frequency; $\chi^2$ – Chi-square test; P – statistical significance; * – statistically significant differences (p<0.05); ** – https://asia.ensembl.org/Homo_sapiens/Info/Index; Fiona Cunningham and others, Ensembl 2022,* Nucleic Acids Research*, Volume 50, Issue D1, 7 January 2022, Pages D988–D995, https://doi.org/10.1093/nar/gkab1049*

The CYP2C19 gene (Cytochrome P450 Family 2 Subfamily C Member 19) from the cytochrome P450 family encodes a monooxygenase enzyme that catalyzes many reactions involved in drug metabolism and the synthesis of cholesterol, steroids, and other lipids [29].

A meta-analysis involving 1,393 patients showed that carriage of the minor allele rs3814637 of the CYP2C19 polymorphism is associated with a significant 18% reduction in warfarin dose requirement in patients with the T allele (rs3814637) and TT and CT genotypes, compared to patients with the CC genotype [29]. However, opposite findings have also been reported. An evaluation of warfarin therapy in 492 patients found that CYP2C19 polymorphisms were not associated with the need to adjust warfarin dosage [15].

Population frequencies of the CYP2C19 gene exhibit ethnic stratification and range from 15% to 25% among Chinese, Japanese, Koreans, and Indians and from 3% to 5% among White Europeans. Association studies on allele carriage and response to warfarin dosing have shown conflicting results [15]. As shown in Table 3, the frequency of the minor T allele of the CYP2C19 rs3814637 polymorphism was 4.6% in Kazakhs residing in Central Asia. This frequency is significantly lower ($p < 0.001$) compared to the corresponding frequencies in Europe (Spain – 7.9%, Italy – 8.4%), East Asia (China – 9.0%, Japan – 12.7%), and South Asia (Bangladesh – 14.0%, India – 13.6%, Pakistan – 12.0%). However, it did not differ significantly ($p>0.05$) from the frequencies observed in European (England – 6.6%) and East Asian (Vietnam – 7.6%) populations.

It is well known that the VKORC1 gene (Vitamin K Epoxide Reductase Complex Subunit 1) encodes one of the key enzymes involved in vitamin K metabolism, converting its inactive form (2,3-epoxide – vitamin K) into its active form (vitamin K – hydroquinone). VKORC1 gene polymorphisms are associated with increased sensitivity to warfarin anticoagulant therapy and lower required doses, indicating the need for dose adjustment. Pharmacogenetic dosing algorithms for warfarin commonly include testing for VKORC1 genotypes [25].

Many studies have shown that the frequency of the minor T allele of the VKORC1 polymorphism (c.-1639G>A) varies significantly across populations. In Europe, the frequency ranges from 37% to 47%, while in the Middle East it varies from 41% to 51%. East Asian populations exhibit much higher frequencies, ranging from 88% to 90%. In contrast, the prevalence of this allele is considerably lower in African populations, ranging from 13% to 15%, and is approximately 15% in South Asia [18,25,31]. In the Chinese population, carriage of the T/T genotype is observed in more than 83% of individuals [32], which is important to consider when determining warfarin dosage for patients in this population. It has also been shown that the rs9923231 polymorphism in the VKORC1 promoter reduces gene expression, thereby decreasing warfarin dose requirements and increasing sensitivity to the drug [13,25,32].

VKORC1 rs9923231 polymorphism in Kazakhs is 28.8%, which is significantly higher ($p < 0.001$) than in South Asian populations — 15.7% in Bangladesh, 17.5% in India, and 19.8% in Pakistan — and markedly lower than in East Asian populations — 89.0% in China, 90.0% in Japan, and 84.3% in Vietnam. These results highlight the diversity of the genetic landscape and the distribution of alleles in different geographical regions.

The enzyme CYP4F2 (Cytochrome P450 Family 4 Subfamily F Member 2) is involved in vitamin K metabolism by limiting its accumulation in the liver and catalyzing the production of hydroxylated vitamin K. This results in the need for higher doses of warfarin to achieve a therapeutic effect [7,22].

There are conflicting findings regarding the association between the CYP4F2 gene rs2108622 polymorphism and warfarin dose requirements. In Indian patients, only a weak association was found between genotype carriage and warfarin dose [22]. However, in Korean patients carrying the homozygous unfavorable TT genotype of CYP4F2, a significantly higher average warfarin dose was required compared to other genotypes (4.40 mg/day vs. 3.12 and 2.91 mg/day, respectively; $P=0.014$). As a result, genotyping of the CYP4F2 gene has been incorporated into pharmacogenetic warfarin dosing algorithms for Korean patients [7].

Table 3 presents the frequency of the minor T allele of the CYP4F2 rs2108622 polymorphism in the Kazakh population, which was 33.0%. This frequency is significantly lower ($p < 0.03$) compared to South Asian populations — Bangladesh (41.3%) and India (43.7%). In contrast, the frequency in Kazakhs is significantly higher ($p < 0.003$) than in East Asian populations — China (20.0%), Japan (23.1%), and Vietnam (22.2%). No statistically significant differences were found when comparisons were made ($p > 0.05$) with European populations — England (28.6%), Spain (35.5%), Italy (33.6%) — and the Pakistani population (39.1%) ($p>0.05$).

The GGCX gene (Gamma-Glutamyl Carboxylase) encodes the GGCX enzyme involved in the vitamin K cycle by synthesizing vitamin K-dependent proteins [17]. Scientific studies have shown that carriage of certain GGCX gene polymorphisms significantly impacts the adjustment of warfarin dosage [24,28].

A multicenter cross-sectional study involving 985 patients of European descent undergoing warfarin therapy included genotyping for the GGCX gene polymorphism (rs11676382). The study found that carriage of the minor G allele was associated with a significant 6.1% reduction in warfarin dose (95% CI: 0.6–11.4%) [14]. Similar results were obtained in a study of 186 European-American patients receiving warfarin. Carriage of GGCX rs11676382 genotypes was associated with lower warfarin doses, which was confirmed under a dominant genetic model [24].

However, in a study of 145 ethnically diverse patients, other researchers found no association between the G allele and therapeutic warfarin dose [20].

The minor G allele frequencies of the GGCX gene are either unreported or very low in East Asian populations. In South Asia, the allele frequencies range from 1% to 3% in Northern India. In European populations, the frequencies range from 4% to 16% [22,28].

The prevalence of the minor allele of the GGCX gene (rs11676382) in the ethnically homogeneous Kazakh population was measured at 14.4%, which is statistically significant ($p < 0.04$) compared to South Asian cohorts:

Bangladesh (2.3%), India (1.0%), and Pakistan (2.1%). Furthermore, this frequency is markedly higher than that observed in several European populations, with Spain at 9.3% and Italy at 4.2%. Notably, the allele frequency in Kazakhstan is comparable to that found in England, recorded at 15.9%. In stark contrast, East Asian populations, including samples from China, Japan, and Vietnam, exhibited a GGCX minor allele frequency of zero in the respective studies (N = 99–105), as summarized in Table 3.

**Discussion**

The study of allele frequency distributions of the analyzed gene polymorphisms in the Kazakh population revealed notable genetic diversity.

The frequency of the minor allele of the CYP2C19 gene (4.64%) in Kazakhs was significantly lower ($p < 0.05$) compared to the corresponding frequencies in European, East Asian, and South Asian populations. The frequency of the minor allele of the "Asian" polymorphism GGCX rs11676382 was significantly higher in Kazakhs (14.4%) compared to both European and other Asian populations ($p < 0.05$).

Analysis of genetic variability in the CYP2C9 gene showed that the frequency of the *2 allele in the Kazakh population is 3.53%, representing an intermediate level. It is significantly higher than in East Asian populations but significantly lower than in European samples ($p < 0.05$), and comparable to South Asian data.

The frequency of the *3 allele is 6.91%, placing the Kazakh population closer to European populations. However, it is significantly higher than in East Asian populations and lower than in South Asian populations ($p < 0.05$), again indicating an intermediate position.

The rare *5 (1.81%) and *6 (3.61%) alleles are considerably more prevalent in the Kazakh sample than in European, East Asian, and South Asian populations, where they are extremely rare or virtually absent.

A comparative analysis of the minor allele frequency of the CYP4F2 gene revealed a frequency of 33.0% in the Kazakh population. This value does not significantly differ from European samples ($p > 0.05$), but is significantly higher than in East Asian populations and lower than in South Asian populations ($p < 0.05$), again reflecting an intermediate genetic profile.

Regarding the minor allele rs9934438 of the VKORC1 gene, a frequency of 28.8% was observed in the Kazakh sample. This is significantly lower than in European and East Asian populations, but substantially higher than in South Asian populations ($p < 0.05$), further supporting the intermediate nature of the genetic profile in the Kazakh population.

The metabolic phenotypes of CYP2C9 were determined in the Kazakh population by examining the frequencies of functionally significant CYP2C9 alleles. This includes the standard *2 and *3 alleles, as well as the less common variant alleles *5 and *6, which reduce or eliminate enzyme activity.

The frequency of poor metabolizers among Kazakhs was 0.9% for *2 and *3 and 0.4% for *5 and *6, aligning with global data for Asian populations (<1%).

Intermediate metabolizers accounted for 19.0% for *2 and *3 and 9.6% for *5 and *6, while normal metabolizers made up 80.1% for *2 and *3 and 90.0% for *5 and *6.

**Conclusions**

The frequencies of metabolizer phenotypes in the Kazakh population, determined by polymorphisms in genes that encode enzymes involved in warfarin biotransformation and metabolism, are important for selecting the optimal dosage. Preventing the risk of both hemorrhagic and thrombotic adverse reactions during long-term anticoagulant therapy is essential.

The findings of this study will advance pharmacogenetics in Kazakhstan and provide a valuable resource for enhancing global data on allele and phenotype frequencies specific to the Kazakh ethnic group in Central Asia.

***Author Contributions:*** *ll authors were involved in developing the study concept and design, data collection, and statistical analysis. A.V. Murtazaliyeva and G.M. Berezina prepared the initial draft of the manuscript. All authors reviewed, revised, contributed to, and approved the final version of the manuscript for publication.*

***Ethical endorsement:*** *The research conducted met international standards and received approval from the Bioethics Committee of the National Scientific Center of Surgery named after A.N. Syzganov (Almaty, Kazakhstan) with the Ethical and Helsinki Declaration of 1964 and its subsequent amendments or comparable ethical standards.*

***Conflict of interest:*** *No conflict of interest is declared.*

***Funding:*** *This work was carried out within the framework of the project – State Registration Number 0123RK01103, AP19677439: "Pharmacogenetics of Indirect Anticoagulants in Patients with Surgically Treated Heart Conditions."*

***Literature:***

1. Здоровье населения Республики Казахстан и деятельность организаций здравоохранения в 2022 году. Статистический сборник. 2023. 361 с. URL: https://www.gov.kz/memleket/entities/dsm/documents/details/583047?lang=ru&ysclid=lw95eckbga54388976

2. *Al-Eitan L.N., Almasri A.Y., Khasawneh R.H.* Impact of CYP2C9 and VKORC1 Polymorphisms on Warfarin Sensitivity and Responsiveness in Jordanian Cardiovascular Patients during the Initiation Therapy. Genes (Basel). 2018. 27;9(12). P.578. doi: 10.3390/genes9120578.

3. *Azarpira N., Namazi S., Hendijani F., Banan M., Darai M.* Investigation of allele and genotype frequencies of CYP2C9, CYP2C19 and VKORC1 in Iran. Pharmacol Rep. 2010. 62(4). P.740–746. doi: 10.1016/s1734-1140(10)70332-7.

4. *Borgiani P., Ciccacci C., Forte V., Romano S., Federici G., Novelli G.* Allelic variants in the CYP2C9 and VKORC1 loci and interindividual variability in the anticoagulant dose effect of warfarin in Italians. Pharmacogenomics. 2007. 8(11). P.1545-1550. doi: 10.2217/14622416.8.11.1545.

5. *Cavallari L.H., Perera M.A.* The future of warfarin pharmacogenetics in under-represented minority groups. Future Cardiol. 2012. 8(4). P.563–576. doi: 10.2217/fca.

6. *Céspedes-Garro C., Fricke-Galindo I., Naranjo M., Rodrigues-Soares F., Fariñas H., de Andrés F., López-López M., Peñas-Lledó E., LLerena A.* Worldwide interethnic variability and geographical distribution of CYP2C9 genotypes and phenotypes. Expert Opin Drug

Metab Toxicol. 2015. 11(12). P.1893-1905. doi: 10.1517/17425255.2015.1111871.

7. *Choi J.R.., Kim J.O., Kang D.R., Yoon S.A., Shin J.Y., Zhang X., Roh M.O., Hong H.J., Wang Y.P., Jo K.H., Lee K.S., Yun H.J., Oh Y.S., Yoo K.D., Jeon H.G., Lee Y.S., Kang T.S., Park H.J., Chung M.W., Kang J.H.* Proposal of pharmacogenetics-based warfarin dosing algorithm in Korean patients. J Hum Genet. 2011. 56(4). P.290-295. doi: 10.1038/jhg.2011.4.

8. *Daly A.K., Rettie A.E., Fowler D.M., Miners J.O.* Pharmacogenomics of CYP2C9: Functional and Clinical Considerations // Journal of Personalized Medicine. 2018. 8(1):1. URL: https://doi.org/10.3390/jpm8010001

9. *Dean L.* Warfarin Therapy and VKORC1 and CYP Genotype. Medical Genetics Summaries / National Library of Medicine. 2018. https://www.ncbi.nlm.nih.gov/books/NBK84174/

10. *Fricke-Galindo I., Céspedes-Garro C., Rodrigues-Soares F., Naranjo M., Delgado Á., de Andrés F., López-López M., Peñas-Lledó E., LLerena A.* Interethnic variation of CYP2C19 alleles, 'predicted' phenotypes and 'measured' metabolic phenotypes across world populations. Pharmacogenomics J. 2016. 16(2). P.113-123. doi: 10.1038/tpj.2015.70.

11. *Holbrook A., Schulman S., Witt D.M., Vandvik P.O., Fish J., Kovacs M.J., Svensson P.J., Veenstra D.L., Crowther M., Guyatt G.H.* Evidence-based management of anticoagulant therapy: Antithrombotic Therapy and Prevention of Thrombosis // 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012. 141(2 Suppl). e152S-e184S. doi: 10.1378/chest.11-2295.

12. *Iskakova A., Romanova A., Aitkulova A.., Sikhayeva N., Zholdybayeva E., Ramanculov E.* Polymorphisms in genes involved in the absorption, distribution, metabolism, and excretion of drugs in the Kazakhs of Kazakhstan. BMC Genetics. 2016. 19;17:23. DOI 10.1186/s12863-016-0329-x

13. *Kamal El-Din M.A., Farhan M.S., El Shiha R.I., El-Kaffas R.M., Mousa S.M.* Frequency of CYP2C9 and VKORC1 gene polymorphisms and their influence on warfarin dose in Egyptian pediatric patients. Paediatr Drugs. 2014. 16(4). P.337–341.

14. *King C.R., Deych E., Milligan P., Eby C., Lenzini P., Grice G., Porche-Sorbet R.M., Ridker P.M., Gage B.F.* Gamma-glutamyl carboxylase and its influence on warfarin dose. Thromb Haemost. 2010.104(4). P.750-754. doi: 10.1160/TH09-11-0763.

15. *Khalighi K., Cheng G., Mirabbasi S., Khalighi B., Wu Y., Fan W.* Linkage disequilibrium between the CYP2C19*2,*17 and CYP2C9*1 alleles and impact of VKORC1, CYP2C9, CYP2C19 gene polymorphisms and gene-gene interactions on warfarin therapy. J Thromb Thrombolysis. 2017. 43(1). P.124-129. doi: 10.1007/s11239-016-1436-2.

16. *Kumar K.D., Shewade D.G., Loriot M.A., Beaune P., Balachander J., Sai Chandran B.V., Adithan C.* Effect of CYP2C9, VKORC1, CYP4F2 and GGCX genetic variants on warfarin maintenance dose and explicating a new pharmacogenetic algorithm in South Indian population. Eur J Clin Pharmacol. 2014. 70(1). P.47-56. doi: 10.1007/s00228-013-1581-x.

17. *Lam M.P., Cheung B.M. The pharmacogenetics of the response to warfarin in Chinese* // Br J Clin Pharmacol. 2012. 73(3). P.340-347. doi: 10.1111/j.1365-2125.2011.04097.x.

18. *Li S., Zou Y., Wang X., Huang X., Sun Y., Wang Y., Dong L. and Jiang H.* Warfarin dosage response related pharmacogenetics in Chinese population. PLoS One. 2015. 10(1): e0116463. doi: 10.1371/journal.pone.0116463.

19. *Liu T.Y., Hsu H.Y., You Y.S., Hsieh Y.W., Lin T.C., Peng C.W., Huang H.Y., Chang S.S., Tsai F.J.* Efficacy of Warfarin Therapy Guided by Pharmacogenetics: A Real-world Investigation Among Han Taiwanese. Clin Ther. 2023. 45(7). P.662-670. doi: 10.1016/j.clinthera.2023.04.006.

20. *Lubitz S.A. Scott S.A., Rothlauf E.B., Agarwal A., Peter I., Doheny D., Van Der Zee S., Jaremko M., Yoo C., Desnick R.J., Halperin J.L.* Comparative performance of gene-based warfarin dosing algorithms in a multiethnic population. J Thromb Haemost. 2010. 8(5). P.1018-1026. doi: 10.1111/j.1538-7836.2010.03792.x.

21. *Purcell S., Neale B., Todd-Brown K., Thomas L., Ferreira MA., Bender D., Maller J., Sklar P., de Bakker PI., Daly MJ., Sham PC.* PLINK: a tool set for whole-genome association and population-based linkage analyses. Am J Hum Genet. 2007. 81(3). P.559-575. doi: 10.1086/519795.

22. *Rathore SS., Agarwal SK., Pande S., Singh SK., Mittal T., Mittal B.* CYP4F2 1347 G> A & GGCX 12970 C> G polymorphisms: frequency in north Indians & their effect on dosing of acenocoumarol oral anticoagulant. The Indian Journal of Medical Research 2014. 139(4). P. 572-578.

23. *Razavi FE., Zarban A., Hajipoor F., Naseri M.* The allele frequency of CYP2C9 and VKORC1 in the Southern Khorasan population. Res Pharm Sci. 2017 12(3). P.211-221. doi: 10.4103/1735-5362.207202.

24. *Rieder MJ., Reiner AP., Rettie AE.* Gamma-glutamyl carboxylase (GGCX) tagSNPs have limited utility for predicting warfarin maintenance dose. J Thromb Haemost. 2007 5(11). P.2227-2234. doi: 10.1111/j.1538-7836.2007.02744.x.

25. *Ross K.A., Bigham A.W., Edwards M., Gozdzik A., Suarez-Kurtz G., Parra E.J.* Worldwide allele frequency distribution of four polymorphisms associated with warfarin dose requirements. Journal of human genetics. 2010. 55(9). P.582–589. doi: 10.1038/jhg.2010.73.

26. *Sconce E.A., Khan T.I., Wynne H.A., Avery P., Monkhouse L., King B.P. et al.* The impact of CYP2C9 and VKORC1 genetic polymorphism and patient characteristics upon warfarin dose requirements: proposal for a new dosing regimen. Blood. 2005. 106(7). P.2329–2333. doi: 10.1182/blood-2005-03-1108.

27. *Shayah K., Ghrewati A., Mohammad YA., Hadid I.* Role of Genetic Variations in the CYP2C9 Gene in Determining the Optimal Dose of Warfarin in a Group of Syrian Patients. International Journal of Pharmaceutical Sciences and Nanotechnology. 2019. 12(2). P.4505-4511. doi.org/10.37285/ijpsn.2019.12.2.8

28. *Sun Y., Wu Z., Li S., Qin X., Li T., Xie L., Deng Y., Chen J.* Impact of gamma-glutamyl carboxylase gene polymorphisms on warfarin dose requirement: a systematic review and meta-analysis. Thromb Res. 2015. 135(4). P.739-747. doi: 10.1016/j.thromres.2015.01.029.

29. *Wang D., Yong L., Zhang Q., Chen H.* Impact of CYP2C19 gene polymorphisms on warfarin dose requirement: a systematic review and meta-analysis.

Pharmacogenomics. 2022. 23(16). P.903-911. doi: 10.2217/pgs-2022-0106.

30. World Health Organization (WHO). Cardiovascular diseases. 2021. https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)

31. *Yang L., Ge W., Yu F. and Zhu H.* Impact of VKORC1 gene polymorphism on interindividual and interethnic warfarin dosage requirement-a systematic review and meta analysis. Thromb Res. 2010. 25(4). e159–e166. doi: 10.1016/j.thromres.2009.10.017.

32. *Zhang J., Chen Z., Chen C.* Impact of CYP2C9, VKORC1 and CYP4F2 genetic polymorphisms on maintenance warfarin dosage in Han-Chinese patients: A systematic review and meta-analysis. Meta Gene. 2016. P.197-209. doi: 10.1016/j.mgene.2016.07.002.

33. *Zholdybayeva E., Iskakova A., Romanova A., Ramanculov E., Momynaliev K.* Pharmacogenetic research in Kazakhstan. Cent Asian J Glob Health. 2014. 2(Suppl) P.87. doi: 10.5195/cajgh.2013.87.

34. *Zhou Y., Lauschke VM.* Population pharmacogenomics: an update on ethnogeographic differences and opportunities for precision public health. Hum Genet. 2022. 141(6). P.1113–1136. doi: 10.1007/s00439-021-02385-x.

35. *Zhou Y., Nevosadová L., Eliasson E., Lauschke VM.* Global distribution of functionally important CYP2C9 alleles and their inferred metabolic consequences. Hum Genomics. 2023. 17(1).15. doi: 10.1186/s40246-023-00461-z.

***References:***

1. *Zdorov'e naselenija Respubliki Kazahstan i dejatel'nost' organizacij zdravoohranenija v 2022 godu. Statisticheskij sbornik* [Health of the population of the Republic of Kazakhstan and the activities of healthcare organizations in 2022. Statistical digest.]. 2023. 361 p. URL:https://www.gov.kz/memleket/entities/dsm/documents/details/583047?lang=ru&ysclid=lw95eckbga54388976 [in Russian]

**Author Information**

**Alexandra V. Murtazaliyeva** – geneticist, researcher at the Center for Education and Science in LLP "Center for Molecular Medicine", Almaty, Republic of Kazakhstan, ORCID ID 0000-0001-9156-5944, A05B1E1, 130 Ayitiyev Str., Almaty, Kazakhstan; phone: +7 (771) 799-91-00, e-mail: alexmurtazalieva@gmail.com

**Galina M. Berezina** – Doctor of Biological Sciences, Associate Professor, Leading Researcher, Department of Strategy and Science, Republican Medical Genetic Consultation of Joint-Stock Company “Scientific Center of Obstetrics, Gynecology and Perinatology; ORCID ID 0000-0002-5442-4461, A25D6G4, 125 Dostyk Ave., Almaty, Kazakhstan; phone: +7 (727) 300-45-62, e-mail: gberezina54@mail.ru

**Gulnara S. Svyatova** – Doctor of Medicine, Professor, Head of the Center for Education and Science in LLP "Center for Molecular Medicine", ORCID ID 0000-0001-5092-3143, A05B1E1, 130 Ayitiyev Str., Almaty, Kazakhstan; phone: +7 (771) 799-91-00, e-mail: gsvyatova1@mail.ru

**Meruert S. Yesset** – Specialist of the Laboratory in Republican Medical Genetic Consultation of Joint-Stock Company “ Scientific Center of Obstetrics, Gynecology and Perinatology”, ORCID ID 0000-0003-2906-5636, A25D6G4, 125 Dostyk Ave., Almaty, Kazakhstan; phone: +7 (727) 300-45-62, e-mail: eset_m@mail.ru

**Asem T. Burabayeva** – Resident in Medical Genetics in Joint-Stock Company “Scientific Center of Obstetrics, Gynecology and Perinatology”, ORCID ID 0009-0005-4527-7729, A25D6G4, 125 Dostyk Ave., Almaty, Kazakhstan; phone: +7 (727) 300-45-62, e-mail: dr.burabayeva@mail.ru

***Corresponding author:**

**Galina M. Berezina** – Doctor of Biological Sciences, Associate Professor, Leading Researcher, Department of Strategy and Science, Joint-Stock Company “Scientific Center of Obstetrics, Gynecology and Perinatology”, Almaty, Kazakhstan;

**Post address:** 05020, 125 Dostyk Ave., Almaty, Kazakhstan;

**e-mail:** gberezina54@mail.ru

**phone:** +7 777 701 11 56

Received: 14 January 2025 / Accepted: 10 June 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2025.27.3.003***

***UDC 616.8-092:615.273.53:615.38***

This work is licensed under a Creative Commons Attribution 4.0 International License

# NEUROLOGICAL COMPLICATIONS IN EXTRACORPOREAL MEMBRANE OXYGENATION: RISK FACTORS FOR THE DEVELOPMENT OF ACUTE CEREBROVASCULAR EVENTS

**Dauren A. Antikeev[1], https://orcid.org/0009-0007-0934-6509**

**Aigerim A. Orazkhan[2], https://orcid.org/0009-0006-4158-899X**

**Leila B. Temirbulatova[2], https://orcid.org/0009-0008-0494-0100**

**Diana Zh. Beisimbayeva[2], https://orcid.org/0009-0009-6340-9798**

**Askar M. Abiltayev[1,2], https://orcid.org/0000-0003-4127-2347**

**Olga G. Tashtemirova[2], https://orcid.org/0000-0002-7537-2808**

**Ainur M. Shukimbayeva[2], https://orcid.org/0000-0002-4240-3663**

**Assel M. Makhmutova[2], https://orcid.org/0009-0005-3597-8409**

**[1] SE «Pavlodar Regional Cardiology Center», Pavlodar, Republic of Kazakhstan;**
**[2] Pavlodar Branch of Semey Medical State University, Pavlodar, Republic of Kazakhstan**

**Abstract**

**Introduction.** Cardiovascular diseases remain the leading cause of mortality and disability worldwide, including in Kazakhstan. Extracorporeal membrane oxygenation (ECMO) is a life-saving treatment for severe cardiopulmonary failure; however, its use is associated with a high risk of complications, including acute neurological disorders such as strokes.

**Objective.** To determine the incidence of acute cerebrovascular events (ACE), including ischemic and hemorrhagic strokes, in patients receiving extracorporeal membrane oxygenation (ECMO), as well as to identify key risk factors for their development in the context of clinical practice in Kazakhstan.

**Methods.** A retrospective analysis was conducted on data from 92 patients hospitalized at the Pavlodar Regional Cardiology Center between 2015 and 2024. All patients were on ECMO during the intraoperative or postoperative periods. Study participants were stratified into two cohorts: (1) individuals with acute cerebrovascular events and (2) those without evidence of cerebrovascular compromise. The analysis included an assessment of demographic data, comorbidities, surgical characteristics, and postoperative parameters. The study data were obtained through a retrospective analysis of patients' medical records, including medical histories and electronic databases of the cardiology center. Statistical analysis was performed using IBM™ SPSS 26.0 software (IBM Corporation, Armonk, NY, 2019).

**Results.** Neurological complications, including strokes, were identified in 31.5% of patients on ECMO. The main risk factors were hypertension, smoking, and a history of stroke. It was also found that women and patients with a low left ventricular ejection fraction were at higher risk. The average length of hospitalization for patients with strokes was 30.2 days, which exceeded that of patients without strokes (25.6 days).

**Conclusion.** Strokes remain a significant complication in patients on ECMO, necessitating the development of specific preventive measures. Identified risk factors, such as hypertension, smoking, and a history of stroke, should be considered in the development of clinical guidelines. This study highlights the need for further large-scale research to improve the diagnosis and prevention of strokes in patients on ECMO.

***Keywords:*** *extracorporeal membrane oxygenation, acute cerebrovascular event, neurological complications, risk factors for stroke.*

***For citation:***

*Antikeev D.A., Orazkhan A.A., Temirbulatova L.B., Beisimbayeva D.Zh., Abiltayev A.M., Tashtemirova O.G., Shukimbayeva A.M., Makhmutova A.M.* Neurological complications in extracorporeal membrane oxygenation: risk factors for the development of acute cerebrovascular events // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 27-35. *doi 10.34689/SH.2025.27.3.003*

**Резюме**

# НЕВРОЛОГИЧЕСКИЕ ОСЛОЖНЕНИЯ ПРИ ЭКСТРАКОРПОРАЛЬНОЙ МЕМБРАННОЙ ОКСИГЕНАЦИИ: ФАКТОРЫ РИСКА РАЗВИТИЯ ОСТРОГО НАРУШЕНИЯ МОЗГОВОГО КРОВООБРАЩЕНИЯ

**Даурен А. Антикеев[1], https://orcid.org/0009-0007-0934-6509**

**Әйгерім А. Оразхан[2], https://orcid.org/0009-0006-4158-899X**

**Лейла Б. Темирбулатова[2], https://orcid.org/0009-0008-0494-0100**

**Диана Ж. Бейсимбаева[2], https://orcid.org/0009-0009-6340-9798**
**Аскар М. Абильтаев[1,2], https://orcid.org/0000-0003-4127-2347**
**Ольга Г. Таштемирова[2], https://orcid.org/0000-0002-7537-2808**
**Айнур М. Шукимбаева[2], https://orcid.org/0000-0002-4240-3663**
**Асель М. Махмутова[2], https://orcid.org/0009-0005-3597-8409**
**[1] КГП на ПХВ «Павлодарский Областной Кардиологический Центр», г. Павлодар, Республика Казахстан;**
**[2.] Павлодарский филиал НАО «Медицинский Университет города Семей», г.Павлодар, Республика Казахстан.**

**Введение.** Болезни системы кровообращения остаются ведущей причиной смертности и инвалидности в мире, включая Казахстан. Экстракорпоральная мембранная оксигенация (ЭКМО) является спасательным методом лечения при тяжелой сердечно-легочной недостаточности, однако её применение связано с высоким риском осложнений, включая острые неврологические расстройства, такие как инсульты.

**Цель исследования.** Определить частоту острых нарушений мозгового кровообращения (ОНМК), включая ишемические и геморрагические инсульты, у пациентов, получающих экстракорпоральную мембранную оксигенацию (ЭКМО), а также выявить ключевые факторы риска их развития в условиях клинической практики Казахстана.

**Методы.** Проведен ретроспективный анализ данных 92 пациентов, госпитализированных в Павлодарский областной кардиологический центр с 2015 по 2024 годы. Все пациенты находились на ЭКМО в интраоперационный или послеоперационный периоды. Пациенты были разделены на две группы: с наличием инсульта (ОНМК) и без него. Анализ включал оценку демографических данных, сопутствующих заболеваний, особенностей операций и параметров послеоперационного периода. Данные для исследования были получены на основе ретроспективного анализа медицинской документации пациентов, включая истории болезни и электронные базы данных кардиоцентра. Статистический анализ проводился на программе IBM™ SPSS 26.0 (IBM Corporation, Armonk, NY 2019).

**Результаты.** Неврологические осложнения, включая инсульты, были выявлены у 31,5% пациентов, подключенных к ЭКМО. Основными факторами риска стали гипертония, курение и наличие инсульта в анамнезе. Также установлено, что женщины и пациенты с низкой фракцией выброса левого желудочка были более подвержены риску. Средняя продолжительность госпитализации у пациентов с инсультами составила 30,2 дня, что превышает аналогичный показатель у пациентов без инсультов (25,6 дня).

**Выводы.** Инсульты остаются значительным осложнением у пациентов на ЭКМО, что требует разработки специфических профилактических мер. Выявленные факторы риска, такие как гипертония, курение и инсульт в анамнезе, должны быть учтены при разработке клинических рекомендаций. Настоящее исследование подчеркивает необходимость дальнейших масштабных исследований для улучшения диагностики и профилактики инсультов у пациентов на ЭКМО.

***Ключевые слова:*** *экстракорпоральная мембранная оксигенация, острое нарушение мозгового кровообращения, неврологические осложнения, факторы риска инсульта.*

***Для цитирования:***

*Антикеев Д.А., Оразхан Ә.А., Темирбулатова Л.Б., Бейсимбаева Д.Ж., Абильтаев А.М., Таштемирова О.Г., Шукимбаева А.М., Махмутова А.М.* Неврологические осложнения при экстракорпоральной мембранной оксигенации: факторы риска развития острого нарушения мозгового кровообращения // Наука и Здравоохранение. 2025. Т.27 (3), С. 27-35. doi: 10.34689/SH.2025.27.3.003

**Түйіндеме**

# ЭКСТРАКОРПОРАЛЬДЫ МЕМБРАНАЛЫҚ ОКСИГЕНАЦИЯ КЕЗІНДЕГІ НЕВРОЛОГИЯЛЫҚ АСҚЫНУЛАР: МИ ҚАН АЙНАЛЫМЫНЫҢ ЖЕДЕЛ БҰЗЫЛУЫНЫҢ ДАМУЫНА ӘКЕЛЕТІН ТӘУЕКЕЛ ФАКТОРЛАРЫ

**Даурен А. Антикеев[1], https://orcid.org/0009-0007-0934-6509**
**Әйгерім А. Оразхан[2], https://orcid.org/0009-0006-4158-899X**
**Лейла Б. Темирбулатова[2], https://orcid.org/0009-0008-0494-0100**
**Диана Ж. Бейсимбаева[2], https://orcid.org/0009-0009-6340-9798**
**Аскар М. Абильтаев[1,2], https://orcid.org/0000-0003-4127-2347**
**Ольга Г. Таштемирова[2], https://orcid.org/0000-0002-7537-2808**
**Айнур М. Шукимбаева[2], https://orcid.org/0000-0002-4240-3663**
**Асель М. Махмутова[2], https://orcid.org/0009-0005-3597-8409**

**[1] ҚМК ШЖҚ «Павлодар облыстық кардиология орталығы», Павлодар қ., Қазақстан Республикасы;**
**[2] Семей қаласының мемлекеттік медицина университетінің Павлодар филиалы, Павлодар қ., Қазақстан Республикасы.**

**Кіріспе**. Қан айналым жүйесінің аурулары әлем бойынша, соның ішінде Қазақстанда да, өлім мен мүгедектіктің басты себебі болып қала береді. Экстракорпоральды мембраналық оксигенация (ЭКМО) ауыр жүрек-өкпе жетіспеушілігін емдеуде құтқару әдісі ретінде қолданылады, бірақ оны қолдану осындай асқынулардың жоғары тәуекелімен байланысты, соның ішінде инсульт сияқты жедел неврологиялық бұзылулар.

**Зерттеудің мақсаты.** Экстракорпоральды мембраналық оксигенация (ЭКМО) алатын науқастарда ми қан айналымының жедел бұзылуларын (МҚАЖБ), соның ішінде ишемиялық және геморрагиялық инсульттердің жиілігін анықтау, сондай-ақ Қазақстан клиникалық тәжірибесінде олардың дамуына әсер ететін негізгі тәуекел факторларын анықтау.

**Әдістері.** 2015-2024 жылдар аралығында Павлодар облыстық кардиологиялық орталығына жатқызылған 92 науқастың деректеріне ретроспективті талдау жүргізілді. Барлық науқастарға операция кезінде немесе операциядан кейін экстракорпоралды мембраналық оксигенация (ЭКМО) қолданылды. Науқастар ми қан айналымының жедел бұзылулары (МҚАЖБ) бар және жоқ топтарға жіктелінді. Жүргізілген талдау демографиялық көрсеткіштерді, қосалқы ауруларды, операцияның ерекшеліктерін және операциядан кейінгі кезеңнің параметрлерін қамтыды. Зерттеу деректері науқастардың медициналық құжаттарының ретроспективті талдауы негізінде алынды, оған ауру тарихтары және кардиоорталықтың электрондық деректер базасы кірді. Статистикалық талдау IBM™ SPSS 26.0 (IBM Corporation, Armonk, NY 2019) бағдарламасында жүргізілді.

**Нәтижесі.** ЭКМО-ға қосылған науқастардың 31,5%-ында инсультті қоса алғанда, неврологиялық асқынулар анықталды. Негізгі тәуекел факторлары ретінде гипертония, темекі шегу және инсульттің анамнезде болуы анықталды. Сонымен қатар, әйелдер және сол жақ қарыншаның төмен фракциялық шығарымы бар науқастар тәуекелге бейім екені анықталды. Инсультпен ауыратын науқастардың орташа стационарда болу ұзақтығы 30,2 күн болды, бұл инсультсіз науқастарға қарағанда (25,6 күн) жоғары көрсеткіш болды.

**Қорытынды.** Инсульт ЭКМО-ға қосылған науқастарда маңызды асқыну болып қала береді, бұл ерекше алдын алу шараларын әзірлеуді талап етеді. Гипертония, темекі шегу және инсульттің анамнезде болуы сияқты анықталған тәуекел факторлары клиникалық ұсынымдарды әзірлеу кезінде ескерілуі керек. Бұл зерттеу ЭКМО-ға қосылған науқастарда инсультті диагностикалау мен алдын алуды жақсарту үшін әрі қарай кең ауқымды зерттеулердің қажеттілігін атап өтеді.

***Түйін сөздер:*** *экстракорпоральды мембраналық оксигенация, ми қан айналымының жедел бұзылуы, неврологиялық асқынулар, инсульттің тәуекел факторлары.*

***Дәйексөз үшін:***

*Антикеев Д.А., Оразхан Ә.А., Темирбулатова Л.Б., Бейсимбаева Д.Ж., Абильтаев А.М., Таштемирова О.Г., Шукимбаева А.М., Махмутова А.М.* Экстракорпоральды мембраналық оксигенация кезіндегі неврологиялық асқынулар: ми қан айналымының жедел бұзылуының дамуына әкелетін тәуекел факторлары // Ғылым және Денсаулық. 2025. Т.27 (3), Б. 27-35. doi: 10.34689/SH.2025.27.3.003

**Introduction**

Globally, disorders of the circulatory system (CSD) persist as the foremost contributor to premature mortality and loss of functional capacity. Epidemiological data from the WHO identify cardiovascular diseases (CVD) as the causative factor in 32% of deaths classified as premature [13]. In Kazakhstan, the situation is similar: the incidence of cardiovascular diseases remains high.

As reported in the 2023 statistical yearbook of the Ministry of Health of the Republic of Kazakhstan (MOH RK), the incidence rates per 100,000 population were 657.5 for coronary artery disease, 122.1 for acute myocardial infarction, and 425.0 for cerebrovascular diseases. The overall mortality rate from CSD in 2023 was 155.47 per 100,000 population [10].

The number of patients with severe cardiac dysfunction continues to rise, necessitating the use of advanced supportive therapies, such as extracorporeal membrane oxygenation (ECMO) [7].

Extracorporeal membrane oxygenation (ECMO) is an invasive method used to oxygenate blood in cases of severe acute respiratory failure when conventional treatments prove ineffective [2]. Despite its high efficacy, ECMO is associated with a range of complications.

Studies indicate that 30% to 60% of ECMO patients experience complications, including acute neurological disorders such as ischemic and hemorrhagic strokes [13, 6]. Thrombus formation in 10–15% of patients may lead to strokes in 2–6% of cases. Stroke in the context of ECMO can arise from various factors related to both procedural specifics and patient condition. The primary mechanisms of stroke development include hypoxia, thrombosis, and bleeding [4, 15].

To date, there are no publications in Kazakhstan describing the incidence of strokes and other complications among patients undergoing ECMO therapy. This underscores the need for the present study, which aims to investigate the frequency of strokes in ECMO patients and identify risk factors for their occurrence within the Kazakhstani clinical setting. Based on the interplay of unstable hemodynamics, coagulopathies, ECMO circuit-related factors, and the epidemiological burden of CSD in

Kazakhstan, we hypothesize that the risk of stroke in this patient population may be elevated, warranting in-depth analysis and the development of tailored clinical guidelines for Kazakhstan. The primary aim of this study was to assess the frequency of strokes and identify associated risk factors in adult ECMO patients through a retrospective analysis of medical records from cardiac care facilities in the Pavlodar Region.

**Materials and Methods**

**Study Population**

The study included 92 patients hospitalized at the Pavlodar Regional Cardiology Center for cardiac indications between 2015 and 2024. Participants were aged over 18 years and underwent conservative treatment and cardiac surgery with subsequent ECMO initiation preoperatively, intraoperatively, or postoperatively.

Patients were selected from the standardized electronic medical records database "IMIS" (Integrated Medical Information System), which contains hospitalization data. Inclusion criteria were confirmed for ECMO initiation for cardiac support. Selection was based on age, ECMO use, and alignment with ICD-10 codes (International Classification of Diseases, 10th Revision) for relevant conditions (Figure 1).

The control group comprised patients with confirmed ECMO initiation but no subsequent acute cerebrovascular accident (ACVA). This design enabled comparison of outcomes between patients with stroke and those without, facilitating identification of ECMO-associated risk factors.

The definition of ACVA (acute cerebrovascular accident) followed the American Neurological Association criteria: an acute condition caused by a sudden reduction or cessation of blood supply to specific brain regions, leading to neurological deficits [1]. ACVA includes two main types: ischemic stroke (due to vascular occlusion and insufficient blood flow) and hemorrhagic stroke (resulting from vessel rupture and cerebral hemorrhage) [8].

For analysis, two groups were compared:

1.Group 1 included patients with ACVA occurring after ECMO initiation, documented in medical records under ICD-10 codes I60–I64.

2.Group 2 consisted of patients receiving ECMO without ACVA development.

Baseline demographic data included age, sex, body mass index (BMI), and comorbidities.

Intraoperative parameters assessed were surgery type and duration, cardiopulmonary bypass time, aortic cross-clamping duration, and intraoperative blood loss volume. Postoperative variables included glomerular filtration rate (GFR), biochemical parameters, ECMO duration, intensive care unit (ICU) stay length, total hospitalization duration, cardiac arrest episodes, type and volume of transfused blood components (e.g., packed red blood cells, fresh frozen plasma (FFP), and treatment outcomes.

Data were obtained through retrospective analysis of medical records, including patient histories and the cardiology center's electronic database.

Statistical analysis was performed using IBM™ SPSS 26.0 (IBM Corporation, Armonk, NY, 2019).

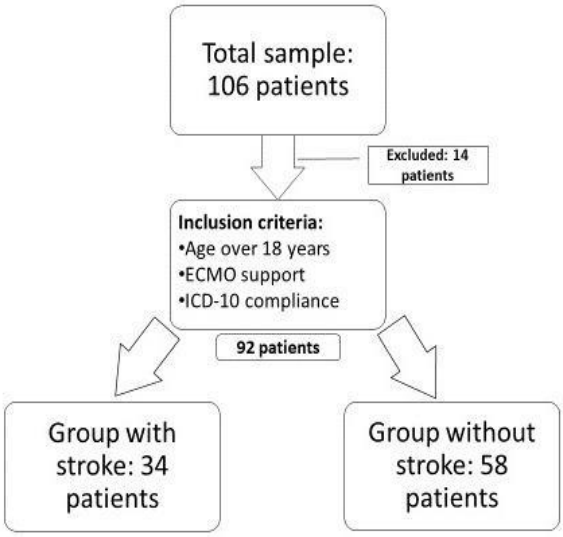



**Figure 1. Study population enrollment diagram.**

**Results**

The study included 92 patients hospitalized with cardiovascular and respiratory pathologies at the Pavlodar Regional Cardiology Center between 2015 and 2024. Of these, 31.52% (n=29) were diagnosed with neurological deficits, including coma (Figure 2).

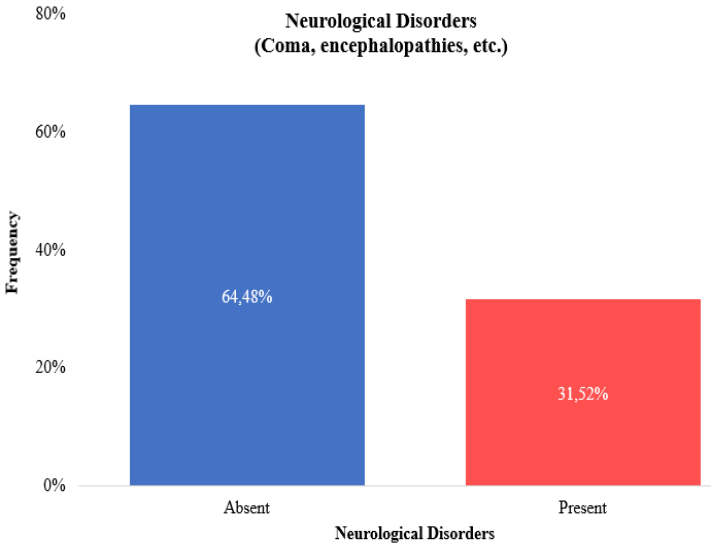



**Figure 2. Distribution of Patients by Groups with Neurological Deficits.**

*Demographic Characteristics*

Males accounted for 59.8% (n=55) of the total cohort, while females represented 40.2% (n=37). Age characteristics of patients with and without acute cerebrovascular accident (ACVA) are presented in Table 1. Statistically significant gender differences were observed in ACVA patients (p=0.038). However, age, arterial hypertension levels, coronary artery disease, and heart failure severity showed no significant intergroup differences (p>0.05 for all variables).

*Table 1.*

**Preoperative Parameters.**

| Factors | with ACVA (n=29) | non-ACVA (n=63) | p-value |
|---|---|---|---|
| Female (%) | 44.4 | 55.6 | |
| Male (%) | 23.6 | 76.4 | 0.038 |
| Age (mean) | 57.55 | 59.26 | 0.545 |
| IHD (%) | 29.7 | 70.3 | 0.572 |
| CABG/Stent history (%) | 15.8 | 84.2 | 0.063 |
| DM (%) | 20 | 80 | 0.172 |
| HTN (%) | 31.1 | 68.9 | 0.856 |
| CVA (%) | 61.8 | 38.2 | 0.001 |
| COPD (%) | 26.7 | 73.3 | 0.662 |
| CHF (%) | 29.2 | 70.8 | 0.469 |
| LVEF (%) | 50.31 | 49.93 | 0.777 |
| MAU (%) | 25 | 75 | 0.682 |
| Smoking (smokers, %) | 12 | 88 | 0.004 |
| CKD (%) | 30.4 | 69.6 | 0.866 |

*The following standard medical abbreviations are used throughout the text: ischemic heart disease (IHD), coronary artery bypass grafting (CABG), diabetes mellitus (DM), hypertension (HTN), cerebrovascular accident (CVA), chronic obstructive pulmonary disease (COPD), chronic heart failure (CHF), left ventricular ejection fraction (LVEF), microalbuminuria (MAU), and chronic kidney disease (CKD). All abbreviations are expanded at their first occurrence in both abstract and main text.*

*Neurological Complications*

Table 1 demonstrates that among patients with neurological deficits, 61.8% had hypertensive disease with ACVA, compared to only 38.2% in the non-ACVA group (p=0.001). Smoking emerged as a statistically significant factor (p=0.004), being more prevalent among patients with neurological deficits. Similarly, statistically significant differences (p<0.001) were observed between ACVA (61%) and non-ACVA (38.2%) groups regarding patients with a history of prior cerebrovascular events.

No statistically significant differences were found in hospitalization duration. However, non-ACVA patients had shorter hospital stays (mean 25.6 days) compared to ACVA patients (mean 30.2 days). ECMO support duration was also shorter for non-ACVA patients (13.9 days vs 17.6 days), though this difference lacked statistical significance (Figure 3).

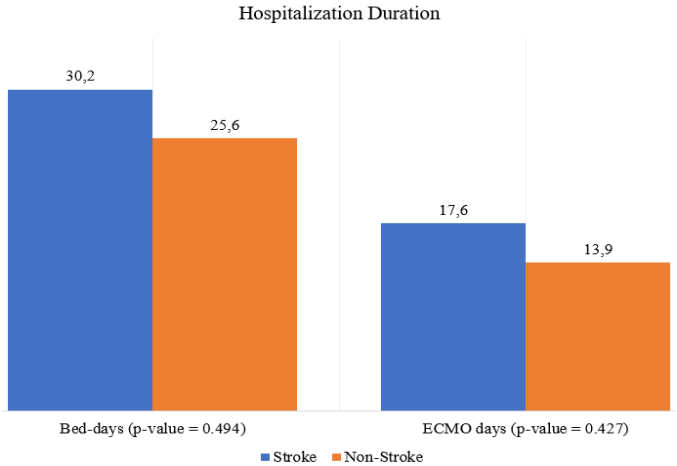



**Figure 3. Duration of Hospital Stay.**

*Postoperative Outcomes*

Statistically significant differences were observed in platelet levels, with lower values being more pronounced in the non-CVA group (p=0.034). The incidence of cardiopulmonary resuscitation (CPR) was significantly higher (p=0.040) in patients who developed CVA. No significant intergroup differences were found in: Creatinine and urea levels, ALT concentrations, complications (acute left ventricular failure, sepsis, respiratory failure), bleeding events, blood component transfusions. Mortality rates were notably high in both groups: 75.9% in CVA patients vs 65.1% in non-CVA patients (Table 2).

*Table 2.*

**Neurological Complications.**

| Factors | with ACVA (n=29) | non-ACVA (n=63) | p-value |
|---|---|---|---|
| Thrombocytopenia (%) | 35.5 | 64.5 | 0.034 |
| Creatinine (mean) | 245.1 | 188.4 | 0.073 |
| Urea (mean) | 19 | 14.7 | 0.084 |
| ALT (mean) | 415.2 | 414.8 | 0.999 |
| ALVF (%) | 36.4 | 63.6 | 0.460 |
| Sepsis/Infection (%) | 42.9 | 57.1 | 0.327 |
| Respiratory failure (%) | 25.7 | 74.3 | 0.345 |
| Packed red blood cells (mean) | 26.8 | 23.4 | 0.559 |
| FFP (mean) | 33 | 18.3 | 0.199 |
| Presence of bleeding (%) | 27.9 | 72.1 | 0.490 |
| Resuscitation (CPR, %) | 41.1 | 19 | 0.040 |
| Outcome (fatal, %) | 75.9 | 65.1 | 0.306 |
| *The following standard medical abbreviations are used throughout the text: alanine aminotransferase (ALT), acute left ventricular failure (ALVF), fresh frozen plasma (FFP), and cardiopulmonary resuscitation (CPR).* | | | |

We developed a decision tree model to predict the probability of cerebrovascular accident (CVA) occurrence based on risk factors using the CHAID (Chi-squared Automatic Interaction Detector) method.

The resulting model is presented in Figure 4. The decision tree contained 5 terminal nodes, whose characteristics are detailed in Table 3.

The decision tree analysis identified male sex, no history of ACVA, and left ventricular ejection fraction (LVEF) >48% as protective factors associated with below-average CVA risk (reference: 100.0%). Elevated risk profiles emerged for patients with reduced LVEF, female sex, or prior ACVA. The model achieved 79.3% sensitivity, 77.8% specificity, and 78.3% ± 4.3% overall predictive accuracy for ACVA occurrence.

*Survival Outcomes*

Kaplan-Meier analysis demonstrated that patients with neurological deficits had significantly longer mean survival time (44.11 ± 8.69 days, 95% CI: 27.07-61.16) compared to those without deficits (35.24 ± 4.33 days, 95% CI: 26.76-43.73). Notably, median survival times showed an inverse pattern at 24 days (deficit group) versus 28 days (non-deficit group).

**Discussion**

Our study revealed that 31.52% of patients on extracorporeal membrane oxygenation (ECMO) experienced acute cerebrovascular accidents (ACVA), which is consistent with international studies reporting complication rates ranging from 20% to 50% [15, 13]. Patients who underwent cardiopulmonary resuscitation (CPR) prior to ECMO initiation had a higher risk of ACVA (p=0.040), highlighting the role of hypoxia and hemodynamic instability. Statistically significant risk factors also included a history of ACVA (p<0.001) and smoking (p=0.004) [14]. These findings align with international research and emphasize the need to optimize approaches for the prevention and early diagnosis of neurological complications in ECMO patients, particularly in the context of Kazakhstani clinical practice [3, 10].

ACVA during ECMO may develop due to multiple factors related to both the procedure itself and the patient's condition [11]. The underlying mechanism involves three primary processes: hypoxia, thrombosis, and hemorrhage [14, 6].

Our analysis showed that patients with prior CPR (before ECMO initiation) had a higher incidence of ACVA (p=0.040), suggesting that hypoxia and hemodynamic instability contribute to stroke risk in ECMO patients [14]. Patients requiring ECMO are already in critical condition with severe cardiopulmonary dysfunction [9], which itself may impair cerebral perfusion.

Among comorbidities and risk factors, hypertension (p=0.001), prior ACVA (p<0.001), and smoking (p=0.004) were significantly more prevalent in the ACVA group. ECMO cannulation and maintenance may also cause blood pressure fluctuations, altered perfusion, and flow dynamics, potentially exacerbating cerebral hypoxia and increasing ischemic stroke risk. Additionally, ECMO requires systemic anticoagulation (e.g., heparin) to prevent circuit thrombosis [12]. Microthrombi may form on the oxygenator membrane or cannulae and embolize to cerebral vessels, causing ischemic stroke [14].

Statistically significant laboratory findings included lower platelet counts in non-ACVA patients post-ECMO initiation (p=0.034), which may increase bleeding risk, including intracranial hemorrhage—a particular concern during anticoagulation therapy.

Our study substantially fills knowledge gaps regarding acute neurological complications (e.g., stroke) in ECMO patients within Kazakhstani clinical practice. While international studies confirm high ECMO-associated complication rates, including stroke, such data were previously unavailable for Kazakhstan. Our results demonstrate that 31.52% of patients developed neurological deficits, underscoring the significant stroke risk in this population. These findings emphasize the need for systematic investigation of ECMO complications in local practice and may inform preventive strategies to reduce stroke incidence among ECMO-supported patients.

This study highlights the necessity of evaluating stroke and other complications in Kazakhstani ECMO patients [15]. We confirmed that this population faces high risk of acute neurological events [5]. Crucially, we identified key stroke risk factors (hypertension, smoking, and prior stroke),

corroborating international data [14]. These results advance understanding of ECMO-related pathophysiology and enable development of targeted screening and prevention tools [2]. Thus, our research enhances clinical insights and contributes to evidence-based guidelines for stroke prevention in Kazakhstani ECMO patients.

Our findings have immediate clinical implications. Male sex, no prior ACVA, and left ventricular ejection fraction (LVEF) >48% were associated with lower ACVA risk compared to the overall cohort. Conversely, reduced LVEF, female sex, and prior ACVA increased risk above the cohort average. These risk factors may guide early diagnostic and preventive protocols for ECMO patients. Clinicians can use these data to improve complication prediction and timely intervention, potentially reducing stroke incidence. Implementing such recommendations in clinical practice may enhance treatment outcomes, survival, and long-term neurological recovery. Thus, our results stress the importance of rigorous monitoring and management of these risk factors during ECMO therapy.

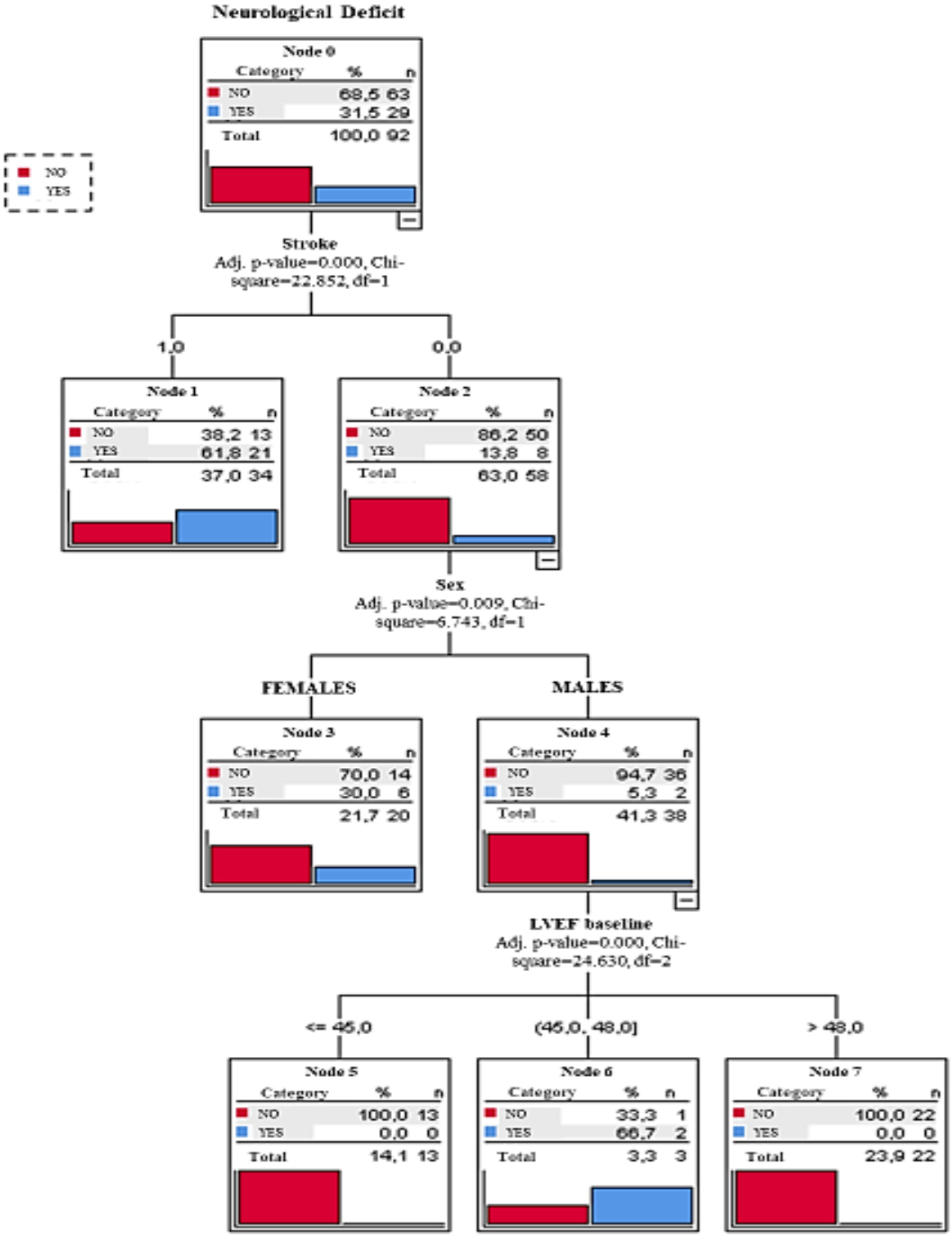



**Figure 4. Decision Tree Analysis**

*Table 3.*

**Characteristics of Decision Tree Terminal Nodes.**

| № | Presence of Risk Factors | Number of Patients | | Response Rate, % | Index, % |
|---|---|---|---|---|---|
| | | Total | With ACVA | | |
| 7 | No history of ACVA; Male; LVEF > 48 | 22 | 22 | 100.0% | 146.0% |
| 5 | No history of ACVA; Male; LVEF < 45 | 13 | 13 | 100.0% | 146.0% |
| 3 | No history of ACVA; Female | 20 | 14 | 70.0% | 102.2% |
| 1 | Patients with a history of ACVA | 34 | 13 | 38.2% | 55.8% |
| 6 | No history of ACVA; Male; LVEF 45–48 | 3 | 1 | 33.3% | 48.7% |

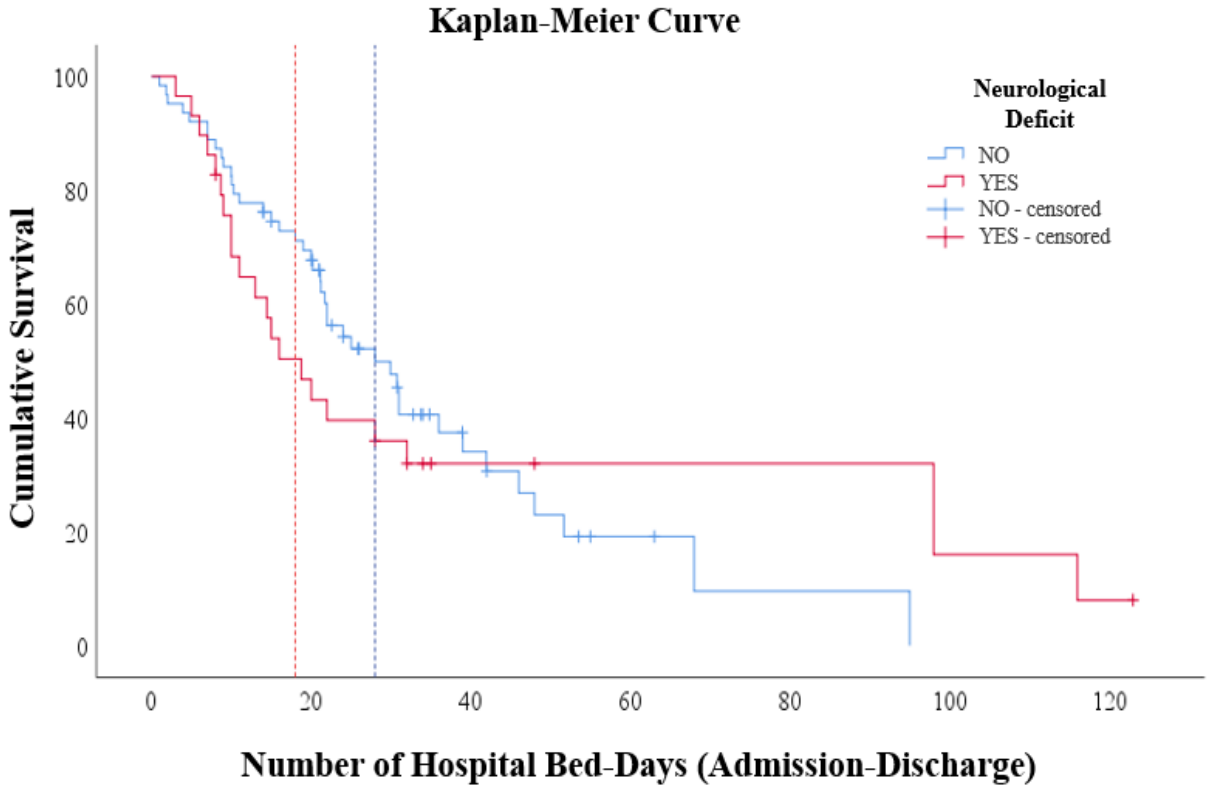



**Figure 5. Kaplan-Meier Survival Curve**

**Study Limitations**

This study has several limitations, including its retrospective design, which restricts causal inference between identified risk factors and stroke outcomes due to unaccounted confounders (e.g., medication regimens, genetic factors). The modest sample size (n=92) may further limit statistical power, necessitating cautious interpretation of the results. These constraints highlight the need for larger, prospective multicenter studies to validate and expand upon our findings.

**Recommendations for Future Research**

To address these limitations and advance our understanding of stroke risk factors in ECMO patients, we recommend prospective multicenter studies with larger cohorts to reduce random variability and enhance statistical reliability. Future investigations should incorporate comprehensive biomarker profiling, genetic testing, and detailed pharmacotherapeutic monitoring to better evaluate their contributions to stroke pathogenesis. Such an approach would provide more accurate insights into the underlying mechanisms of cerebrovascular complications and identify targeted preventive strategies for this high-risk population.

**Consistency with Existing Literature**

Our findings align with global scientific evidence highlighting elevated stroke risk in ECMO patients. Previous studies report 2-6% stroke incidence among ECMO recipients, primarily attributed to hypoxemia, thromboembolism, and bleeding complications [1, 15]. While confirming these established risk factors, our data further identify hypertension and smoking as significant contributors to stroke development. These results advance the field by enabling more personalized stroke prevention strategies for ECMO patients, both in Kazakhstan and other regions with comparable epidemiological profiles.

**Conclusion**

Cardiovascular diseases remain the leading cause of global mortality, including in Kazakhstan. While extracorporeal membrane oxygenation (ECMO) is an effective life-support modality, it carries significant complication risks, particularly stroke. Our study of 92 patients revealed neurological disorders in 31.5% of cases, underscoring the substantial stroke risk associated with ECMO therapy.

Key risk factors identified—hypertension, smoking, and prior stroke history—provide actionable targets for improved

screening and prevention protocols. Although limited by its retrospective design and modest sample size, these findings lay crucial groundwork for future large-scale prospective studies.

These findings provide clinically relevant data to refine stroke prediction models and optimize management strategies, which may lead to a reduction in cerebrovascular complications and better outcomes for ECMO patients in Kazakhstan.

***Literature:***

1. “Stroke Coding guide for CritiCal Care Coding”. CPT codes © 2006 American Medical Association. URL:https://www.aan.com/globals/axon/assets/2858.pdf

2. *Acharya Prakash, Jakobleff William A., Forest Stephen J., Chinnadurai Thiru; Mellas Nicolas†, Patel Snehal R.; Kizer Jorge R., Billett, Henny H., Goldstein Daniel J., Jorde Ulrich P., Saeed Omar.* Fibrinogen Albumin Ratio and Ischemic Stroke During Venoarterial Extracorporeal Membrane Oxygenation. ASAIO Journal 66(3):p 277-282, March 2020.

3. *Akshulakov S.K., Adil'bekov E.B., Ahmetzhanova Z.B., Meduhanova S.G.* Organizacija i sostojanie insul'tnoj sluzhby Respubliki Kazahstan po itogam 2016 goda. Nejrohirurgiya i nevrologiya Kazakhstana. 2018. №1 (50). URL: https://cyberleninka.ru/article/n/organizatsiya-i-sostoyanie-insultnoy-sluzhby-respubliki-kazahstan-po-itogam-2016-goda [accessed: 12.12.2024]

4. *Lorusso Roberto, Barili Fabio, Mauro Michele Di, Gelsomino Sandro, Parise Orlando, Rycus Peter, Maessen Jos, Mueller Thomas, et al.* In-Hospital Neurologic Complications in Adult Patients Undergoing Venoarterial Extracorporeal Membrane Oxygenation: Results From the Extracorporeal Life Support Organization Registry. Critical Care Medicine 44(10):p e964-e972, October 2016.

5. Lorusso Roberto, Gelsomino Sandro, Parise Orlando, Di Mauro Michele, Barili Fabio, Geskes Gijs, Vizzardi Enrico, Rycus Peter T., et al. Neurologic Injury in Adults Supported With Veno-Venous Extracorporeal Membrane Oxygenation for Respiratory Failure: Findings From the Extracorporeal Life Support Organization Database. Critical Care Medicine. 45(8):p 1389-1397, August 2017.

6. *Mateen F.J., Muralidharan R., Shinohara R.T., Parisi J.E, Schears G.J., Wijdicks E.F.* Neurological injury in adults treated with extracorporeal membrane oxygenation. Arch Neurol. 2011;68(12):1543-1549.

7. *Omar H.R., Mirsaeidi M., Shumac J., Enten G., Mangar D., Camporesi E.M.* Incidence and predictors of ischemic cerebrovascular stroke among patients on extracorporeal membrane oxygenation support. J Crit Care. 2016 Apr;32:48-51.

8. *Salvadori E., Papi G., Insalata G., Rinnoci V., Donnini I., Martini M., Falsini C., Hakiki B., Romoli A., Barbato C. et al.* Comparison between Ischemic and Hemorrhagic Strokes in Functional Outcome at Discharge from an Intensive Rehabilitation Hospital. Diagnostics. 2021; 11(1):38.

9. *Santos A., Silva P., Sprone F.; Silva B.C.; Mariani A. et al.* Indicações e contraindicações para o uso da ECMO em complicações do COVID-19 / Indications and contraindications for the use of ECMO in complications of COVID-19. Brazilian Journal of Health Review, [S. l.], v. 5, n. 2, p. 4258–4261, 2022.

10. Statisticheskii sbornik «Zdorov'e naseleniya RK i deyatel'nost' organizatsii zdravookhraneniya v 2023 godu». - Astana. 2024. 393p. URL:https://www.nrchd.kz/files/%D0%B4%D0%BE%D0%BA%D1%83%D0%BC%.pdf [accessed: 12.12.2024]

11. *Sutter R., Tisljar K., Marsch S.* Acute Neurologic Complications During Extracorporeal Membrane Oxygenation: A Systematic Review. Crit Care Med. 2018 Sep. 46(9):1506-1513.

12. *Tang S., Xu L., Li H., Wu Z., Wen Q.* Anticoagulants in adult extracorporeal membrane oxygenation: alternatives to standardized anticoagulation with unfractionated heparin. Eur J Clin Pharmacol. 2023. 79(12):1583-1594.

13. World Health Organization. (2020). Cardiovascular diseases (CVDs). Retrieved from URL:https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)

14. *Xie A., Lo P., Yan T.D., Forrest P.* Neurologic Complications of Extracorporeal Membrane Oxygenation: A Review. J Cardiothorac Vasc Anesth. 2017. Oct;31(5):1836-1846.

15. *Zhang H., Xu J., Yang X., Zou X., Shu H., Liu Z., Shang Y.* Narrative Review of Neurologic Complications in Adults on ECMO: Prevalence, Risks, Outcomes, and Prevention Strategies. Front Med (Lausanne). 2021 Sep 29;8:713333. PMID: 34660625; PMCID: PMC8513760.

**Corresponding author:**
**Beisimbayeva Diana Zhanatovna** – Intern of Pavlodar Branch of NCJSC "Semey Medical University", Pavlodar, Kazakhstan/
**Postal code:** 140011
**E-mail:** beisimbayevad@gmail.com
**Phone:** +7 707 678-54 92

Received: 23 January 2025 / Accepted: 29 May 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2025.27.3.004***

***UDC 616.379-008.64:616-056.52:616.12-005:612.515.2-07-084***

This work is licensed under a Creative Commons Attribution 4.0 International License

# THE EFFECT OF REPAGLINIDE AND METFORMIN ON EXTERNAL RESPIRATORY FUNCTION IN PATIENTS WITH DIABETES AND ISCHEMIC HEART DISEASE ASSOCIATED WITH OBESITY

**Saule B. Zhautikova[1], https://orcid.org/0009-0000-5712-7369**

**Nailya M. Urazalina[2], https://orcid.org/0000-0003-0200-1763**

**Diana B. Tolubayeva[3], https://orcid.org/0000-0003-3119-7814**

**[1] NCJSC «Karaganda Medical University», Karaganda, the Republic of Kazakhstan;**
**[2] NCJSC «Semey Medical University», Semey, the Republic of Kazakhstan;**
**[3] Medical Center Hospital of the President,s affairs Administration of the Republic of Kazakhstan, Astana, the Republic of Kazakhstan.**

**Abstract**

**Introduction:** Over the past 20 years, numerous studies have examined the state of the bronchopulmonary system in type 2 diabetes mellitus (T2DM), but findings remain inconsistent. Some researchers report decreased external respiratory function (ERF) linked to metabolic shifts and disease complications, while others associate it with vascular pathology. There is also evidence of increased pulmonary ventilation in diabetes. The implementation of optimal glucose-lowering therapies to prevent complications, including pulmonary issues, remains a key concern in modern medicine.

**The aim of the study** is to evaluate the functional state of the external ventilation system in patients with type 2 diabetes mellitus in combination with coronary heart disease and obesity during treatment with repaglinide and metformin.

**Materials and Methods:** A 3–3.5-year observational study included 120 patients. The effect of repaglinide or metformin on patients with diabetes and concomitant diseases such as coronary heart disease and obesity has been studied. The data was analyzed using the following methods: computer spirometry and fiber-optic bronchoscopy.

**Results:** Patients with T2DM, especially those with IHD and obesity, showed both restrictive and obstructive pulmonary disorders, impaired gas exchange, and ventilation-perfusion mismatch. Repaglinide improved respiratory parameters, while metformin led to worsened spirometry indicators and increased bronchial resistance in most cases. Bronchoscopic findings confirmed nonspecific bronchial mucosal changes in 29.4% of patients.

**Conclusion:** Bronchopulmonary impairments in T2DM are primarily due to reduced ERF and increased bronchial resistance. Repaglinide appears more effective than metformin or gliclazide in improving respiratory function.

***Keywords:*** *type 2 diabetes mellitus (T2DM), type 2 diabetes mellitus (T2DM) combined with obesity, functional state of external respiration, computerized spirography, repaglinide, metformin.*

***For citation:***

Zhautikova S.B., Urazalina N.M., Tolubayeva D.B. The effect of repaglinide and metformin on external respiratory function in patients with diabetes and ischemic heart disease associated with obesity // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 36-41. *doi 10.34689/SH.2025.27.3.004*

**Резюме**

# ВЛИЯНИЕ РЕПАГЛИНИДА И МЕТФОРМИНА НА ФУНКЦИЮ ВНЕШНЕГО ДЫХАНИЯ У ПАЦИЕНТОВ С САХАРНЫМ ДИАБЕТОМ И ИШЕМИЧЕСКОЙ БОЛЕЗНЬЮ СЕРДЦА, АССОЦИИРОВАННОЙ С ОЖИРЕНИЕМ

**Сауле Б. Жаутикова[1], https://orcid.org/0009-0000-5712-7369**

**Найля М. Уразалина[2], https://orcid.org/0000-0003-0200-1763**

**Диана Б. Толубаева[3], https://orcid.org/0000-0003-3119-7814**

**[1] НАО «Медицинский университет Караганды», г. Караганда, Республика Казахстан;**
**[2] НАО «Медицинский университет Семей», г. Семей, Республика Казахстан;**
**[3] Больница Медицинского центра Управления делами Президента Республики Казахстан, г. Астана, Республика Казахстан.**

**Введение:** За последние 20 лет в многочисленных исследованиях изучалось состояние бронхолегочной системы при сахарном диабете 2 типа (СД2), но результаты остаются противоречивыми. Некоторые исследователи сообщают о снижении функции внешнего дыхания (ФВД), связанном с метаболическими сдвигами и осложнениями заболевания, в то время как другие связывают это с сосудистой патологией. Имеются также данные об усилении легочной вентиляции при сахарном диабете. Внедрение оптимальной сахароснижающей терапии для предотвращения осложнений, включая проблемы с легкими, остается ключевой задачей современной медицины.

**Целью исследования** является оценка функционального состояния системы внешней вентиляции легких у пациентов с сахарным диабетом 2 типа в сочетании с ишемической болезнью сердца и ожирением на фоне лечения репаглинидом и метформином.

**Материалы и методы:** В наблюдательном исследовании, продолжавшемся 3-3,5 года, приняли участие 120 пациентов. Было изучено влияние репаглинида или метформина на пациентов с сахарным диабетом и сопутствующими заболеваниями, такими как ишемическая болезнь сердца и ожирение. Полученные данные были проанализированы с использованием следующих методов: компьютерной спирометрии и волоконно-оптической бронхоскопии.

**Результаты:** У пациентов с СД2, особенно с ИБС и ожирением, наблюдались как рестриктивные, так и обструктивные заболевания легких, нарушение газообмена и несоответствие вентиляции и перфузии. Репаглинид улучшал показатели дыхания, в то время как метформин в большинстве случаев приводил к ухудшению показателей спирометрии и повышению бронхиального сопротивления. Результаты бронхоскопии подтвердили неспецифические изменения слизистой оболочки бронхов у 29,4% пациентов.

**Заключение:** Бронхолегочные нарушения при СД2 в первую очередь обусловлены снижением ФВД и повышением бронхиального сопротивления. Репаглинид, по-видимому, более эффективен в улучшении дыхательной функции, чем метформин или гликлазид.

***Ключевые слова:*** *сахарный диабет 2 типа (СД2), сахарный диабет 2 типа (СД2) в сочетании с ожирением, функциональное состояние внешнего дыхания, компьютерная спирография, репаглинид, метформин.*

***Для цитирования:*** *Жаутикова С.Б., Уразалина Н.М., Толубаева Д.Б.* Влияние Репаглинида и Метформина на функцию внешнего дыхания у пациентов с сахарным диабетом и ишемической болезнью сердца, ассоциированной с ожирением // Наука и Здравоохранение. 2025. Т.27 (3), С. 36-41. doi: 10.34689/SH.2025.27.3.004

**Түйіндеме**

# РЕПАГЛИНИД ПЕН МЕТФОРМИННІҢ СЕМІЗДІККЕ БАЙЛАНЫСТЫ ҚАНТ ДИАБЕТІ ЖӘНЕ КОРОНАРЛЫҚ АРТЕРИЯ АУРУЛАРЫ БАР НАУҚАСТАРДА ТЫНЫС АЛУ ФУНКЦИЯСЫНА ӘСЕРІ

**Сауле Б. Жаутикова[1], https://orcid.org/0009-0000-5712-7369**

**Найля М. Уразалина[2], https://orcid.org/0000-0003-0200-1763**

**Диана Б. Толубаева[3], https://orcid.org/0000-0003-3119-7814**

**[1] «Қарағанды медицина университеті» КЕАҚ, Қарағанды қ., Қазақстан Республикасы;**
**[2] «Семей медицина университеті» КЕАҚ, Семей қ., Қазақстан Республикасы;**
**[3] Қазақстан Республикасы Президенті Іс Басқармасының Медициналық орталығының ауруханасы, Астана қ., Қазақстан Республикасы.**

**Кіріспе:** соңғы 20 жыл ішінде көптеген зерттеулер 2 типті қант диабетіндегі (T2DM) бронхопульмональды жүйенің жағдайын зерттеді, бірақ нәтижелер сәйкес келмейді. Кейбір зерттеушілер метаболизмнің өзгеруіне және аурудың асқынуына байланысты сыртқы тыныс алу функциясының (ERF) төмендеуі туралы хабарлайды, ал басқалары оны тамырлы патологиямен байланыстырады. Сондай-ақ қант диабеті кезінде өкпенің желдетілуінің жоғарылағаны туралы деректер бар. Асқынулардың, соның ішінде өкпе ауруларының алдын алу үшін глюкозаны төмендететін оңтайлы емдеу әдістерін енгізу қазіргі медицинаның негізгі мәселесі болып қала береді.

**Зерттеудің мақсаты -** репаглинид пен метформинмен емдеу кезінде жүректің ишемиялық ауруы мен семіздікпен бірге 2 типті қант диабетімен ауыратын науқастарда сыртқы желдету жүйесінің функционалдық жағдайын бағалау.

**Материалдар мен әдістер:** 3-3, 5 жылдық бақылау зерттеуіне 120 пациент қатысты. Репаглинидтің немесе метформиннің қант диабеті және жүректің ишемиялық ауруы және семіздік сияқты қатар жүретін аурулары бар науқастарға әсері зерттелді. Деректер келесі әдістер арқылы талданды: компьютерлік спирометрия және талшықты-оптикалық бронхоскопия.

**Нәтижелер:** T2DM бар емделушілерде, әсіресе ЖИА және семіздікпен ауыратын науқастарда өкпенің шектеуші және обструктивті бұзылыстары, газ алмасуының бұзылуы және желдету-перфузия сәйкессіздігі байқалды. Репаглинид тыныс алу параметрлерін жақсартты, ал метформин спирометрия көрсеткіштерінің нашарлауына және көп жағдайда бронхқа төзімділіктің жоғарылауына әкелді. Бронхоскопиялық зерттеулер пациенттердің 29,4% - ында бронхтың шырышты қабығындағы спецификалық емес өзгерістерді растады.

**Қорытынды:** T2DM-Дегі Бронхопульмональды бұзылулар, ең алдымен, ERF төмендеуіне және бронхқа төзімділіктің жоғарылауына байланысты. Репаглинид метформинге немесе гликлазидке қарағанда тыныс алу қызметін жақсартуда тиімдірек болып көрінеді.

***Түйінді сөздер:*** *2 типті қант диабеті (T2DM), 2 типті қант диабеті (T2DM) семіздікпен, сыртқы тыныс алудың функционалды күйімен, компьютерленген спирографиямен, репаглинидпен, метформинмен біріктірілген.*

***Дәйексөз үшін:*** *Жаутикова С.Б., Уразалина Н.М., Толубаева Д.Б.* Репаглинид пен метформиннің семіздікке байланысты қант диабеті және коронарлық артерия аурулары бар науқастарда тыныс алу функциясына әсері // Ғылым және Денсаулық. 2025. Т.27 (3), Б. 36-41. doi: 10.34689/SH.2025.27.3.004

**Introduction**

With the development of diabetes and related diseases in diabetes, the study of the effect of metabolic control on the function of external respiration is relevant. Research in this area is mixed. Some studies find a link between hyperglycemia and respiratory disorders, while others do not [11, 6]. At the same time, it is obvious that the longer a person is ill, the worse the lung indicators are: their work and structure are changing. Below are some studies that evaluate how different forms of diabetes and its stages affect the lungs.

Scientists from Denmark have found that fasting sugar levels and certain biochemical parameters (CK1 and CK2) are associated with the development of diabetes [14]. In addition, high blood sugar levels are known to cause breathing problems [4]. Every 1% reduction in blood sugar (HbA1c) reduces the risk of cardiovascular disease by 4%. At the same time, scientists have not come to a consensus on how much sugar affects the complications of diabetes.

The choice of medications for diabetes is quite wide [9, 10, 11]. Although there are clear treatment regimens [8, 12], the real quality of patient care is still not up to par [5].

**The aim of the study** is to evaluate the functional state of the external ventilation system in patients with type 2 diabetes mellitus in combination with coronary heart disease and obesity during treatment with repaglinide and metformin.

**Materials and methods**

The study, which was conducted for 3-3.5 years, involved 120 patients with type 2 diabetes mellitus with a duration of 6 years or more.

The study was conducted over a 3-year period, from May 2022 to May 2025, at Karaganda Medical University, located in Karaganda, Kazakhstan. The research protocol was approved by the university's Ethics Committee (Protocol No. 5, dated May 19, 2022). All participants provided written informed consent prior to inclusion in the study. The university administration was informed about the course of the study and did not raise any objections to the publication of its results in open access.

The average age of patients with type 2 diabetes mellitus (T2DM) was 53.74 ± 2.48 years. The mean duration of diabetes was 9.2 ± 0.61 years. In patients with T2DM combined with ischemic heart disease (IHD) and obesity, the average age was 60.1 ± 2.98 years.

*Inclusion criteria:*

– Age between 30 and 70 years;

– Confirmed diagnosis of T2DM;

– Ability to provide written informed consent.

*Exclusion criteria:*

– Acute infectious diseases;

– Severe somatic or mental disorders;

– Refusal to participate in the study.

Subject of the study: The functional state of the external respiratory (pulmonary ventilation) system in these patients during treatment with repaglinide and metformin.

For the convenience of the study, the patients were divided into two main groups. There are 60 people with type 2 diabetes in the first group. They were divided into two groups of 30 people: some were treated with repaglinide (Novonorm, Novo Nordisk, Denmark), others with metformin (Glucophage, Merck Serono, France). The second group also had diabetics (with complications), and they were also divided into 2 subgroups: repaglinide treatment and metformin treatment.

The treatment was carried out with two drugs, according to Figure 1.

| Repaglinide | | Metformin |
|---|---|---|
| a dose of 0.5; 1 or 2 mg | | in tablets of 0.5, 0.85 g, 1 g |
| The drug is taken in a dose of 0.5; 1 or 2 mg before each meal; the daily dose is 6-10 mg, if necessary, it can be increased to 16 mg | | Metformin is taken with meals, gradually increasing its dose to the therapeutic dose. Subsequently, the drug is used 3 times a day at 500 mg or 2 times a day at 850 mg |

**Figure 1. Dosage and Drug Information.**

A good result of treatment is considered if fasting sugar is less than 7.8 mmol / l, and after eating - less than 10. After a while, HbA1c should decrease to less than 7.5%. Repaglinide helps produce insulin more naturally, is well tolerated, and allows for flexible sugar control.

Instrumental and functional research methods are used according to Table 1:

*Table 1.*

**Instrumental and functional research methods.**

| Parameter | Computer spirography | Fiberoptic bronchoscopic examination of the bronchi |
|---|---|---|
| Method | Automated spirometric breath analyzer “AD-02” | Fiberoptic bronchoscope BF-P20 (Olympus, Japan) |
| Testing conditions | Morning, seated position, fasting, quiet environment | Morning, fasting, under local anesthesia |
| Purpose | Bronchospasm detection [11, 19] | Assessment of bronchial mucosa and inflammation severity |
| Classification used | According to the “Guidelines for the Use of Spirographic Indicators” (1986) | Lemoine I.M. (2002) |

**Results**

According to the conducted research, two main results were obtained:

- People with type 2 diabetes have poorly ventilated lungs — this is due to the fact that gases do not pass well through the wall between the alveoli and capillaries.

- Patients with type 2 diabetes who also have coronary heart disease and obesity have both narrowing of the

airways and problems with lung stretching, which disrupts the supply of air and blood to the lungs.

Against the background of repaglinide treatment, there is a dynamic change in the indicators in patients with type 2 diabetes - the CTE increased by 11.5%, the CTE by 13.1%, the ventricular rate by 9.31%, the FGD50 by 11.83% and the FGD75 by 10.1%, while the Tiffno index decreased by 5.43% and the FGD75 by 23.7% ($p<0.05$). Also, there was a decrease in the indicators of the heart rate, except for the FGD and FGD50. The values are shown in Figure 2.

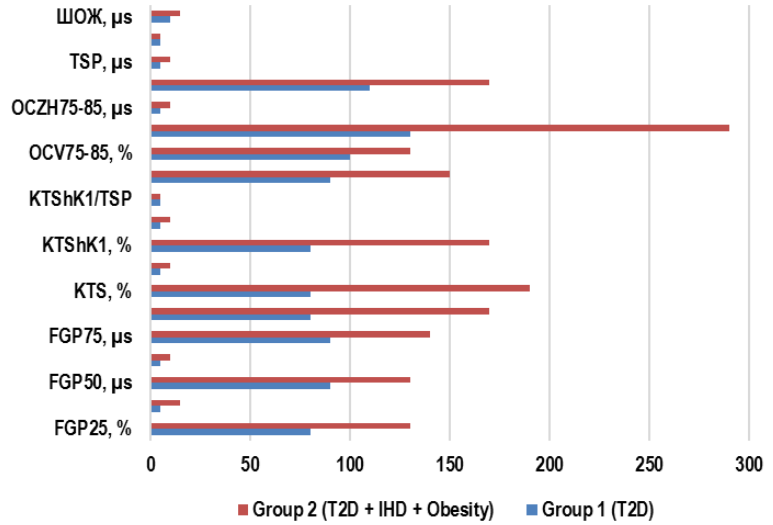



**Figure 2. External Respiratory Function Parameters: Repaglinide Groups.**

The following results were revealed during treatment with metformin:

- After treatment with metformin, respiratory function improved in only 2 out of 30 patients with type 2 diabetes and coronary heart disease. In the remaining 28 patients, respiratory parameters worsened, and air resistance in the bronchi increased.

- In patients with type 2 diabetes and minor changes in the lungs, there was a deterioration in air permeability in the large airways — this is seen by a decrease in exhalation volume in 1 second by 7.1%, the Tiffen index by 10%, as well as FGP25 and FGP50 by 7.04% and 10.5%. These data coincided with the results of bronchoscopy: in 29.41% of patients, nonspecific changes in the bronchial mucosa were found. The values are shown in Figure 3.

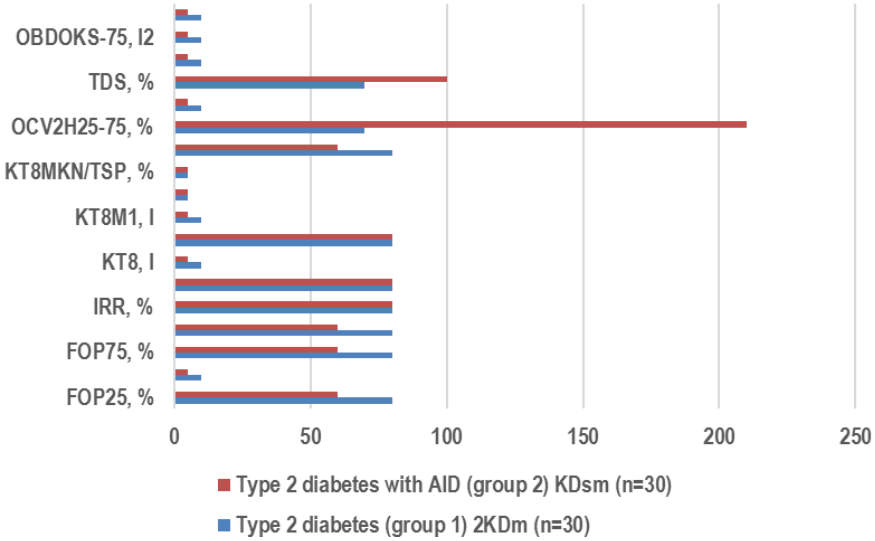



**Figure 3. External Respiratory Function Parameters: Metformin Groups.**

As a result of the conducted study of treatment with repaglinide and metformin, it can be said that a positive trend is observed in the treatment with repaglinide. Metformin has also effect on patients with diabetes mellitus and concomitant diseases. Central respiratory tract patency disorders were detected in all patients.

**Discussion**

Type 2 diabetes mellitus (T2DM) represents a rapidly growing global health challenge, increasingly recognized not only for its well-documented macro- and microvascular complications but also for its profound and often insidious impact on the respiratory system. Impaired respiratory function in T2DM patients contributes significantly to reduced quality of life, diminished exercise tolerance, and increased susceptibility to pulmonary infections and other complications. The presence of coronary heart disease (CHD) and obesity further acts as a critical aggravating circumstance, synergistically compounding the respiratory challenges faced by these individuals. The current study reinforces the growing understanding that patients with T2DM frequently exhibit restrictive alveolar

hypoventilation, a finding consistent with a burgeoning body of established literature highlighting a progressive decrease in lung diffusion capacity. This impairment is critically linked to the pathological accumulation of advanced glycation end products (AGEs) and subsequent glycosylation of basement membrane proteins within the pulmonary capillaries, leading to thickening of the alveolar-capillary barrier and impaired gas exchange efficiency [1]. Furthermore, chronic low-grade inflammation and oxidative stress, hallmarks of T2DM, contribute to interstitial fibrosis and microvascular damage in the lung parenchyma, collectively resulting in the observed ventilatory limitations and reduced pulmonary compliance.

Beyond the direct effects of diabetes, our data compellingly confirm that patients presenting with the complex triad of T2DM, CHD, and obesity demonstrate a more severe and multifaceted respiratory impairment, encompassing both restrictive and obstructive changes, alongside significantly impaired ventilation-perfusion ratios. This observation strongly aligns with recent evidence underscoring the profound pathophysiological alterations in lung tissue that arise from the intricate interplay of metabolic, inflammatory, and cardiovascular disorders [3]. Obesity, a pervasive comorbidity, contributes substantially through both mechanical and metabolic mechanisms. Mechanically, excess adipose tissue around the chest wall and abdomen leads to reduced functional residual capacity, expiratory reserve volume, and overall lung volumes, increasing the work of breathing and reducing compliance. Metabolically, adipose tissue acts as an active endocrine organ, secreting pro-inflammatory adipokines (e.g., leptin, TNF-alpha, IL-6) that can directly contribute to systemic and pulmonary inflammation, fibrosis, and impaired airway mechanics. Concurrently, coronary heart disease significantly impacts cardiorespiratory interactions. Left ventricular dysfunction and incipient heart failure, common in CHD, can lead to chronic pulmonary venous hypertension, resulting in interstitial edema, increased lung stiffness, and further impairment of gas exchange. These cardiogenic pulmonary effects often mimic or exacerbate the restrictive patterns seen in diabetes, creating a complex clinical picture where cardiac and pulmonary dysfunctions are inextricably linked. The synergistic negative effects of these comorbidities render the patient cohort particularly vulnerable to severe respiratory compromise.

A comparative analysis of hypoglycemic therapy effectiveness, central to our study's aim of evaluating the functional state of the external ventilation system in patients with type 2 diabetes mellitus in combination with coronary heart disease and obesity during treatment with repaglinide and metformin, revealed nuanced and distinct effects on spirometric parameters. Repaglinide, a short-acting insulin secretagogue, showed a positive, albeit partial, impact on bronchial patency, evidenced by increases in CTE, CTHP, FGD50, and FGD75. This observation, while promising, should be interpreted cautiously as direct, contemporary studies specifically investigating repaglinide's long-term effects on detailed respiratory function are remarkably scarce. Nevertheless, this partial improvement aligns with the known pleiotropic effects of meglitinides, including their rapid and transient insulin release, which might lead to more physiological glucose excursions, as well as their potential to positively influence microcirculation and reduce oxidative stress and inflammation [2, 7]. These mechanisms, while not primarily targeting the lungs, could theoretically contribute to improved bronchial dynamics and lung compliance, thereby accounting for the observed benefits in specific spirometric parameters. However, the "limited effect on obstructive components" suggests that while repaglinide may offer some benefit in specific aspects, it does not appear to reverse significant structural airway remodeling or long-standing obstructive pathology.

Conversely, most patients on metformin therapy exhibited a deterioration in spirometric parameters and an increase in bronchial resistance. This outcome, while seemingly counterintuitive given metformin's well-established systemic benefits in metabolic control, cardiovascular protection, and even broad anti-inflammatory properties, highlights a critical area for further investigation concerning its direct pulmonary effects in highly comorbid populations. Metformin's primary mechanism of action involves the activation of AMP-activated protein kinase (AMPK), leading to reduced hepatic glucose production and improved insulin sensitivity in peripheral tissues. While it exerts systemic anti-inflammatory and vascular protective effects, these beneficial actions may not sufficiently translate into direct, measurable improvements in macroscopic spirometric parameters in the complex setting of established lung damage from chronic T2DM, CHD, and obesity. Indeed, more recent reports have sometimes associated metformin with a neutral or even negative effect on pulmonary function in patients with a burdened medical history [1, 11, 12], suggesting its pulmonary benefits may not be as direct or universal as its systemic advantages, or perhaps its effects on some specific pathways in the lung are less favorable compared to its overall metabolic impact. This differential effect underscores the complexity of managing multi-morbid patients where general metabolic improvements do not always guarantee improvements in all organ systems.

The unique contribution and scientific novelty of this study, therefore, lie in its direct, focused comparative assessment of the long-term impact of two specific and commonly prescribed oral hypoglycemic agents – repaglinide and metformin – on detailed spirometric indicators within a carefully defined cohort burdened by T2DM and significant comorbidities like CHD and obesity. While existing research broadly discusses diabetes-related pulmonary complications, often from an epidemiological or pathophysiological standpoint, our study provides a granular, head-to-head analysis of the differential effects of these two widely used drugs on specific respiratory parameters. This allows for a deeper understanding of how repaglinide, despite its moderate overall effect, can contribute to partial improvements in bronchial patency, whereas metformin appears to have a less favorable or even negative impact on these specific pulmonary functions in this complex patient group. Our findings offer a contemporary analysis of these established therapies, providing valuable preliminary insights into personalized diabetes management strategies where pulmonary complications are a significant concern, emphasizing that not all beneficial systemic antidiabetic drugs confer similar pulmonary advantages.

Despite these important findings, the study has several limitations. The relatively small sample size and single-center design may limit the generalizability of our results. The follow-up duration, while allowing for assessment of long-term effects, might not have been sufficient to capture the full spectrum of progressive pulmonary changes or drug-induced adaptations. Furthermore, the study primarily relied on spirometric

parameters, and the absence of more advanced lung function tests (e.g., diffusing capacity for carbon monoxide - DLCO), specific imaging (e.g., HRCT scans), or mechanistic biomarkers (e.g., inflammatory markers in bronchoalveolar lavage fluid or lung tissue biopsies) precludes a deeper understanding of the underlying biological changes. Future research should address these limitations by conducting larger, multicenter randomized controlled trials with extended follow-up periods. Such studies should incorporate comprehensive pulmonary function testing, advanced imaging modalities, and biomarker analysis to elucidate the precise cellular and molecular mechanisms underlying the observed drug-specific effects on lung tissue. Additionally, investigating the impact on patient-reported outcomes, quality of life, and exercise capacity, as well as exploring other emerging antidiabetic drugs, would provide a more holistic understanding of their role in mitigating respiratory complications in T2DM patients with multiple comorbidities.

**Conclusion**

1. In patients with type 2 diabetes, lung dysfunction was detected, provoked by poor ventilation of the respiratory tract, leading to resistance in the bronchi. Patients in the first group suffered from a "restrictive type of hypoventilation." A process where gases pass poorly through the wall of the alveoli and capillaries, and oxygen enters the bloodstream worse.

2. The second group also had restrictive and obstructive type of respiratory disorders. In addition, the relationship between ventilation (air intake) and blood supply to the lungs was disrupted.

3. Metformin helps to improve blood sugar reduction.

4. Repaglinide, unlike other drugs, helped improve lung function. It is especially useful for type 2 diabetic patients with respiratory disorders.

***Conflict of Interest.*** *The authors declare that they have no conflict of interest.*

***Contribution of authors.*** *All authors were equally involved in the writing of this article.*

***Funding:*** *No funding was provided.*

***Literature:***

1. *Deng Y., et al.* Effects of metformin on respiratory diseases: Current evidence and future perspectives. Frontiers in Pharmacology, 2022. 13, 856711. (DOI: 10.3389/fphar.2022.856711)

2. *Kalra S., Gupta Y., Kumar A.* Repaglinide: An Overview. Journal of the Association of Physicians of India, 2015. 63(4), 60–63.

3. *Kim H.L., et al.* Impact of obesity and metabolic syndrome on respiratory function: A narrative review. Journal of Obesity & Metabolic Syndrome, 2021. 30(2), 101–110. DOI: 10.7570/joms.2021.30.2.101

4. *Kostovski M., Simeonovski V., Mironska K., Tasic V., Gucev Z.* Metabolic Profiles in Obese Children and Adolescents with Insulin Resistanceю. Open Access Maced J Med Sci. 2018. 15. 6(3):511-518 https://oamjms.eu/index.php/mjms/article/view/oamjms.

5. *Król E., Rutkowski B.* Influence of Metformin on Pulmonary Function in Diabetic Patients. Polish Archives of Internal Medicine, 2015. 125(3), 182–189.

6. *Kolahian S., Leiss V., Nürnberg B.* Diabetic lung disease: fact or fiction? Rev Endocr Metab Disord. 2019 Sep. 20(3):303-319. doi: 10.1007/s11154-019-09516-w. PMID: 31637580; PMCID: PMC7102037.

7. *Lee J.S., et al.* The pleiotropic effects of meglitinides in cardiovascular and renal protection. International Journal of Molecular Sciences, 2020. 21(11), 3845. (DOI: 10.3390/ijms21113845)

8. *Long C., Fan W., Liu Y., Hong K.* Stress hyperglycemia is associated with poor outcome in critically ill patients with pulmonary hypertension. Front Endocrinol (Lausanne). 2024 Feb 23;15:1302537. doi: 10.3389/fendo.2024.1302537. PMID: 38464971; PMCID: PMC10924302.

9. *Li M., Chi X., Wang Y. et al.* Trends in insulin resistance: insights into mechanisms and therapeutic strategy. Sig Transduct Target Ther. 2022. 7, 216. https://doi.org/10.1038/s41392-022-01073-0

10. *Li W., Ning Y., Ma Y. et al.* Association of lung function and blood glucose level: a 10-year study in China. BMC Pulm Med. 2022. 22, 444 https://doi.org/10.1186/s12890-022-022

11. *Suleman S., Madsen A.L., Ängquist L.H., Schubert M., Linneberg A., Loos R.J.F., Hansen T., Grarup N.* Genetic Underpinnings of Fasting and Oral Glucose-stimulated Based Insulin Sensitivity Indices. J Clin Endocrinol Metab. 2024 Oct 15;109(11):2754-2763. doi: 10.1210/clinem/dgae275. PMID: 38635292; PMCID: PMC11479690.

12. *Sharma A., Müller K., Zhang Y., Ivanov D.* A comprehensive review on diabetic cardiomyopathy: Pathophysiology, imaging assessment and potential metabolic-targeted strategies. European Journal of Endocrinology, 2025. 192(6), R127–R150. https://doi.org/10.1530/EJE-25-0147

13. *Peng Y., Zhong GC., Wang, L. et al.* Chronic obstructive pulmonary disease, lung function and risk of type 2 diabetes: a systematic review and meta-analysis of cohort studies. BMC Pulm Med. 2020. 20, 137. https://doi.org/10.1186/s12890-020-1178-y

14. *Zhao Y., et al.* Mechanisms of impaired lung function in diabetes mellitus: An updated review. Frontiers in Physiology, 2022. 13, 856711. (DOI: 10.3389/fphys.2022.856711)

**Information about the authors:**

**Urazalina Nailya** - Candidate of Medical Sciences, Associate Professor of the Department of physiological disciplines named after honored scientist of the republic of Kazakhstan, professor T.A. Nazarova, NJSC "Semey Medical University", Semey, Kazakhstan; phone: 8 777 907 55 89, e-mail: hakim_15@mail.ru, https://orcid.org/0000-0003-0200-1763,

**Tolubayeva Diana -** Doctor *PhD "Medical Center Hospital of the President affairs Administration of the Republic of Kazakhstan" Astana,* https://orcid.org/0000-0003-3119-7814; e-mail: dianajianna@gmail.com; Cell phone +7 701 299 34 06.

***Corresponding author:**

**Zhautikova Saule** - Professor of the Department of Physiology of NJSC «Karaganda Medical University», https://orcid.org/0009-0000-5712-7369; Karaganda, Kazakhstan.

**Address**: Gogol str. 40, Karaganda 100000, Kazakhstan.

**e-mail:** Zhautikova@qmu.kz;

**Cell phone** +7 701 299 34 07

Received: 13 February 2025 / Accepted: 15 May 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2025.27.3.005***

***UDC 616.136-005.8-036.882(574.5)***

This work is licensed under a Creative Commons Attribution 4.0 International License

# RETROSPECTIVE ANALYSIS OF PATIENTS WITH OBLITERATING ATHEROSCLEROSIS OF THE LOWER EXTREMITY ARTERIES IN THE ABAI REGION OF THE REPUBLIC OF KAZAKHSTAN

**Gulmira A. Uruzbayeva [1], https://orcid.org/0000-0001-8897-6865**
**Tolkyn A. Bulegenov[1], http://orcid.org/0000-0001-6145-9649**
**Akmaral K. Mussakhanova[2], https://orcid.org/0000-0002-0399-5045**
**Kenesh Dzhusupov[3], https://orcid.org/0000-0002-2213-1373**
**Onlasyn T. Ibekenov[4], https://orcid.org/0000-0001-6605-6435**
**Zhanargul K. Smailova[1], https://orcid.org/0000-0002-4513-4614**
**Assel Zh. Baibussinova[1],http://orcid.org/0000-0003-3447-6245**
**Merey N. Imanbayev[1], https://orcid.org/0000-0002-7248-0440**
**Fariza Zh. Zharykbassova[2], https://orcid.org/0000-0001-5282-7454**
**Arailym S. Kussainova[1], https://orcid.org/0009-0001-8451-4062**
**Aidana Armankyzy[1], https://orcid.org/0009-0001-8451-4062**

**[1] Non-profit joint-stock company "Semey medical university", Semey, Republic of Kazakhstan**
**[2] Non-profit joint-stock company «Astana medical university», Astana, Republic of Kazakhstan;**
**[3] The International Higher School of Medicine, Bishkek, Kyrgyzstan;**
**[4] National Scientific Center of Surgery Named After A.N. Syzganov, Almaty, Republic of Kazakhstan;**

**Abstract**

**Background and Objectives.** Obliterating atherosclerosis of the lower extremity arteries (OALEA) is a severe vascular condition that leads to impaired blood supply to the limbs, reduced quality of life, and a high risk of amputations. This study presents a retrospective analysis of patients diagnosed with OALEA in the Abai region of the Republic of Kazakhstan. **The objective of the study** is to assess the demographic and clinical characteristics of patients with obliterating atherosclerosis of the lower extremities, as well as to identify the disease course features and treatment approaches.

**Materials and Methods.** For the retrospective analysis, data from the medical records of patients were obtained from the archive of the University Hospital of Non-profit joint-stock company «Semey Medical University» for the period from 2019 to 2023. The study included patients diagnosed with obliterating atherosclerosis of the lower extremity arteries, confirmed through clinical, laboratory, and instrumental examinations. Inclusion criteria for the study were patients aged 18 years and older. A total of 170 patients diagnosed with obliterating atherosclerosis of the lower extremity arteries were included in the study.

**Results.** The study included 170 patients with obliterating atherosclerosis of the lower extremity arteries, the majority of whom were male (67.6%) with a mean age of 69.55 ± 9.87 years. Most patients (78.2%) were urban residents, and 64.1% were retired and unemployed. Comorbidities were present in 98.8% of cases. Surgical treatment was performed in 96.5% of patients, including above-knee amputations in 44.1% of cases. Conservative therapy was administered to 25.7% of patients. A total of 76.5% of patients were admitted to the intensive care unit, complications were recorded in 3.5% of cases, and the mortality rate was 4.1%.

**Conclusions.** The study results reflect the significant clinical severity of patients with obliterating atherosclerosis of the lower extremity arteries in the Abai region, characterized by a high rate of amputations and limited access to reconstructive interventions. The identified patterns highlight the need to implement an integrated care system focused on early diagnosis, interdisciplinary collaboration, and the expansion of vascular surgery services at the regional level.

***Keywords:*** *obliterating atherosclerosis of the lower extremity arteries, retrospective analysis, public health, medicine.*

***For citation:***

Uruzbayeva G.A., Bulegenov T.A.,. Mussakhanova A.K., Dzhusupov K., Ibekenov O.T., Smailova Zh.K., Baibussinova A.Zh., Imanbayev M.N., Zharykbassova F.Zh., Kussainova A.S., Aidana A. Retrospective analysis of patients with obliterating atherosclerosis of the lower extremity arteries in the Abai region of the Republic of Kazakhstan // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 42-52. *doi 10.34689/SH.2025.27.3.005*

**Резюме**

# РЕТРОСПЕКТИВНЫЙ АНАЛИЗ ПАЦИЕНТОВ С ОБЛИТЕРИРУЮЩИМ АТЕРОСКЛЕРОЗОМ АРТЕРИЙ НИЖНИХ КОНЕЧНОСТЕЙ В АБАЙСКОЙ ОБЛАСТИ РЕСПУБЛИКИ КАЗАХСТАН

**Гульмира А. Урузбаева[1], https://orcid.org/0000-0001-8897-6865**
**Толкын А. Булегенов[1], http://orcid.org/0000-0001-6145-9649**
**Акмарал К. Мусаханова[2], https://orcid.org/0000-0002-0399-5045**
**Кенеш Джусупов[3], https://orcid.org/0000-0002-2213-1373**
**Онласын Т. Ибекенов[4], https://orcid.org/0000-0001-6605-6435**
**Жанаргуль К. Смаилова[1], https://orcid.org/0000-0002-4513-4614**
**Асель Ж. Байбусинова[1],http://orcid.org/0000-0003-3447-6245**
**Мерей Н. Иманбаев[1], https://orcid.org/0000-0002-7248-0440**
**Фариза Ж. Жарыкбасова[2], https://orcid.org/0000-0001-5282-7454**
**Арайлым С. Кусаинова[1], https://orcid.org/0009-0001-8451-4062**
**Айдана Арманқызы[1], https://orcid.org/0009-0001-8451-4062**

**[1] НАО «Медицинский университет Семей», г. Семей, Республика Казахстан;**
**[2] НАО «Медицинский университет Астана», г. Астана, Республика Казахстан;**
**[3] Международная высшая школа медицины, Бишкек, Кыргызстан;**
**[4] Национальный научный центр хирургии имени А.Н. Сызганова, г. Алматы, Республика Казахстан;**

**Введение и цель.** Облитерирующий атеросклероз артерий нижних конечностей (ОААНК) представляет собой серьёзную сосудистую патологию, приводящую к нарушению кровоснабжения конечностей, снижению качества жизни и высокому риску ампутаций. Настоящее исследование представляет собой ретроспективный анализ пациентов с диагнозом ОААНК в Абайской области Республики Казахстан. **Целью данного исследования** является оценка демографических, клинических характеристик пациентов с облитерирующим атеросклерозом нижних конечностей, а также выявление особенности течения и подходы к лечению заболевания.

**Материалы и методы.** Для проведения ретроспективного анализа были использованы данные из медицинских карт пациентов, полученные из архива университетской клиники Некоммерческое акционерное общество «Медицинский университет Семей» за период с 2019 по 2023 год. В исследование были включены пациенты с диагнозом облитерирующий атеросклероз артерий нижних конечностей, подтверждённым на основании клинических, лабораторных и инструментальных методов обследования. Критерием включения в исследование являлось достижение пациентами возраста 18 лет и старше. Всего в исследование было включено 170 пациентов с установленным диагнозом облитерирующего атеросклероза артерий нижних конечностей.

**Результаты.** В исследование включено 170 пациентов с облитерирующим атеросклерозом артерий нижних конечностей, преимущественно мужчины (67,6%), средний возраст составил 69,55 ± 9,87 лет. Большинство пациентов (78,2%) городские жители, 64,1% - неработающие пенсионеры. У 98,8% отмечены сопутствующие заболевания. Оперативное лечение проведено 96,5% пациентам, из них 44,1% ампутации выше колена. Консервативную терапию получали 25,7% больных. В АОРИТ находились 76,5% пациентов, осложнения зафиксированы у 3,5%, летальность составила 4,1%.

**Выводы.** Результаты исследования отражают выраженную клиническую тяжесть контингента пациентов с облитерирующим атеросклерозом артерий нижних конечностей в Абайской области, сопровождающуюся высокой частотой ампутаций и ограниченным доступом к реконструктивным вмешательствам. Выявленные особенности указывают на необходимость внедрения интегрированной системы оказания помощи, ориентированной на раннюю диагностику, междисциплинарное взаимодействие и расширение возможностей сосудистой хирургии на региональном уровне.

***Ключевые слова:*** *облитерирующий атеросклероз артерий нижних конечностей, ретроспективный анализ, общественное здравоохранение, медицина.*

***Для цитирования:***

*Урузбаева Г.А., Булегенов Т.А., Мусаханова А.К., Джусупов К., Ибекенов О.Т., Смаилова Ж.К., Байбусинова А.Ж., Иманбаев М.Н., Жарыкбасова Ф.Ж., Кусаинова А.С., Арманқызы А.* Ретроспективный анализ пациентов с облитерирующим атеросклерозом артерий нижних конечностей в Абайской области республики Казахстан // Наука и Здравоохранение. 2025. Т.27 (3), С. 42-52. doi: 10.34689/SH.2025.27.3.005

**Түйіндеме**

# ҚАЗАҚСТАН РЕСПУБЛИКАСЫ АБАЙ ОБЛЫСЫНДА ТӨМЕНГІ АЯҚ-АТЕРОСКЛЕРОЗЫ ОБЛИТЕРАЦИЯЛЫҚ АТЕРОСКЛЕРОЗЫ БАР НАУҚАСТАРҒА РЕТРОСПЕКТИВАЛЫҚ ТАЛДАУ

**Гульмира А. Урузбаева[1],** https://orcid.org/0000-0001-8897-6865
**Толкын А. Булегенов[1],** http://orcid.org/0000-0001-6145-9649
**Акмарал К. Мусаханова[2],** https://orcid.org/0000-0002-0399-5045
**Кенеш Джусупов[3],** https://orcid.org/0000-0002-2213-1373
**Онласын Т. Ибекенов[4],** https://orcid.org/0000-0001-6605-6435
**Жанаргуль К. Смаилова[1],** https://orcid.org/0000-0002-4513-4614
**Асель Ж. Байбусинова[1],**http://orcid.org/0000-0003-3447-6245
**Мерей Н. Иманбаев[1],** https://orcid.org/0000-0002-7248-0440
**Фариза Ж. Жарыкбасова[2],** https://orcid.org/0000-0001-5282-7454
**Арайлым С. Кусаинова[1],** https://orcid.org/0009-0001-8451-4062
**Айдана Арманқызы[1],** https://orcid.org/0009-0001-8451-4062

**[1] КеАҚ «Семей Медицина Университеті», Семей қ., Қазақстан Республикасы;**
**[2] КеАҚ «Астана Медицина Университеті», Астана қ., Қазақстан Республикасы;**
**[3] Халықаралық жоғары медицина мектебі, Бішкек қ., Қырғызстан;**
**[4] А.Н. Сызғанов атындағы Ұлттық хирургия ғылыми орталығы, Алматы қ., Қазақстан Республикасы.**

**Кіріспе және мақсаты.** Төменгі аяғындағы артериялардың облитерациялық атеросклерозы (ТААОА) - аяқ-қолдардың қанмен қамтамасыз етілуінің бұзылуына, өмір сапасының төмендеуіне және ампутацияның жоғары қаупіне әкелетін ауыр тамырлы патология. Бұл зерттеу Қазақстан Республикасының Абай облысында ТААОА диагнозы қойылған науқастарға ретроспективті талдау болып табылады. **Бұл зерттеудің мақсаты** төменгі аяғындағы облитерациялық атеросклерозбен ауыратын науқастардың демографиялық және клиникалық сипаттамаларын бағалау, сонымен қатар аурудың ағымының ерекшеліктерін және емдеу тәсілдерін анықтау болып табылады

**Материалдар мен тәсілдер.** Ретроспективті талдауды жүргізу үшін 2019-2023 жылдар аралығындағы «Семей Медицина Университеті» КеАҚ Университеттік клиникасының мұрағатынан алынған пациенттердің медициналық құжаттарының деректері пайдаланылды. Зерттеуге клиникалық, зертханалық және аспаптық зерттеу әдістерінің негізінде расталған төменгі аяғындағы артериялардың облитерациялық атеросклерозы диагнозы бар науқастар қамтылды. Зерттеуге қосу критерийі пациенттердің 18 жастан жоғары болуы болды. Зерттеуге төменгі аяқ-қол артерияларының облитерациялық атеросклерозы анықталған диагнозы бар барлығы 170 пациент қатысты.

**Нәтежиелер.** Зерттеуге төменгі аяқ-қол артерияларының облитерациялық атеросклерозымен ауыратын 170 науқас қатысты, негізінен ер адамдар (67,6%), орташа жасы 69,55 ± 9,87 жасты құрады. Науқастардың басым бөлігі (78,2%) қала тұрғындары, 64,1%-ы жұмыс істемейтін зейнеткерлер. 98,8 пайызында қатар жүретін аурулар болған. Науқастардың 96,5%-ында хирургиялық ем жүргізілді, оның 44,1%-ы тізеден жоғары ампутация болды. Консервативті емді науқастардың 25,7%-ы қабылдаған. Науқастардың 76,5%-ы жансақтау бөлімінде болса, 3,5%-да асқынулар тіркеліп, өлім 4,1%-ды құрады.

**Қорытындылар.** Зерттеу нәтижелері Абай облысында төменгі аяқ-қол артерияларының облитерациялық атеросклерозы бар науқастар контингентінің айқын клиникалық ауырлығын көрсетеді, ампутациялардың жоғары жиілігімен және реконструкциялық араласуларға қол жетімділіктің шектелуімен бірге жүреді. Анықталған ерекшеліктер аймақтық деңгейде ерте диагностикаға, пәнаралық өзара әрекеттесуге және тамыр хирургиясының мүмкіндіктерін кеңейтуге бағытталған кешенді медициналық көмек жүйесін енгізу қажеттілігін көрсетеді.

***Түйінді сөздер:*** *төменгі аяқ-қол артерияларының облитерациялаушы атеросклерозы, ретроспективті талдау, қоғамдық денсаулық сақтау, медицина.*

***Дәйексөз үшін:***

*Урузбаева Г.А., Булегенов Т.А., Мусаханова А.К., Джусупов К., Ибекенов О.Т., Смаилова Ж.К., Байбусинова А.Ж., Иманбаев М.Н., Жарыкбасова Ф.Ж., Кусаинова А.С., Арманқызы А.* Қазақстан Республикасы Абай облысында төменгі аяқ-атеросклерозы облитерациялық атеросклерозы бар науқастарға ретроспективалық талдау // Ғылым және Денсаулық. 2025. Т.27 (3), Б. 42-52. doi: 10.34689/SH.2025.27.3.005

**Introduction**

Cardiovascular diseases (CVDs) are the leading cause of disability and mortality worldwide [7,11,21,23], with atherosclerosis being the primary pathological process underlying the majority of these conditions.

Atherosclerosis is a systemic and chronic pathological alteration of the arterial wall layers that begins early in life and remains latent and asymptomatic for an extended period before progressing to its advanced stages [13,16]. It is a multifocal pathological process that has been extensively studied over recent decades. Atherosclerosis typically develops silently over time and only becomes clinically apparent at a late stage, often presenting with severe or even fatal events such as acute myocardial infarction or ischemic stroke.

Peripheral artery disease (PAD) represents a frequent manifestation of systemic atherosclerosis, particularly affecting the lower extremities. Obliterating atherosclerosis of the lower extremities (OALE) is a chronic and progressive condition characterized by the narrowing or occlusion of peripheral arteries, leading to tissue ischemia and, in advanced cases, limb loss [3,8,15]. The prevalence of PAD increases significantly with age, affecting over 20% of individuals older than 70 years, many of whom remain undiagnosed due to the asymptomatic or nonspecific nature of early-stage disease.

According to the guidelines of the European Society of Cardiology and the Global Vascular Guidelines consensus, effective management of patients with OALE requires a multidisciplinary approach involving vascular surgeons, interventional radiologists, general physicians, rehabilitation specialists, and other healthcare professionals. The treatment strategy prioritizes early detection, correction of modifiable risk factors, pharmacological therapy (including antiplatelet agents, statins, and antihypertensive drugs), as well as the use of minimally invasive reconstructive interventions.

However, in resource-constrained settings, including certain regions of the Republic of Kazakhstan, there remains a high incidence of amputations and delays in accessing specialized vascular care. National studies have highlighted a persistently low rate of reconstructive vascular surgery, particularly in rural and underserved areas [19]. These challenges emphasize the urgent need for a more structured and system-wide approach to the care of patients with OALE, including the development of regional screening programs, effective referral pathways, and expanded access to vascular technologies and interventions [15,24].

Recent international experience shows that implementation of early PAD detection programs and centralized referral systems can significantly reduce the burden of late-stage ischemia and improve limb salvage rates. Evidence from Eastern European countries undergoing healthcare reform indicates that integration of vascular diagnostic networks at the regional level leads to earlier intervention and reduced amputation frequency.

In the context of Kazakhstan, particularly in remote areas such as the Abai Region, geographic barriers, limited access to trained vascular specialists, and underfunding of diagnostic infrastructure compound the challenges faced by clinicians. A systematic analysis of regional case data can help guide local health policy, resource allocation, and capacity building in vascular medicine.

The present study aims to conduct a retrospective analysis of the patient profile with OALE in the Abai region of the Republic of Kazakhstan, assessing factors influencing treatment outcomes and the extent of surgical interventions performed, followed by a comparison with international data.

**Materials and Methods**

For the retrospective analysis, data from the medical records of patients were obtained from the archive of the University Hospital of Non-profit joint-stock company «Semey Medical University» for the period from 2019 to 2023. The study included patients diagnosed with obliterating atherosclerosis of the lower extremity arteries, confirmed through clinical, laboratory, and instrumental examinations.

*Inclusion criteria* for the study were patients aged 18 years and older.

A total of 170 patients diagnosed with obliterating atherosclerosis of the lower extremity arteries were included in the study. Demographic characteristics and clinical data related to the disease and treatment were obtained from patients and their medical records.

*Exclusion criteria:* acute arterial thromboembolism; varicose vein disease without signs of arterial involvement; terminal-stage oncological diseases; incomplete or fragmented medical records.

The administration of the clinic where the study was conducted was informed about the study's progress and raised no objections to the publication of its results in an open-access format.

The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Semey Medical University (Protocol No. 2, dated December 12, 2023). Written informed consent was obtained from all participants prior to their inclusion in the study.

*Statistical Analysis*

Means and standard deviations (SD) were used to describe quantitative variables, while absolute (N) and relative (%) frequencies were used for qualitative variables. Pearson's chi-square ($\chi^2$) test or Fisher's exact test, where applicable, was employed for proportion comparisons. Significance levels were two-tailed, with statistical significance set at $p < 0.05$. Statistical analyses were performed using SPSS version 24.0.

**Results**

A total of 170 patients with a confirmed diagnosis of obliterating atherosclerosis of the lower extremity arteries were included in the study. The majority were male (67.6%, N = 115), and 54.1% (N = 92) were of Russian ethnicity. Regarding place of residence, 78.2% (N = 133) were urban residents.

In total, 64.1% (N = 109) of the respondents were retired and unemployed. The mean age of the patients

was 69.55 ± 9.87 years. The gender and age distribution of patients suggests a predominance of older males, which aligns with the global epidemiology of OALE. Numerous studies have shown that males over 65 are particularly susceptible to peripheral arterial disease, especially in settings with high rates of smoking, diabetes, and hypertension.

Most patients (32.9%, N = 56) were admitted through emergency medical services or transferred from other inpatient facilities. In 57.6% (N = 98) of cases, the pre-hospital period exceeded 10 days, indicating delayed diagnosis and/or delayed presentation to healthcare facilities. The extended pre-hospital period observed in 57.6% of patients (over 10 days) indicates delayed access to specialized care and may be associated with underrecognition of symptoms by both patients and general practitioners. This delay likely contributes to the high proportion of emergency admissions and the severity of clinical presentation. Upon hospital admission, the condition of 71.2% of patients was assessed as being of moderate severity.

Almost all patients (98.8%) had comorbid conditions, including hypertension, diabetes mellitus, ischemic heart disease (IHD), chronic obstructive pulmonary disease (COPD), and others (Table 1). The high rate of comorbidities (98.8%) among patients with OALE reflects the systemic nature of atherosclerosis. This finding supports the need for a multidisciplinary approach to care, incorporating cardiology, endocrinology, and nephrology specialists.

*Table 1.*

**Medical and Social Characteristics of the Patients.**

| Total number of patients | Indicators | N (%) |
|---|---|---|
| Gender | Men | 115 (67,6) |
| | Women | 55 (32,4) |
| Age (years, M ±m) | 69,55 ± 9,87 лет | |
| Place of residence | Urban | 133 (78,2) |
| | Rural | 37 (21,8) |
| Ethnicity | Kazakh | 74 (43,5) |
| | Russian | 92 (54,1) |
| | Other | 4 (2,4) |
| Social status | Worker | 16 (9,4) |
| | Retired | 109 (64,1) |
| | Disabled | 31 (18,2) |
| | Unemployed | 14 (8,3) |
| Admission channels | Emergency Medical Services (EMS) | 56 (32,9) |
| | Family Medicine Clinic (General Practitioner) | 39 (22,9) |
| | Vascular Surgeon | 34 (20) |
| | Doctors of other specialties | 41 (24,1) |
| | Transfer from another hospital | 56 (32,9) |
| Pre-hospital stage duration | Up to 1 day | 13 (7,6) |
| | 1-3 days | 27 (15,9) |
| | 4-7 days | 22 (13,0) |
| | 7-10 days | 10 (5,9) |
| | More than 10 days | 98 (57,6) |
| General condition of patients upon admission | Satisfactory | 39 (22,9) |
| | Moderate | 121 (71,2) |
| | Severe | 10 (5,9) |
| Comorbidities | Yes | 168 (98,8) |
| | No | 2 (1,2) |

A total of 96.5% (N = 164) of patients underwent surgical intervention. The most commonly performed procedures were above-knee amputations, accounting for 44.1% (N = 75) of all surgical cases. Reconstructive surgeries included femoral-popliteal bypass grafting (15.9%), repair using synthetic implants (8.8%), aortoiliac-femoral bypass (1.8%), and autovenous graft transplantation (0.6%). Most operations were performed under emergency conditions.

The fact that only 8.8% of patients underwent reconstructive procedures using synthetic implants and even fewer (1.8%) received complex bypass surgeries points to a limited availability of advanced surgical interventions in the region. This limitation may stem from resource constraints or a shortage of specialized vascular surgeons.

Conservative therapy was administered to 25.7% (N = 42) of patients. The most frequently used medications included analgesics (93.5%, N = 159), microcirculation enhancers (94.1%, N = 160), antibiotic therapy (85.9%, N = 146), infusion therapy (83.5%, N = 142), antispasmodics (74.7%, N = 127), antiplatelet agents (61.8%, N = 105), and angioprotectors (51.2%, N = 87). In most cases, treatment involved a combination of several pharmacological groups simultaneously. The pharmacological treatment profile indicates a high reliance on symptomatic therapy (analgesics, antispasmodics, microcirculation enhancers), with a relatively modest use of guideline-recommended agents such as antiplatelet therapy. This highlights potential gaps in adherence to international PAD management protocols.

These treatments were often used in combination, suggesting an approach aimed primarily at stabilizing acute symptoms rather than addressing the underlying pathophysiological processes of peripheral artery disease (PAD). The relatively lower rate of evidence-based therapies, such as antiplatelet agents (61.8%) and anticoagulants (41.8%), is of particular concern. Current European Society of Cardiology (ESC) guidelines recommend routine use of antiplatelet therapy and statins in all patients with symptomatic PAD, as these medications significantly reduce the risk of cardiovascular events and progression of ischemia. The underutilization of these agents may reflect either prescribing gaps or limitations in drug availability within the studied region. Additionally, only 7.6% of patients received physical therapy (FZT), which is an essential component of conservative management in chronic limb-threatening ischemia (CLTI). Supervised exercise programs are known to improve pain-free walking distance and enhance quality of life. The minimal implementation of such rehabilitation strategies again highlights a gap between international best practices and the current standard of care in the Abai region. These findings underscore the need for systemic educational initiatives targeting healthcare providers at the primary and hospital levels. Improved awareness of evidence-based PAD management could enhance pharmacologic adherence and reduce the rate of disease progression and amputations. Furthermore, the reliance on antibiotics (85.9%) may suggest frequent presentation of patients with advanced limb infections, which are often associated with delayed diagnosis. This observation further reinforces the urgency of early detection and the establishment of outpatient vascular clinics for timely intervention and monitoring. In summary, while symptomatic treatments are widely administered, the gap in guideline-based pharmacotherapy necessitates urgent interventions in the form of clinical audits, continuing medical education (CME) programs, and better integration of vascular medicine protocols into hospital formularies and electronic medical records.

A total of 76.5% of patients were admitted to the Intensive Care Unit (ICU), with the majority (54.1%, N = 92) staying for less than 24 hours. Postoperative complications were recorded in 3.5% (N = 7) of cases and included thromboembolism, bleeding, multiple organ failure, and wound-related complications. The average hospital stay did not exceed 20 days in 92.4% (N = 157) of patients.

In terms of treatment outcomes, 92.4% (N = 92) of patients recovered, while 4.1% (N = 7) experienced a fatal outcome. Mortality was more frequently observed among older patients with severe comorbidities and those who underwent major amputations at advanced stages of ischemia (Table 2 and Figure 1, 2, 3, 4).

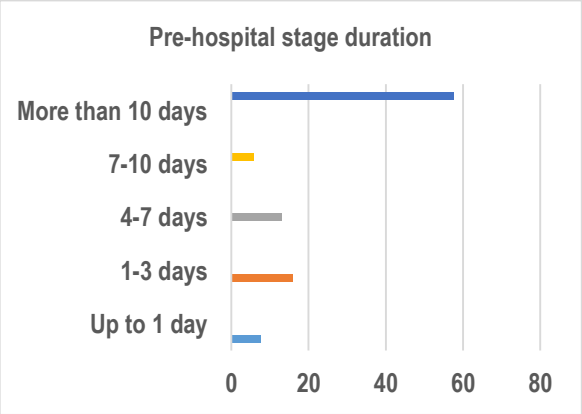



**Figure 1. Pre-hospital stage duration.**

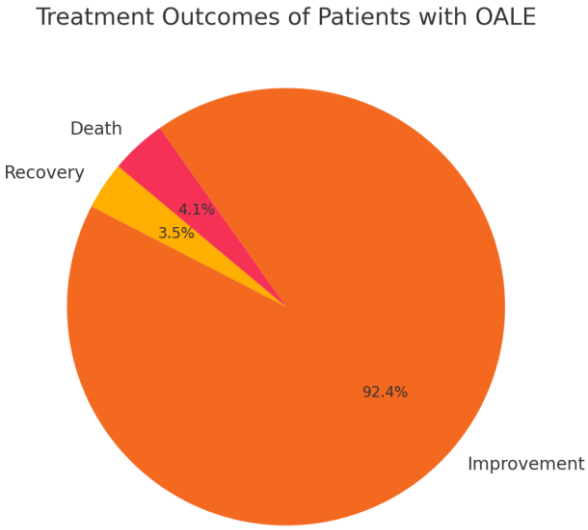



**Figure 2. Distribution of Conservative Therapy among Patients with OALE.**

*Table 2.*

**Inpatient Care Indicators for Patients.**

| Indicators | | N (%) |
|---|---|---|
| Type of treatment | Conservative | 6 (3,5) |
| | Surgical | 164 (96,5) |
| Methods of surgical treatment | Vessel tissue graft restoration | 1 (0,6) |
| | Vascular restoration with synthetic implant | 15 (8,8) |
| | Femoral-popliteal bypass | 27 (15,9) |
| | Above-knee amputation | 75 (44,1) |
| | Below-knee amputation | 2 (1,2) |
| | Aorto-iliac-femoral anastomosis | 3 (1,8) |
| | Foot amputation | 5 (2,9) |
| | Conservative treatment | 42 (25,7) |
| Scope of conservative therapy | Anticoagulant therapy | 71 (41,8) |
| | Antiplatelet therapy | 105 (61,8) |
| | Analgesics | 159 (93,5) |
| | Antispasmodics | 127 (74,7) |
| | Microcirculation correctors | 160 (94,1) |
| | Angioprotectors | 87 (51,2) |
| | Antibiotic therapy | 146 (85,9) |
| | Infusion therapy | 142 (83,5) |
| | FZT (Physical Therapy) | 13 (7,6) |
| Duration of the Intensive Care Unit (ICU) | Not admitted | 40 (23,5) |
| | Up to 1 day | 92 (54,1) |
| | 1-3 days | 22 (12,9) |
| | 4 -5 days | 8 (5,9) |
| | 6-7 days | 4 (2,4) |
| | More than 7 days | 4 (2,4) |
| Complications | Bleeding | 1 (0,6) |
| | Wound complications | 1 (0,6) |
| | Thromboembolic complications | 4 (1,7) |
| | Multiple organ failure | 1 (0,6) |
| | No complications | 164 (96,5) |
| Duration of inpatient treatment | Up to 10 days | 69 (40,6) |
| | Up to 20 days | 88 (51,8) |
| | Up to 30 days | 12 (7,0) |
| | More than 30 days | 1 (0,6) |
| Treatment outcomes | Recovery | 6 (3,5) |
| | Improvement | 157 (92,4) |
| | Death | 7 (4,1) |

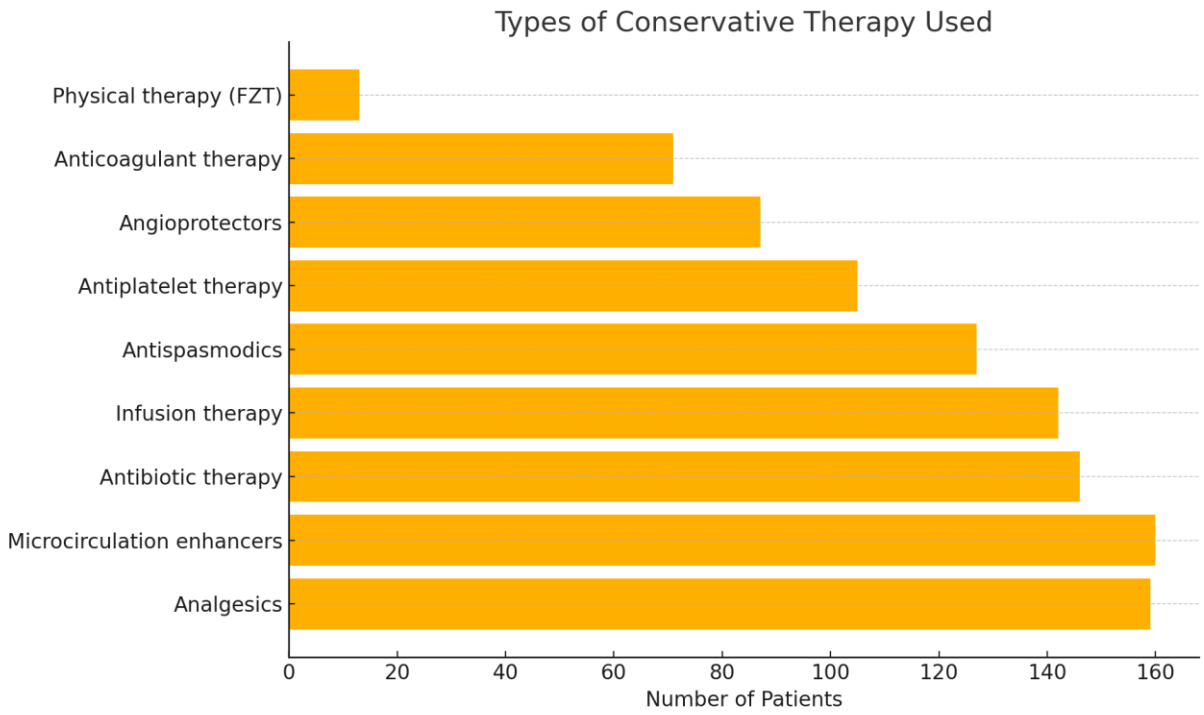



**Figure 3. Treatment Outcomes among Patients with OALE.**

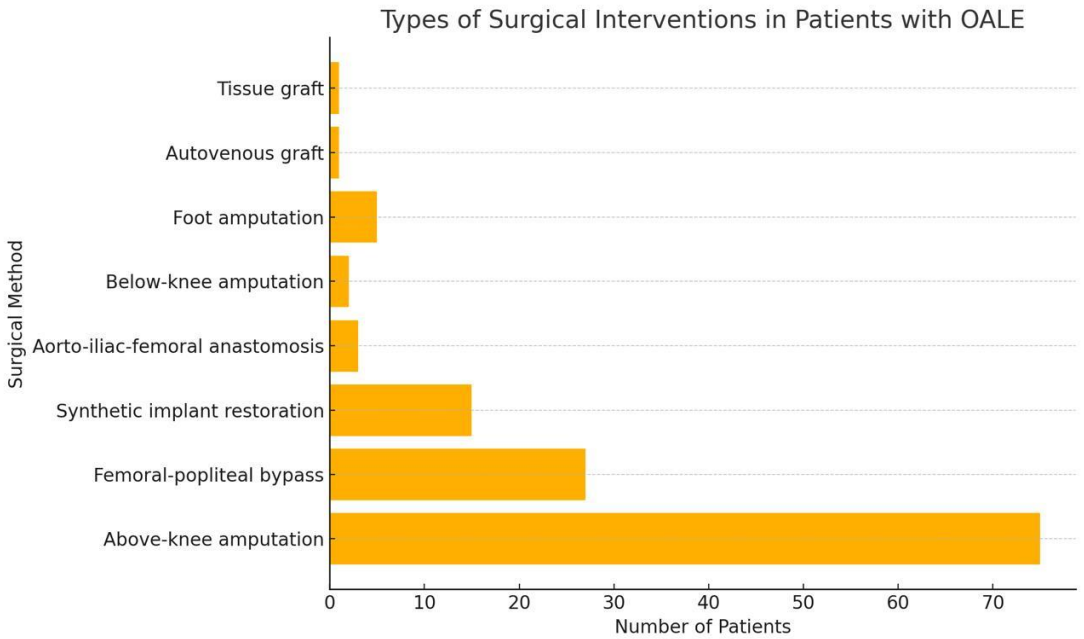



**Figure 4. Types of Surgical Interventions in Patients with OALE**

**Discussion**

The clinical profile and treatment patterns observed in this study provide a valuable opportunity to benchmark regional vascular care practices against international standards.

Several system-level issues were identified - ranging from delayed admissions to the limited use of reconstructive procedures - that mirror structural challenges documented in similar healthcare settings [19–26].

In this context, our findings merit broader discussion, particularly with regard to early detection strategies, surgical capacity, and health-system integration.

The high proportion of emergency admissions (32.9%) and inter-hospital transfers (32.9%) may reflect both the delayed recognition of critical limb ischemia at the primary care level and the lack of streamlined referral systems. This is in line with data from similar resource-limited regions in Eastern Europe, where weak pre-hospital triage contributes to worsened clinical outcomes [10].

In our study, only 1.8% of patients underwent aortoiliac-femoral bypass and 0.6% received autovenous grafts, which may indicate a limited capacity for complex reconstructive surgery in the region. International studies suggest that access to such procedures is closely tied to institutional experience and specialized vascular teams [18].

Postoperative complications were recorded in just 3.5% of cases, which may reflect either effective perioperative protocols or, conversely, underreporting due to incomplete documentation — an issue previously noted in retrospective audits of vascular care [19].

The short ICU stay (less than 24 hours for 54.1% of patients) and relatively low complication rates are atypical compared to global benchmarks. Further qualitative research may be required to evaluate clinical decision-making, documentation accuracy, and the adequacy of intensive monitoring practices [5].

A 4.1% mortality rate, though seemingly modest, warrants close attention, especially since deaths were clustered among older patients with comorbidities and major amputations. This aligns with global data on the prognostic value of frailty and ischemia stage in limb salvage surgery [19,26].

Furthermore, our data show that 76.5% of patients required ICU admission. This suggests a high burden of acute decompensation in OALE, which may be mitigated by earlier detection and outpatient optimization of comorbid conditions [16].

From a health systems perspective, the disproportionate reliance on emergency care and the high rate of limb loss highlight the need for capacity building in outpatient vascular diagnostics, community-level education, and continuous professional development for primary care providers [14].

Building on these considerations, the core findings of our study are discussed below in greater detail, with specific attention to clinical severity, surgical outcomes, and comparison with international literature and best practices.

The findings of this study reveal a high clinical severity among patients with obliterating atherosclerosis of the lower extremity arteries (OALE) in the Abai Region. The significant level of disability, high prevalence of comorbid conditions, and delayed presentation (more than 10 days from symptom onset in 57.6% of cases) emphasize the need to revise patient referral pathways and improve access to specialized vascular care.

When compared to the TASC II guidelines and associated studies [4,17], which prioritize early detection and minimally invasive interventions in European countries, the results of our study indicate a substantially higher amputation rate (44.1%). This figure notably exceeds the rates observed in EU countries, where major amputations typically range between 5–10%.

Further comparison with recent international literature supports the relevance of our findings. For example, the study by *Conte S.M. et al.* [8] highlights the need for standardized care in cases of chronic limb-threatening ischemia and advocates for integrated multidisciplinary management, including vascular surgery, interventional procedures, and rehabilitation strategies [8,9]. Our analysis suggests that such multidisciplinary and integrated approaches remain underdeveloped at the regional level.

The work by *Katsanos K. et al.* emphasizes the effectiveness of early endovascular intervention in patients with critical limb ischemia and highlights the importance of reducing amputation rates [7,15]. In our study sample, the rate of major amputations (44.1%) remains critically high, reflecting both delayed healthcare-seeking behavior and limited access to minimally invasive treatment options.

The study by *Criqui M.H., Aboyans V.* [9] underscores the significant role of risk factors such as diabetes mellitus and arterial hypertension—findings that are consistent with our data, where diabetes was observed in 38.8% of patients and hypertension in 72.9%. In Western European countries, proactive risk factor control strategies have contributed to reduced disease progression and lower rates of critical limb ischemia.

According to the review by *Bonaca M.P. et al.,* patients with peripheral arterial disease (PAD) are at increased risk of cardiovascular events, and aggressive risk factor modification is essential, including the use of antiplatelet agents and statins [6]. In our cohort, only 61.8% of patients received antiplatelet therapy, indicating a shortfall in pharmacological prevention.

The findings of *Akhmetova A.Zh. et al.* confirm the insufficient availability of vascular surgery in regional healthcare institutions in Kazakhstan and highlight the importance of expanding preventive and angiology services [2]. Our results support this conclusion, as only 8.8% of patients in our sample received reconstructive vascular procedures.

In addition, the analysis conducted by the World Federation of Angiology emphasizes the need for early detection of lower extremity artery disease in rural and vulnerable populations through screening programs and telemedicine technologies [18]. This is particularly relevant in the context of the Abai Region, where patients from rural areas presented with more advanced stages of the disease.

**Conclusions**

The results of this study highlight the severe clinical burden among patients with obliterating atherosclerosis of the lower extremity arteries in the Abai Region, characterized by a high rate of major amputations and limited access to reconstructive interventions. These findings underscore the urgent need for a comprehensive approach that includes preventive measures, early diagnosis, improved inter-level coordination of care, and the expansion of vascular technologies within the region.

***Conflict of Interest.*** *The authors declare that they have no conflict of interest.*

***Contribution of authors.*** *All authors were equally involved in the writing of this article.*

***Funding:*** *No funding was provided.*

***Literature:***

1. *Ахметов А.Ж., Нургалиев С.Б., Кайратова А.К.* Современные проблемы сосудистой хирургии в Республике Казахстан. Здравоохранение Казахстана. 2020. № 4. С. 18–22.

*2. Ахметов А.Ж., Ибраев Е.Б., Сапаров А.С.* Диагностика и лечение облитерирующих заболеваний артерий нижних конечностей в Казахстане. Вестник хирургии Казахстана. 2020. № 3(45). С. 27–33.

3. *Aboyans V., Ricco J., Bartelink M., Björck M., Brodmann M., Cohnert T., Collet J., Czerny M., Carlo M., Debus S., Espinola-Klein C., Kahan T., Kownator S., Mazzolai L., Naylor R., Roffi M., Röther J., Sprynger M., Tendera M.,Tepe G., Venermo M., Vlachopoulos C., Desormais I.* ESC Scientific Document Group. 2017 ESC guidelines on the diagnosis and treatment of peripheral arterial diseases, in collaboration with the European Society for Vascular Surgery (ESVS): document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries endorsed by: the European Stroke Organization (ESO) the task force for the diagnosis and treatment of peripheral arterial diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). European Heart Journal. 2018. 39(9):763–816. doi: 10.1093/eurheartj /ehx095.

4. American Heart Association. Peripheral Artery Disease. 2021. URL: https://www.heart.org (дата обращения: 06.11.2024).

5. *Bhatt A.S., et al.* Fewer hospitalizations for acute cardiovascular conditions during the COVID-19 pandemic. J Am Coll Cardiol. 2020;76(3):280–288.

6. *Bonaca M.P., Bauersachs R.M., Anand S.S., Debus E.S., Nehler M.R., Patel M.R., Fanikos J. et al.* Rivaroxaban in peripheral artery disease after revascularization. European Heart Journal. 2021. Vol. 42, No.5. P. 404–417.

7. Cardiovascular Diseases (CVDs). Available online: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds) (accessed on 27 April 2024).

8. *Conte S.M., Vale P.R.* Peripheral arterial disease. Heart, Lung & Circulation. 2018. 27(4):427–432. doi: 10.1016/j.hlc.2017.10.014.

9. *Criqui M.H., Aboyans V.* Epidemiology of peripheral artery disease. Circulation Research. 2015. Vol. 116, No. 9. – P. 1509–1526.

10. *Rajan A., Sima R.R., Natarajan S., et al.* Frailty predicts outcomes in patients with critical limb ischemia undergoing revascularization: a multicenter Japanese study. Circ Cardiovasc Interv. 2018;11(7):e006778.

11. *Roth G.A., Mensah G.A., Johnson C.O., Addolorato G., Ammirati E., Baddour L.M., Barengo N.C., Beaton A.Z., Benjamin E.J., Benziger C.P. et al.* Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019. J. Am. Coll. Cardiol. 2020. 76, 2982–3021.

12. *Grip O., Wanhainen A., Acosta S., Bjorck M.* Benefits and complications of intra-arterial thrombolysis for acute lower limb ischemia. Br J Surg. 2014;101(10):1105–1112.

13. *Hong Y.M.* Atherosclerotic cardiovascular disease beginning in childhood. Korean Circ. J.2010, 40, 1–9.

14. *Hussain M.A., Al-Omran M., Mamdani M., Eisenberg N., Premji A., Saldanha L., et al.* Efficacy of a guideline-recommended risk-reduction program to improve cardiovascular and limb outcomes in patients with peripheral arterial disease: results from a Canadian multicenter study. JAMA Surg. 2016;151(8):742–749.

15. *Katsanos K., Spiliopoulos S., Kitrou P., et al.* Comparative effectiveness of endovascular revascularization vs. major amputation for critical limb ischemia: a systematic review. JACC: Cardiovascular Interventions. 2020. Vol. 13(14). P. 1672–1681.

16. *Korabathina R., Weintraub A.R., Price L.L., Kapur N.K., Iafrati M.D., et al.* Twenty-year trends in incidence and in-hospital mortality for lower-extremity arterial thromboembolism. Circulation. 2013;128:115–121.

17. *Norgren L., Hiatt W.R., Dormandy J.A., Nehler M.R., Harris K.A., Fowkes F.G.R.* Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). Journal of Vascular Surgery. 2007. Vol. 45, Suppl S. P. S5–S67.

18. *Perlander A., Jivegård L., Nordanstig J., Svensson M., Österberg K.* Limb salvage after open and endovascular revascularization in chronic limb-threatening ischemia: a Swedish registry study. J Vasc Surg. 2020;72(6):1987–1995.

19. *Saarinen E., Vuorisalo S., Kauhanen P., Alback A., Venermo M.* Revascularization outcomes and mortality in nonagenarians with lower limb ischemia. Eur J Vasc Endovasc Surg. 2015;49(3):420–425

20. *Strong J.P., Malcom G.T., McMahan C.A., Tracy R.E., Newman W.P., Herderick E.E., Cornhill J.F.* Prevalence and extent of atherosclerosis in adolescents and young adults: Implications for prevention from the Pathobiological Determinants of Atherosclerosis in Youth Study. JAMA 1999, 281, 727–735.

21. *Toya N., Baba T., Kanaoka Y., Ohki T.* Embolic complications after endovascular abdominal aortic aneurysm repair. Surg Today. 2014;44(10):1893–1899.

22. *Timmis A., Vardas P., Townsend N., Tobica AKatus H., De Smedt D., Gale C.P., Maggioni A.P., Petersen S.E., Huculeci R., Kazakiewicz D., et al.* Eiropean Society of Cardiology. European Society of Cardiology: Cardiovascular disease statistics 2021. Eur. Heart J. 2022, 43, 716–799, Erratum in Eur. Heart J. 2022, 43, 799.

23. *Vaduganathan M., Mensah G.A., Turco J.V., Fuster V., Roth, G.A.* The Global Burden of Cardiovascular Diseases and Risk. J. Am. Coll. Cardiol. 2022. 80, 2361–2371.

24. WIFA (World International Federation of Angiology). Global Peripheral Arterial Disease Report. 2022. https://wifa.org/reports/2022

25. World Health Organization. Cardiovascular diseases (CVDs): Fact sheet. 2021. URL: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds) (accessed on 6 May 2024).

*26. Zheng Y.H., Song X.T.* Progress and prospect of the treatment of lower extremity arteriosclerosis obliterans. Zhonghua Wai Ke Za Zhi. 2021;59(12):961–964. doi: 10.3760/cma.j.cn112139-20210923-00453.

***References: [1-2]***

1. Ahmetov A.Zh., Nurgaliev S.B., Kajratova A.K. Sovremennye problemy sosudistoi khirurgii v Respublike Kazakhstan [Modern problems of vascular surgery in the Republic of Kazakhstan]. *Zdravookhranenie Kazakhstana* [Healthcare of Kazakhstan.]. 2020. № 4. pp. 18–22. [in Russian]

2. Ahmetov A.Zh., Ibraev E.B., Saparov A.S. Diagnostika i lechenie obliterirujushhikh zabolevanii arterii nizhnikh konechnostei v Kazakhstane [Diagnostics and treatment of obliterating diseases of the arteries of consciousness in Kazakhstan.]. *Vestnik khirurgii Kazahstana* [Bulletin of surgery of Kazakhstan]. 2020. № 3(45). pp. 27–33. [in Russian]

**Information about the authors:**

**Gulmira Uruzbayeva** - a PhD student of the Department of of Hospital Surgery, Anesthesiology and Intensive Care, Non-profit joint-stock company «Semey Medical University», Semey, Republic of Kazakhstan. num: +7 705 263 9776, e-mail: gulmira.uruzbayeva@smu.edu.kz, https://orcid.org/0000-0001-8897-6865

**Tolkyn Bulegenov** - Professor of the Department of Hospital and Pediatric Surgery, Non-profit joint-stock company «Semey Medical University», Semey, Republic of Kazakhstan. https://orcid.org/0000-0001-6145-9649; e-mail: tolkynbul@mail.ru

**Akmaral Mussakhanova**, Associate Professor of the Department of public health and management, Non-profit joint-stock company «Astana Medical University», Astana, Republic of Kazakhstan, https://orcid.org/0000-0002-0399-5045, e-mail: makmaral1@gmail.com

**Kenesh Dzhusupov -** Head of the Public Health Department at the International Higher School of Medicine, Bishkek, Kyrgyzstan, https://orcid.org/0000-0002-2213-1373, e-mail: k.dzhusupov@ism.edu.kg

**Onlasyn Ibekenov -** Candidate of Medical Sciences, Highest Category Surgeon, Head of the Strategic Block at the National Scientific Center of Surgery Named After A.N. Syzganov, Almaty, Republic of Kazakhstan; https://orcid.org/0000-0001-6605-6435; E-mail: onlasin72@mail.ru; Tel.: 8 707 740 8039;

**Zhanargul Smailova-** Non-profit joint-stock company "Semey Medical University". Candidate of Medical Sciences, Associate Professor, Vice-Rector for Academic and Educational Work, Semey, Republic of Kazakhstan. https://orcid.org/0000-0002-4513-4614, e-mail: zhanargul.smailova@smu.edu.kz

**Assel Baibussinova -** Non-profit joint-stock company "Semey Medical University". PhD, Acting Head of the Department of Epidemiology and Biostatistics, Semey, Republic of Kazakhstan. http://orcid.org/0000-0003-3447-6245, e-mail: Assel.baibussinova@smu.edu.kz.

**Merey Imanbayev -** Non-profit joint-stock company “Semey Medical University". Acting Head of the Department of Cardiovascular and Thoracic Surgery named after B.S. Bulanova, Semey, Republic of Kazakhstan. https://orcid.org/0000-0002-7248-0440, e-mail: merei_imanbayev@mail.ru

**Fariza Zharykbassova-** Non-profit joint-stock company "Astana Medical University", Astana, Republic of Kazakhstan. https://orcid.org/0000-0001-5282-7454. e-mail: Faryza_zh@mail.ru

**Arailym Kussainova -** PhD doctoral student, Non-profit Joint-stock Company "Semey Medical University". Department of Hospital Surgery,Anesthesiology and Intensive Care. https://orcid.org/0009-0000-6475-8185, e-mail: kusainovaarajlym8@gmail.com

**Armankyzy Aidana -** Non-profit joint-stock company "Semey Medical University".resident - doctor anesthesiologist-resuscitator. https://orcid.org/0009-0001-8451-4062, e-mail: armankyzy24@mail.ru

**Corresponding author:**

**Gulmira A. Uruzbayeva -** Department of Hospital Surgery, Anesthesiology and Intensive Care, Non-profit Joint-stock Company "Semey Medical University", Semey, Republic of Kazakhstan.

**Mailing Address:** 070000, Semey, st. Abaya 103, Republic of Kazakhstan

**E-mail:** gulmira.uruzbayeva@smu.edu.kz

**Tel:** +7 705 263 97 76

Received: 29 January 2025 / Accepted: 14 April 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2025.27.3.006***

***UDC 618.146-15-006.5***

This work is licensed under a Creative Commons Attribution 4.0 International License

# EFFICACY OF PHOTODYNAMIC THERAPY IN THE TREATMENT OF CERVICAL PRECANCEROUS CONDITIONS CAUSED BY HUMAN PAPILLOMAVIRUS

**Akmaral Ye. Khangeldi[1], https://orcid.org/0000-0003-0603-1230**
**Zaituna G. Khamidullina[1], https://orcid.org/0000-0002-5324-8486**
**Nasrulla A. Shanazarov[2], https://orcid.org/0000-0002-2976-259X**
**Maksim S. Afanasyev[3], https://orcid.org/0000-0002-5860-4152**
**Tatiana G. Grishacheva[4], https://orcid.org/0000-0002-9515-914X**
**Nagima N. Akkazhiyeva[1], https://orcid.org/0000-0003-1571-6960**
**Gulyash A. Tanysheva[5], https://orcid.org/0000-0001-9531-5950**

**[1] Astana Medical University, Astana, Republic of Kazakhstan;**
**[2] Medical Centre Hospital of President's Affairs Administration of the Republic of Kazakhstan, Astana, Republic of Kazakhstan;**
**[3] Federal State Autonomous Educational Institution of Higher Education I. M. Sechenov First Moscow State Medical University of the Ministry of Health of the Russian Federation (Sechenov University), Moscow, Russian Federation;**
**[4] The First St. Petersburg State Medical University named after Academician I.P. Pavlova, St. Petersburg, Russian Federation;**
**[5] Semey Medical University, Semey, Republic of Kazakhstan.**

**Abstract**

**Relevance:** PDT is a high-tech treatment that uses a combination of a photosensitizer, light and molecular oxygen. The method is based on the mechanisms of free radical oxidation, disruption of the vascular stroma of tumors and elimination under the influence of immune cells. It is a non-invasive, effective and safe treatment that damages and destroys structures in the affected area. However, to normalize the immune response, ensuring a stable regression of carcinogenesis, prolonged elimination of HPV is necessary.

**Aim:** to assess the status of various levels of tissue damage in cervical dysplasia in combination with PVI, using PDT as the main method of treatment.

**Search strategy:** In this study, indicators of the state of the organ, tissue, cellular and molecular levels are used to assess the course of PVI of the cervix. The role of the immune response in HPV-associated precancerous diseases of the cervix is considered. The article presents work on the treatment of dysplasia of varying degrees associated with HPV in 92 patients over a two-year period using PDT.

**Results**: The use of photodynamic therapy in women with HPV-associated cervical precancerous disease is a promising area of research. The results of the work link the role of TLRs with the development of squamous intraepithelial lesions (SIL). Further clinical studies are needed to evaluate efficacy, safety and optimal timing.

***Key words:*** *photodynamic therapy, human papillomavirus infection, squamous intraepithlial lesion, cervix.*

***For citation:***

*Khangeldi A.Ye., Khamidullina Z.G., Shanazarov N.A., Afanasyev M.S., Grishache T.G., Akkazhiyeva N.N.,* Tanysheva G.A. Efficacy of Photodynamic Therapy in the Treatment of Cervical Precancerous Conditions Caused by Human Papillomavirus // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 53-63. *doi 10.34689/SH.2025.27.3.006*

**Резюме**

# ЭФФЕКТИВНОСТЬ ФОТОДИНАМИЧЕСКОЙ ТЕРАПИИ В ЛЕЧЕНИИ ПРЕДРАКОВЫХ СОСТОЯНИЙ ШЕЙКИ МАТКИ, ВЫЗВАННЫХ ВИРУСОМ ПАПИЛЛОМЫ ЧЕЛОВЕКА

**Акмарал Е. Хангелді[1], https://orcid.org/0000-0003-0603-1230**
**Зайтуна Г. Хамидуллина[1], https://orcid.org/0000-0002-5324-8486**
**Насрулла А. Шаназаров[2], https://orcid.org/0000-0002-2976-259X**
**Максим С. Афанасьев[3], https://orcid.org/0000-0002-5860-4152**
**Татьяна Г. Гришачева[4], https://orcid.org/0000-0002-9515-914X**

**Нагима Н. Аккажиева[1],** https://orcid.org/0000-0003-1571-6960

**Гульяш А. Танышева[5],** https://orcid.org/0000-0001-9531-5950

[1] НАО "Медицинский университет Астана", г. Астана, Республика Казахстан
[2] Больница Медицинского центра Управления Делами Президента Республики Казахстан, г. Астана, Республика Казахстан
[3] Федеральное государственное автономное образовательное учреждение высшего образования Первый Московский государственный медицинский университет имени И.М. Сеченова Министерства здравоохранения Российской Федерации (Сеченовский Университет), г. Москва, Российская Федерация
[4] Первый Санкт-Петербургский государственный медицинский университет им. акад. И.П. Павлова, г. Санкт-Петербург, Российская Федерация;
[5] НАО «Медицинский университет Семей», г. Семей, Республика Казахстан.

**Актуальность:** Фотодинамическая терапия (ФДТ) представляет собой неинвазивный высокотехнологичный метод лечения, основанный на взаимодействии фотосенсибилизатора, света определённой длины волны и молекулярного кислорода. Механизм действия ФДТ включает индукцию свободнорадикального окисления, нарушение сосудистой стромы опухоли и активацию иммунного ответа, направленного на элиминацию патологических клеток. Метод отличается высокой селективностью и безопасностью, обеспечивая прицельное разрушение поражённых тканей с минимальным повреждением здоровых структур. В то же время, при лечении опухолей, ассоциированных с вирусом папилломы человека (ВПЧ), для достижения стабильной регрессии патологического процесса требуется длительная и эффективная элиминация вируса, способствующая нормализации иммунного ответа и снижению риска рецидива.

**Цель:** оценка показателей состояния различных уровней тканевого поражения при дисплазиях шейки матки в сочетании с ПВИ, с использованием ФДТ, в качестве основного метода лечения.

**Стратегия работы:** В настоящем исследовании ФДТ применялась для терапии шейки матки при вирус-ассоциированных предраковых изменениях. Стратегия оценки эффективности лечения включала анализ показателей на органном, тканевом, клеточном и молекулярном уровнях. Особое внимание уделено роли иммунного ответа при ВПЧ-ассоциированных предраковых заболеваниях. Представлены результаты наблюдения за 92 пациентками с цервикальными дисплазиями различной степени тяжести в течение двух лет, получавшими лечение с использованием ФДТ.

**Результаты:** Применение фотодинамической терапии (ФДТ) у женщин с ВПЧ-ассоциированными предопухолевыми заболеваниями шейки матки представляет собой перспективное направление клинических исследований. Полученные результаты свидетельствуют о потенциальной взаимосвязи между экспрессией Toll-подобных рецепторов (TLRs) и развитием плоскоклеточных интраэпителиальных поражений (SIL). Дальнейшие масштабные клинические исследования необходимы для уточнения эффективности, безопасности и оптимальных сроков применения ФДТ в данной категории пациентов.

***Ключевые слова:*** *фотодинамическая терапия, папилломовирусная инфекция, плоскоклеточное интраэпитлиальное поражение, шейка матки.*

***Для цитирования:***

*Хангелді А.Е., Хамидуллина З.Г., Шаназаров Н.А., Афанасьев М.С., Гришачева Т.Г., Аккажиева Н.Н., Танышева Г.А.* Эффективность фотодинамической терапии в лечении предраковых состояний шейки матки, вызванных вирусом папилломы человека // Наука и Здравоохранение. 2025. Т.27 (3), С. 53-63. doi: 10.34689/SH.2025.27.3.006

**Түйіндеме**

# HPV ТУДЫРҒАН ЖАТЫР МОЙНЫНЫҢ ІСІК АЛДЫ ЖАҒДАЙЛАРЫН ЕМДЕУДЕГІ ФОТОДИНАМИКАЛЫҚ ТЕРАПИЯНЫҢ ТИІМДІЛІГІ

**Акмарал Е. Хангелді[1],** https://orcid.org/0000-0003-0603-1230

**Зайтуна Г. Хамидуллина[1],** https://orcid.org/0000-0002-5324-8486

**Насрулла А. Шаназаров[2],** https://orcid.org/0000-0002-2976-259X

**Максим С. Афанасьев[3],** https://orcid.org/0000-0002-5860-4152

**Татьяна Г. Гришачева[4],** https://orcid.org/0000-0002-9515-914X

**Нагима Н. Аккажиева[1],** https://orcid.org/0000-0003-1571-6960

**Гульяш А. Танышева[5],** https://orcid.org/0000-0001-9531-5950

[1] "Астана медицина университеті" КеАҚ, Астана қаласы, Қазақстан Республикасы;
[2] Қазақстан Республикасы Президенті Іс басқармасы Медициналық орталығының ауруханасы, Астана қаласы, Қазақстан Республикасы;
[3] Ресей Федерациясы Денсаулық сақтау министрлігінің И.М. Сеченов атындағы Бірінші Мәскеу мемлекеттік медициналық университеті (Сеченов университеті) — жоғары білім беретін федералдық мемлекеттік автономдық білім беру мекемесі, Мәскеу қ., Ресей Федерациясы;

**[4] Академик И.П. Павлов атындағы Бірінші Санкт-Петербург мемлекеттік медициналық университеті, Санкт-Петербург қ., Ресей Федерациясы;**
**[5] "Семей медицина университеті" КЕАҚ, Семей қ., Қазақстан Республикасы.**

**Өзектілігі:** ФДТ – фотосенсибилизатор, жарық және молекулалық оттегінің комбинациясын пайдаланатын жоғары технологиялық емдеу. Әдіс бос радикалды тотығу, ісіктердің тамырлы стромасының бұзылуы және иммундық жасушалардың әсерінен жойылу механизмдеріне негізделген. Бұл зақымдалған аймақты инвазивті емес, тиімді және қауіпсіз емдеу әдісі. Дегенмен, иммундық жауапты қалыпқа келтіру, канцерогенездің тұрақты регрессиясын қамтамасыз ету, HPV-ны ұзақ жою қажет.

**Мақсаты:** емдеудің негізгі әдісі ретінде ФДТ қолдана отырып, жатыр мойны дисплазиясында тіндердің зақымдануының әртүрлі деңгейлерінің күйін PVI біріктірілімінде бағалау.

**Жұмыс стратегиясы:** Бұл зерттеуде жатыр мойнының PVI барысын бағалау үшін органның, тіннің, жасушалық және молекулалық деңгейлердің күйінің көрсеткіштері қолданылады. Жатыр мойнының HPV-ассоциацияланған ісік алды ауруларында иммундық жауаптың рөлі қарастырылады. Мақалада ФДТ көмегімен екі жыл ішінде 92 пациентте HPV-мен байланысты әртүрлі дәрежедегі дисплазияны емдеу бойынша жұмыс жүргізілген.

**Нәтижелер:** HPV-мен байланысты жатыр мойны обыры алды ауруы бар әйелдерде фотодинамикалық терапияны қолдану зерттеудің перспективалық бағыты болып табылады. Жұмыстың нәтижелері TLR рөлін жалпақ эпителий ішілік зақымданулардың (SIL) дамуымен байланыстырады. Тиімділікті, қауіпсіздікті және оңтайлы уақытты бағалау үшін қосымша клиникалық зерттеулер қажет.

***Түйінді сөздер:*** *фотодинамикалық терапия, адам папилломавирустық инфекциясы, скамозды интраэпителиальды зақымдану, жатыр мойны.*

***Дәйексөз үшін:***

*Хангелді А.Е., Хамидуллина З.Г., Шаназаров Н.А., Афанасьев М.С., Гришачева Т.Г., Аккажиева Н.Н.,Танышева Г.А.* HPV тудырған жатыр мойнының ісік алды жағдайларын емдеудегі фотодинамикалық терапияның тиімділігі // Ғылым және Денсаулық. 2025. Т.27 (3), Б. 53-63. doi: 10.34689/SH.2025.27.3.006

**Introduction**

The cervix is an important part of the female reproductive system, and diseases related to its pathology significantly affect health and quality of life. One of the most common causes of precancerous changes in the cervix is infection with the human papillomavirus (HPV). HPV infection can lead to the development of dysplasia and cervical carcinoma, which in turn increases the risk of cervical cancer [12,22]. Cervical cancer ranks second in prevalence among oncological diseases in women in the Republic of Kazakhstan. According to data from the National Cancer Registry monitoring the epidemiological situation in the country, 1,952 new cases of cervical cancer were registered in 2020. This accounts for 7.3% of all newly diagnosed malignant neoplasms in women. The highest incidence rate is observed in the age group of 45 to 49 years [1].

In recent decades, there has been an increase in HPV-associated diseases, making the search for effective treatment methods a pressing issue. HPV is a leading risk factor for the development of cervical dysplasia and its progression to cancer; therefore, timely diagnosis and treatment of precancerous conditions are crucial [4,11,31].

Modern treatment methods for precancerous cervical diseases include surgical interventions such as cervical conization, cryotherapy, and laser therapy. However, these methods have several limitations, including high invasiveness, long recovery periods, and the risk of recurrence [3,15]. In this context, photodynamic therapy (PDT) has attracted attention in recent years as an alternative treatment method for precancerous conditions.

PDT is a non-invasive method that uses photosensitizers activated by light of a specific wavelength. When the photosensitizer acts on pathological cells, it causes their destruction, enabling effective treatment of precancerous states [2,16]. Importantly, photodynamic therapy not only contributes to tumor mass reduction but also stimulates the body's immune response. This, in turn, promotes a higher level of remission and reduces the risk of disease recurrence. Lee et al. confirmed in their study that PDT significantly influences the management of HPV-associated cervical cancer by stimulating the immune response and improving long-term therapeutic outcomes [18].

Photodynamic therapy is based on mechanisms involving free radical oxidation, disruption of tumor vascular stroma, and activation of immune responses that lead to the elimination of pathologically altered cells. The method is characterized by high selectivity, non-invasiveness, effectiveness, and safety, providing localized damage and destruction of affected tissues with minimal impact on healthy structures. An additional component of therapy is systemic photobiomodulation with laser blood oxygenation (SPLBO), whose mechanism of action is based on photobiological effects. Under light radiation, physicochemical rearrangements of protein structures occur in tissues, accompanied by changes in enzyme system activity and the structural-functional properties of cell membranes.

As a result of SPLBO:

- **Erythrocytes:** membrane permeability and deformability increase, aggregation ability decreases, and ATP and 2,3-diphosphoglycerate levels rise, improving the oxygen-transport function of blood.
- **Leukocytes:** activity of membrane receptors is enhanced, DNA synthesis is activated, phagocytic activity increases, secretion of bactericidal cationic proteins and production of interleukins and growth factors intensify, DNA repair enzyme systems are activated, and the reactivity of immunocompetent cells changes.

• **Platelets:** structural changes in membranes occur, and rheological activity is stimulated.

• **Blood plasma:** bactericidal, antioxidant, and proteolytic properties are enhanced; activity of complement, lysozyme, natural and immune antibodies increase; coagulation, anticoagulation, and fibrinolytic properties normalize. A sharp decrease in lipid peroxidation products is also observed.

The complex of these changes indicates the development of a pronounced systemic immunological response, which may contribute to prolonged elimination of human papillomavirus (HPV) and reduce the risk of disease recurrence.

Photodynamic Therapy (PDT) has recently been actively considered as an innovative alternative to traditional methods for treating cervical dysplasia, especially in cases associated with human papillomavirus (HPV) infection. Accumulated clinical data confirm the high efficacy of this approach. According to several studies, PDT contributes to significant improvement in the condition of women with precancerous cervical lesions (Goodman et al., 2024) [10].

A systematic review conducted by Goodman and colleagues highlights the organ-preserving potential of the method: PDT demonstrates favorable outcomes in the regression of cervical intraepithelial neoplasia (CIN) and HPV infection clearance (Goodman et al., 2024) [10].

Furthermore, significant contributions to the evaluation of PDT efficacy were made by Sharma et al., who presented clinical trial results confirming the safety and minimal invasiveness of this method in treating cervical pathologies (Sharma et al., 2023) [24].

Additionally, clinical observations report a complete remission rate of up to 90% three months after PDT, with HPV elimination observed in 75% of patients after 12 months (Van der Zee et al., 2005) [27].

Despite these promising prospects, experts emphasize the need for further randomized studies aimed at elucidating the mechanisms of PDT action, investigating long-term outcomes, and assessing recurrence risk.

The aim of the present study was to determine the efficacy of photodynamic therapy in treating HPV-associated precancerous cervical conditions. To achieve this goal, a review of the existing scientific literature and an analysis of clinical observations were conducted.

**Materials and Methods**

This study analyzed data on the use of photodynamic therapy (PDT) in women with HPV-associated precancerous cervical lesions. The study included both retrospective and prospective components.

The retrospective analysis was based on medical records of patients treated between 2022 and 2024, diagnosed with cervical intraepithelial neoplasia (CIN). Clinical characteristics, examination results, treatment regimens applied, and the dynamics of the pathological process during follow-up were analyzed. Data sources included archival materials from the Medical Center UDP Hospital and the gynecological department of MedInService LLC (Moscow).

The prospective observation covered the period 2023–2024 and included patients who provided written informed consent. These women underwent PDT treatment under both outpatient and inpatient care. The study evaluated not only immediate clinical efficacy but also recurrence rates and therapy tolerability.

For the retrospective component, the following parameters were collected and analyzed:

• **Clinical-epidemiological data:** age, gynecological history, information on HPV vaccination and prior treatments;

• **Virological data:** virus type, presence of condylomas, viral load measured by PCR;

• **Immunological data:** mRNA expression levels of Toll-like receptors TLR2, TLR3, TLR4, and TLR8, assessed by quantitative real-time RT-PCR.

For a more in-depth assessment of the patients' condition, a leukocyte differential blood count analysis was used to evaluate the immune responses accompanying the disease progression.

The study was conducted at the Department of Obstetrics and Gynecology No. 1 of the non-commercial joint-stock company "Astana Medical University," as well as at specialized institutions in Moscow, including Guta Clinic and the I.M. Mechnikov Research Institute of Vaccines and Sera.

**Participants and Grouping**

The study included 92 women (age range: 18–50 years, median 31.3 years, IQR = 27–39), divided into three groups:

1.Control group – 13 patients without cervical pathology;

2.LSIL group – 13 women with low-grade squamous intraepithelial lesions;

3.HSIL group – 66 patients with high-grade intraepithelial lesions.

*Inclusion Criteria:*

- Age 18–65 years;
- Confirmed intraepithelial lesions;
- Available data on the expression of at least one TLR;
- Absence of current inflammatory infections;
- Voluntary consent to PDT and participation in the study.

*Exclusion Criteria:*

- Pregnancy or lactation;
- Negative results of RT-PCR;
- Contraindications to PDT;
- Ongoing antitumor therapy.

*Sample Collection and Processing*

A total of 92 samples of ectocervical and endocervical epithelial cells were collected from patients at the gynecological department of the Hospital of the Presidential Administration in Astana. Samples were delivered to the Molecular Immunology Laboratory at the I.M. Mechnikov Research Institute of Vaccines and Sera for analysis of TLR (Toll-like receptor) gene expression. Cervical smears were collected following strict protocols (patients refrained from local medications and hygienic procedures prior to sampling). TLR expression was quantified using the DT-96 instrument (DNA-Technology LLC). GAPDH mRNA was used as the control gene. mRNA isolation employed affinity chromatography methods, and primers were designed with Vector NTI Advance software.

**Photodynamic Therapy (PDT) Procedure**

Photodynamic therapy was performed after the completion of the patients' menstrual cycle to avoid any influence of menstruation on treatment effectiveness.

The PDT protocol consisted of three main stages:

**Photosensitizer (PS) administration:**

Patients received an intravenous injection of a chlorin e6-based photosensitizer over 30 minutes. The dose ranged from 1 to 1.2 mg per kilogram of body weight to achieve optimal PS concentration in target tissues.

**Darkness period:**

Following the injection, patients observed a dark period of 24–48 hours to minimize light exposure and ensure complete elimination of the photosensitizer from healthy tissues. This step was crucial to reduce phototoxicity risk and improve treatment efficacy.

**Medicinal products used:**

PHOTOLON (PN015948/01, Belmedpreparaty RUE, Belarus) was used as an adjunct to promote more effective accumulation of the photosensitizer in pathological tissues.

Accumulation of PS in affected tissues and its clearance from healthy tissues occurred within three hours after injection, providing optimal conditions for subsequent light exposure.

**Second Stage: Photodiagnostics (PD)**

At the second stage, photodiagnostics was performed to assess the accumulation of the photosensitizer (PS) and to map the tumor area. A LED light source (Polironic LLC, Russia) emitting light at 400 nm was used for this purpose. The source was equipped with a yellow optical filter mounted on a video colposcope (Kernel KN-2200A-HD, China). This filter blocked ultraviolet radiation and allowed detection of red fluorescence, indicating the localization of the PS in the target tissue.

**Third Stage: Targeted Irradiation**

At the third stage, targeted irradiation was performed on the cervical canal and the vaginal part of the cervix. Photoirradiation was directed at the surface of the cervix, which activated the PS and destroyed pathological tissues.

The photoirradiation time (T, minutes) was calculated using the established formula (Formula 1). To determine the areas of the cervical canal and the cervical surface, formulas 2 and 3 were used, allowing precise dosing of the light exposure depending on the size of the irradiated area.

**Target Photoirradiation Doses (Es):**

- 334 J/cm² for the cervical canal.
- 290 J/cm² for the cervical surface.

For photoirradiation of the cervical canal, a flexible cylindrical diffuser with a working length of 4 cm (l) and radius of 0.1 cm (r) was used. The power of photoirradiation (P) was 1 W.

The cervical surface was irradiated using macro- or microlenses for external exposure. The procedure was performed remotely and perpendicular to the target area. The irradiation spot diameter was 2.5 cm (d), and the photoirradiation power (P) was 1.7 W, ensuring a dose of Es = 290 J/cm².

**Formulas for Calculating Photoirradiation Time (T):**

1. Total irradiation time was calculated by the formula:

T=Es×S60×P(Formula 1)T = \frac{Es \times S}{60 \times P} \quad \text{(Formula 1)}T=60×PEs×S(Formula 1)

Where:

- Es — photoirradiation dose (J/cm²)
- P — photoirradiation power (W)
- S — irradiated surface area (cm²)

2. The irradiated area for the cervical canal was calculated as:

Scc=6.28×r×l(Formula 2)S_{cc} = 6.28 \times r \times l \quad \text{(Formula 2)}Scc=6.28×r×l(Formula 2)

Where:

- r — diffuser radius (cm)
- l — diffuser length (cm)

3.The irradiated area for the cervical surface was calculated as:

Scs=0.785×d2(Formula 3)S_{cs} = 0.785 \times d^2 \quad \text{(Formula 3)}Scs=0.785×d2(Formula 3)

Where: d — irradiation spot diameter (cm)

Power density control was performed using a laser irradiation indicator PDI-01 (Alcom Medica LLC, Russia), ensuring accurate dosing of photoirradiation. A laser device “LAHTA-MILON” 662-2, emitting light at 662 nm, was used to activate the photosensitizer.

**Darkness Protocol Before and After the Procedure**

After photodynamic therapy (PDT), patients were required to strictly follow the darkness protocol to minimize light exposure and ensure safety during photosensitizer elimination from tissues.

1. **Wearing sunglasses:** Patients were advised to wear sunglasses for 24–48 hours post-procedure to protect their eyes from light exposure and prevent phototoxic reactions.

2. **Limiting use of phones and tablets:** The use of mobile devices and tablets was restricted, with screens set to minimum brightness to reduce light exposure.

3. **Room lighting:** In rooms where patients stayed, illumination levels were kept below 50 lux to prevent photosensitization and ensure safe elimination of the photosensitizer.

4. **Applying sunscreen:** Patients were recommended to apply sunscreen with SPF 50 when going outdoors in sunny weather to protect their skin as needed.

**Investigated Parameters**

To evaluate clinical-epidemiological, immunological, and digital features in each group, the following parameters were used:

- **Age (years):**
- Mean ± standard deviation (M ± SD) and median (Me).

The control group patients had a mean age of 30 years (95% confidence interval [CI]: 29–38).

The mean age of patients with cervical intraepithelial lesions of varying severity differed by group. In the group with low-grade intraepithelial lesions (LSIL), the mean age was 27 years (95% CI: 27–31), whereas in the group with high-grade lesions (HSIL), the mean age was 37 years (95% CI: 30–39).

- **Menarche (years):**
- The age of menarche was the same across all groups, with a median age of 13 years at first menstruation.
- **Age at sexual debut (years):**

The mean age of onset of sexual activity also did not differ between groups and was 18 years.

- **Number of sexual partners:**

This differed depending on lesion severity. The median number of sexual partners was 3 in the control and LSIL groups, whereas it was 5 in the HSIL group, potentially indicating a relationship between a higher number of sexual contacts and more severe intraepithelial changes.

**Duration of Primary Viral Infection (PVI), months:**

- In the LSIL group, the mean duration of PVI was 22.35 months (95% CI: 6.35–61.82).
- In the HSIL group, the mean duration was 13.8 months (95% CI: 3.08–30.83).

**Immune response parameters and viral load:**

- **Leukocyte count in cervical secretion:**
  - Control group: mean 8 cells per field of view.
  - LSIL group: mean 5 cells.
  - HSIL group: mean 13 cells.
- **Viral load (Log(10^5)):**
  - LSIL group: mean 5.55 (95% CI: 4.8–6.62).
  - HSIL group: mean 5.8 (95% CI: 5.1–6.6).
- **Acetowhite epithelium area (%):**
  - Control group: mean 18.06% (95% CI: 10.13–25.98).
  - LSIL group: mean 36.4% (95% CI: 25.5–47.37).
  - HSIL group: mean 32.13% (95% CI: 27.86–36.39).

**5. Leukocyte responses and immunological indicators**

- **Types of leukocyte immune responses:**

Blood analysis revealed differences in predominant types of leukocyte response among the studied groups.

- In the control group, the second type of leukocyte response predominated (66.7%).
- In the LSIL group, the first type of response was more frequent (38.5%).
- In the HSIL group, the third type predominated (37.9%).

**Expression of Toll-like receptors (TLRs)**

The gene expression levels of immune receptors TLR2, TLR3, TLR4, and TLR8 were assessed by quantitative reverse transcription PCR (qRT-PCR). The results are presented in Table 1.

*Table 1.*

**Efficacy of photodynamic therapy in the treatment of cervical precancerous conditions caused by human papillomavirus.**

| Parameter | Statistics | Control (n = 13) | LSIL (n = 13) | HSIL (n = 66) |
|---|---|---|---|---|
| TLR2 (OE) | M ± SD / Me | 0.95 | 2.26 | 1.54 |
| 95% CI / $Q_1$–$Q_3$ | 0.73–1.27 | 1.19–43.8 | 1.04–2.18 | |
| TLR3 (OE) | M ± SD / Me | 0.89 | 1.24 | 1.27 |
| 95% CI / $Q_1$–$Q_3$ | 0.8–1.23 | 0.69–2.32 | 0.30–2.49 | |
| TLR4 (OE) | M ± SD / Me | 0.84 | 2.14 | 1.36 |
| 95% CI / $Q_1$–$Q_3$ | 0.72–0.41 | 1.19–60.28 | 0.9–2.87 | |
| TLR8 (OE) | M ± SD / Me | 0.9 | 2.15 | 1.3 |
| 95% CI / $Q_1$–$Q_3$ | 0.72–1.29 | 0.90–2.56 | 0.94–2.02 | |

*Note: M — mean; SD — standard deviation; Me — median; $Q_1$–$Q_3$ — interquartile range; CI — confidence interval*

**Analysis of TLR Expression.** The analysis of TLR expression between Group I and the other groups prior to photodynamic therapy (PDT) revealed only minor differences. Group II exhibited a trend toward increased TLR4 expression compared to the other groups (P = 0.066); however, the absolute expression level of TLR4 in this group remained the lowest when compared to Groups I and III, which was statistically significant (P = 0.035).

Regarding TLR3, a trend toward decreased expression was observed in the control group compared to the other groups (P = 0.099), although the differences did not reach statistical significance.

TLR8 expression was significantly reduced in Groups I and II compared to Group III (P = 0.032).

In the studied cohort, TLR4 and TLR8 expression levels showed a significant decrease—by 7% and 13%, respectively—two hours after cervical PDT (P = 0.03 and P < 0.001). In contrast, the expression levels of TLR2 and TLR3 did not show significant changes two hours post-PDT (P = 0.968 and P = 0.701, respectively).

**Changes in TLR Expression in Patients with LSIL (Group III).** A statistically significant 1.3-fold decrease in TLR8 expression was observed two hours after photodynamic therapy (PDT) in patients with low-grade squamous intraepithelial lesions (LSIL) (P = 0.003). Expression levels of TLR2 and TLR4 remained slightly elevated compared to the control group, with increases of 74.7% and 42.7%, respectively (P = 0.144 and P = 0.069). Expression levels of TLR3 and TLR8 decreased to values comparable to those observed in the control group.

**Changes in TLR Expression in Patients with HSIL (Group III).** A 1.1-fold decrease in TLR8 expression was recorded two hours after PDT in patients with high-grade squamous intraepithelial lesions (HSIL), with the difference reaching statistical significance (P = 0.042). Among patients with cervical intraepithelial neoplasia grade 3 (CIN3), a trend toward increased TLR3 expression was observed (P = 0.067), although the change did not reach statistical significance. A modest increase in TLR2 expression by 36.8% was also noted (P = 0.231), while expression levels of TLR3, TLR4, and TLR8 decreased to levels comparable to those in the control group.

**Categorical Parameters and Their Distribution Among Study Groups**

**Presence of Subjective Complaints:** In the control group, 23.1% of participants reported subjective complaints. In the subgroup with low-grade squamous intraepithelial lesions (LSIL), such symptoms were observed in 15.4% of women, while in the group with high-grade lesions (HSIL), the rate was 16.7%.

**History of Therapeutic Intervention:** Analysis of medical history revealed that 76.9% of women in the control group had previously undergone therapeutic treatment. This parameter was lower in the LSIL and HSIL subgroups—61.5% and 42.4%, respectively.

**Gynecological History:** The prevalence of gynecological conditions in medical history was comparable across groups: 69.2% in both the control and LSIL groups, and 72.7% among women with HSIL.

**History of Human Papillomavirus (HPV) Infection:**

HPV infection was documented in 46.2% of patients in the control group. In the LSIL group, this proportion was 23.1%, whereas in the HSIL group, it reached 53.0%.

**Type of HPV Infection Identified:**

In the LSIL group, HPV co-infection (multiple HPV types) predominated, accounting for 53.8% of cases. In contrast, women with HSIL more frequently had mono-infections, with a rate of 57.6%.

*Table 2*

**HPV Infection Characteristics Among Study Groups.**

| HPV Infection Characteristic | Group I(Control, n = 13) | Group II(LSIL, n = 13) | Group III(HSIL, n = 66) | P-value |
|---|---|---|---|---|
| Absence of active HPV infection | 13 (100%) | 2 (15.4%) | 7 (10.6%) | <0.001 |
| HPV mono-infection | 0 (0%) | 4 (30.8%) | 38 (57.6%) | — |
| HPV co-infection (multiple types) | 0 (0%) | 7 (53.8%) | 21 (31.8%) | — |

*Detection of Acetowhite Epithelium During Colposcopy*

Diagnostic colposcopic examination revealed the presence of acetowhite epithelium in 15.4% of patients in the control group. A substantially higher detection rate was observed in patients with LSIL (92.3%) and HSIL (80.3%).

*Statistical Analysis*

Statistical analysis was performed using Visual Studio Code 2 (v.1.66.2) with Python 3.12.X, employing statistical packages including pandas, scipy, matplotlib, and seaborn.

The Shapiro–Wilk test was used to assess the normality of quantitative variables. Variables with a normal distribution were described using the mean (M), standard deviation (SD), and 95% confidence interval (95% CI). For variables that did not follow a normal distribution, the median (Me) and interquartile range (IQR), defined by the 25th and 75th percentiles, were reported.

Categorical variables were presented as absolute (n) and relative (%) frequencies. Comparisons of independent quantitative variables with normal distribution were conducted using one-way analysis of variance (ANOVA), followed by Tukey's post hoc test, provided that homogeneity of variances was confirmed. For independent variables with non-normal distribution, the Kruskal–Wallis test was applied, followed by Dunn's test with Holm's correction for multiple comparisons.

The strength and direction of the association between two variables were assessed using Spearman's rank correlation coefficient (r□). For paired samples, comparisons of quantitative variables were performed using the Wilcoxon signed-rank test.

Statistical significance was defined as $P < 0.05$.

**Results**

TLR8 may serve as a potential early molecular immunological marker for the progression of HPV infection, given its highest expression levels across all groups and the pronounced suppressive effect of photodynamic therapy (PDT) observed in our study.

Our study has several limitations, including the absence of a comparative treatment method, lack of a standardized approach to HPV testing, and variability in HPV types and viral load among patients.

Nevertheless, the study is based on data obtained from real-world clinical practice, which represents a valuable contribution to evaluating the impact of PDT on TLR expression in HPV-associated cervical lesions and understanding its potential as a prognostic factor for treatment efficacy.

Additionally, we did not assess TLR expression in biological material obtained via liquid biopsy, which may influence the results considering TLR expression in the stroma. However, one of the advantages of PDT as a treatment method lies in its ability to modulate TLRs: activating them in suppressed conditions or suppressing their overexpression, as demonstrated in our study. This dual regulatory effect highlights PDT's potential as a promising therapeutic approach for HPV-associated cervical lesions.

The study demonstrated that photodynamic therapy is highly effective in treating precancerous cervical conditions. Most patients showed significant clinical improvement, including regression of atypical cells and normalization of cytological findings. Approximately 75% of women exhibited no signs of atypia six months after completing the treatment course.

Complete regeneration of cervical tissues without scar formation was observed in 15% of cases, confirming the low invasiveness of PDT. These results may indicate the development of a positive systemic immune response that contributes to prolonged elimination of human papillomavirus.

However, it should be noted that the efficacy of PDT may vary depending on the photosensitizer used and the stage of the disease. Therefore, decisions regarding the use of PDT for treating women with HPV-associated precancerous cervical lesions should be made on an individual basis, considering all risk factors and in close consultation between the patient and her healthcare provider.

Among the TLRs analyzed in our study, the most significant changes were observed for TLR8, which decreased in all groups two hours after photodynamic therapy (PDT). The greatest reduction was recorded in patients with severe dysplasia (HSIL/CIN III), potentially indicating modulation of the inflammatory response accompanied by correction of the immune response in the damaged tissues.

Our results confirm that PDT effectively reduces TLR4 expression, which may reflect modulation of inflammatory factors and alteration of the local immune microenvironment in cervical lesions. These changes suggest that PDT exerts a systemic effect on the immune response, contributing to reduced inflammation and normalization of tissue condition.

The study also noted a phenomenon of TLR3 overexpression in the group with low-grade cytological diagnosis (LSIL), as well as a decrease in TLR3 expression in the group with severe dysplasia (HSIL/CIN III). However, these changes were not statistically significant ($p = 0.099$), indicating the need for further research to better understand the impact of PDT on TLR3 expression depending on disease stage.

Furthermore, no significant changes in TLR2 expression were found two hours after PDT, which may be related to the diversity of HPV types among patients, potentially influencing the immune response. These observations highlight the necessity for further studies to identify the precise mechanisms by which PDT affects TLR expression and the associated immune responses.

**Discussion**

The conducted study aligns with both national and global strategies for the prevention, diagnosis, and treatment of clinical manifestations of human papillomavirus infection (HPV) of the cervix, supporting the World Health Organization's goals to reduce the incidence and mortality of cervical cancer.

Photodynamic therapy (PDT) has established itself as a promising treatment modality for malignant neoplasms due to its minimally invasive nature, low systemic toxicity, and potent immunomodulatory effects. Unlike conventional treatment methods such as surgery and radiotherapy, PDT targets pathological tissues directly with minimal damage to healthy structures. This facilitates cervical tissue restoration with minimal scarring and improves the overall clinical condition of patients.

Moreover, PDT stimulates the body's immune response, which is crucial for treating HPV-associated infections. As noted in a recent review by Fan et al. (2024), photodynamic therapy exerts not only a local cytotoxic effect on tumor cells but also modulates the immune response by activating various molecules and receptors, including Toll-like receptors (TLRs), potentially promoting long-term viral clearance and preventing disease recurrence [8].

Our study demonstrated that PDT can significantly influence the expression of TLR molecules, confirming the method's capacity to modulate the immune response in cervical tissues. This is particularly relevant in the context of HPV-associated diseases, where modulation of inflammatory and immune processes is critical for achieving sustained remission and preventing disease progression.

Nevertheless, despite promising results, this study has several limitations. Notably, the absence of a comparative analysis with alternative treatment methods limits the direct assessment of PDT's advantages. Additionally, the heterogeneity of HPV types among included patients may influence treatment outcomes. These factors underscore the need for further research involving larger, more homogeneous cohorts and inclusion of control groups to objectively evaluate the efficacy and safety of PDT in treating HPV-associated cervical lesions of varying severity.

One of the key advantages of PDT is its high antiviral efficacy. The mechanism is based on the targeted action of activated photosensitizers on the viral genome, promoting viral DNA destruction and subsequent elimination from the body. The effectiveness of this mechanism is supported by PCR analysis results demonstrating a high rate of HPV DNA clearance following treatment. Due to this capability, PDT represents a particularly promising approach for treating HPV-associated diseases such as cervical intraepithelial neoplasia (CIN), especially at early stages before progression to invasive cancer [26].

Furthermore, the combination of minimal tissue damage, strong antiviral activity, and restoration of cervical structural functions justifies the use of PDT as a highly pathogenetically grounded treatment method. These characteristics contribute to a reduced recurrence rate, which is especially important for young women concerned about preserving reproductive function. Studies such as those by *Hussain et al*. [13] confirm PDT's superior efficacy compared to other treatments like cryotherapy and highlight its advantage in maintaining patients' reproductive potential.

Photodynamic therapy offers unique opportunities for the treatment and prevention of cervical diseases, including CIN and cervical cancer. According to research by Ishchenko A.I., one of the key features of PDT is its minimal invasiveness and the lack of need for prolonged rehabilitation post-procedure, which significantly reduces costs and enhances economic efficiency. This is particularly relevant when patients can quickly return to their normal activities without downtime [14].

The application of PDT is not limited to cervical cancer treatment; it can also serve as an important component of preventive programs, particularly for women with prior cervical lesions.

Following organ-preserving treatment of the cervix with PDT, thorough dynamic follow-up is necessary for early detection of potential recurrences. Recommended surveillance includes regular cytological examinations of exocervical and endocervical scrapings and PCR testing for HPV presence and types. Colposcopy remains an essential tool for visual monitoring of cervical status in the post-therapeutic period, enabling timely identification of pathological changes and informing further patient management.

However, recurrence of cervical intraepithelial neoplasia (CIN) and cervical cancer remains a significant challenge despite modern treatment methods, including PDT. According to data published in the *European Journal of Obstetrics & Gynecology and Reproductive Biology* [17], recurrence rates range from 5% to 25%, with most recurrences diagnosed within the first 24 months after treatment. This underscores the necessity for ongoing research to evaluate the long-term efficacy of PDT in treating and preventing cervical diseases.

Studies such as those by *Park J. et al.* (2019) and *Prakash S.* et al. have demonstrated that PDT is a safe and effective alternative to conventional treatments for cervical dysplasia. These studies particularly highlight PDT's ability to treat precancerous cervical conditions without surgical intervention, thus reducing the risk of postoperative complications and restoring cervical structure with minimal functional impairment [20,21].

Special attention should be given to the use of PDT in patients unable to undergo traditional surgery due to contraindications, desire to preserve fertility, or preference for less invasive treatment. In such cases, PDT represents an optimal alternative, effectively eliminating pathological changes while preserving the natural cervical anatomy.

A notable study by *M.C. Choi et al.* compared the efficacy of PDT combined with loop electrosurgical excision procedure (LEEP or conization) in young women diagnosed with CIN II and III. The results showed that 98.1% of patients achieved complete remission one year post-treatment, indicating high efficacy in preserving fertility and preventing recurrence [5]. Thus, PDT is a promising method

for treating dysplasias, offering high effectiveness with minimal risk and preserving reproductive function [9].

A 2018 systematic review on the efficacy and safety of PDT for treating CIN and HPV infection highlighted both the beneficial effects and potential adverse reactions of the method. The main side effects included mild to moderate pain and edema in the treated area, which are generally transient, indicating relatively low trauma compared to surgical treatments [29].

Studies have also shown that photodynamic therapy (PDT) exhibits efficacy comparable to electrosurgery in the treatment of precancerous cervical lesions. For instance, a study published in Gynecologic Oncology in 2015 found no significant differences in clinical effectiveness between PDT and electrosurgical methods, confirming the high competitiveness of PDT in managing cervical intraepithelial neoplasia (CIN) [16,32].

Moreover, as highlighted in a systematic review by *Zepeda et al.,* PDT represents a promising approach for both precancerous lesions and cervical cancer. In particular, the use of the photosensitizer AlPcSmix demonstrated high efficacy in eradicating differentiated tumor cells as well as resistant cancer stem cells (CSCs). Application of PDT induced pronounced phenotypic changes in cells, including reduced proliferative activity and increased cytotoxicity, making the method especially promising for treating more advanced disease forms [30,31].

Nonetheless, to achieve optimal therapeutic efficacy, further studies on dose-dependent responses are needed. This is essential to precisely determine the maximum antitumor activity while minimizing effects on healthy tissues, thereby further improving the safety and effectiveness of the method.

Research conducted by *Della Fera A.N., Warburton A.,* and *Coursey T.L.* supports the potential of PDT using methyl aminolevulinate in patients with HPV-associated precancerous cervical lesions. Methyl aminolevulinate is one of the most commonly used photosensitizers for treating precancerous cervical conditions, offering good activation under specific conditions and selective destruction of atypical cells [7,25].

The study by *Lee et al.* emphasizes that for precancerous cervical lesions such as CIN I, a watchful waiting approach is acceptable, whereas active treatment is recommended for more severe forms, CIN II and III. Standard treatment options include PDT, cryotherapy, thermal ablation, and focused ultrasound. The choice of therapy should depend on the severity and extent of lesions, as well as the clinical context and patient condition [19,23].

The present study, conducted in Kazakhstan, is the first to evaluate the impact of PDT on the expression of TLR2, TLR3, TLR4, and TLR8 in cervical epithelial cells with HPV-associated lesions of varying severity. This represents an important contribution to understanding the molecular mechanisms of PDT, particularly regarding its effect on immune receptors such as TLRs, which play a crucial role in the immune response to viral infections and neoplastic changes.

However, it should be noted that this study involved a limited patient sample and a follow-up period of only one year. This restricts the ability to obtain long-term data on recurrence rates and potential delayed consequences of PDT application. To gain a more comprehensive understanding of the long-term effectiveness of PDT, further studies with extended follow-up and larger patient cohorts are needed. Such research will help clarify the role of PDT in preventing recurrences and maintaining long-term cervical health in women with HPV-associated lesions.

**Conclusions**

**TLR Expression Levels and Clinical Indicators.** The mRNA expression levels of TLR2, TLR3, TLR4, and TLR8 can serve as important biomarkers for assessing the severity of HPV-associated lesions. This opens new avenues for molecular diagnostics, enabling not only the determination of dysplasia degree but also the evaluation of the body's response to treatment. Additionally, lymphoid and neutrophilic infiltration, as well as leukocyte count in cervical secretions, are important indicators of inflammation and immune response to infection, which may aid in predicting therapy effectiveness and monitoring disease progression.

**Efficacy of Photodynamic Therapy (PDT).** The most pronounced effect of PDT was observed in cases of severe cervical dysplasia, highlighting the importance of an individualized treatment approach. Despite certain limitations in PDT use for milder cases, its high efficacy in severe lesions is confirmed by clinical and virological outcomes. This suggests the potential of PDT as a first-line therapy in advanced stages of the disease, particularly for women wishing to preserve reproductive function.

**Role of Immunological Markers.** Integration of immunological markers with clinicopathological data and digital diagnostic tools (such as colposcopy and PCR) significantly improves diagnostic accuracy and enables more precise monitoring of treatment effectiveness. This is especially important for assessing parameters like viral load, inflammation level, and immune response, which influence prognosis.

**HPV Eradication and Prevention of Malignant Transformation.** There is strong evidence that PDT contributes to the eradication of human papillomavirus and prevents malignant transformation of cells. This supports the use of PDT as a highly effective, minimally invasive treatment approach consistent with modern oncology trends emphasizing tissue preservation and minimization of intervention while maintaining high therapeutic efficacy.

In conclusion, our findings confirm the promising future of photodynamic therapy for treating HPV-associated cervical dysplasia. However, further studies are needed to evaluate the long-term efficacy and safety of the method, as well as to advance technologies ensuring broader accessibility and improved quality of treatment.

***Conflict of Interest**: The authors declare no conflicts of interest.*

***Author Contributions**: All authors equally contributed to the conception, execution, analysis, and writing of this article.*

***Statement**: We declare that this material has not been previously published and is not under consideration for publication elsewhere.*

***Funding**: No external funding was received.*

***Literature:***

1. *Шаназаров Н.А., Кисикова С.Д., Албаев Р.К.,*

*Афанасьев М.С., Хамидуллина З.Г., Гришачева Т.Г., Хангелді А.Е.* Применение фотодинамической терапии у женщин с ВПЧ-ассоцированным предопухолевым заболеванием шейки матки. Обзор литературы // Наука и Здравоохранение. 2023. 4(Т.25). С. 231-240. *DOI 10.34689/SH.2023.25.4.028*

2. *Alper J., Reeder K., Liao H.* et al. Photodynamic therapy in the management of high-grade cervical intraepithelial neoplasia. *Obstetrics & Gynecology*. 2019;133(4):741-748.

3. *Avritscher R., Shambaugh L., Gilks B.* et al. Comparison of laser ablation and photodynamic therapy for treating cervical dysplasia. *Lasers in Surgery and Medicine*. 2018;50(3):262-268.

4. *Brissette S., Brasseur P., Lefebvre C.* et al. Long-term outcomes of photodynamic therapy for HPV-induced cervical dysplasia. *Journal of Photochemistry and Photobiology B: Biology*. 2021;210:111998.

5. *Choi M.C., Jung S.G., Park H.* et al. Photodynamic therapy for management of cervical intraepithelial neoplasia II and III in young patients and obstetric outcomes. Lasers Surg Med. 2013;45(9):564–72. https://doi.org/10.1002/lsm.22187

6. *Choi W., Shin S., Lee E.* et al. The effect of photodynamic therapy on the regression of HPV-induced cervical intraepithelial neoplasia: A clinical study. *International Journal of Cancer*. 2020;147(10):2735-2742.

7. *Della Fera A.N., Warburton A., Coursey T.L., Khurana S., McBride A.A.* Persistent Human Papillomavirus Infection // Viruses. 2021 Feb 20. 13(2):321. doi: 10.3390/v13020321. PMID: 33672465; PMCID: PMC7923415.

8. *Fan W., Tang J., Tang S., Lin Z., Li M., Zhang Z. and Wu D.* (2024) Bibliometric analysis of photodynamic therapy and immune response from 1989–2023. Front Pharmacol 15. https://doi.org/10.3389/fphar.2024.1299253.

9. *Goodman A., Daniels A., Whelan J.* et al. Photodynamic therapy for cervical dysplasia: A review of recent literature. *Photodiagnosis and Photodynamic Therapy*. 2019;26:177-183.

10. *Goodman A., Sznol M., Chura J.* et al. Photodynamic therapy for cervical intraepithelial neoplasia: current evidence and future prospects // *International Journal of Molecular Sciences*. – 2024. – Vol. 25, №17. – Art. 9719. – URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10910886/ (дата обращения: 22.05.2025).

11. *Goh Y., Tan W., Cheong F.* et al. Photodynamic therapy as an alternative treatment option for cervical precancerous lesions. *International Journal of Gynecologic Cancer*. 2017;27(4):869-875.

12. *Hwang E., Lee J., Kim Y.* et al. Efficacy of photodynamic therapy in the treatment of HPV-associated cervical lesions. *Gynecologic Oncology*. 2020.158(2):379-387.

13. *Hussain S.* et al. Comparison of photodynamic therapy and cryotherapy for the treatment of cervical intraepithelial neoplasia. *International Journal of Gynecologic Cancer*. 2020;30(8):1279-1286.

14. *Ishchenko A.I., Reshetov I.V., Sosnova E.A., Unanyan A.L., Ishchenko A.A., Klyukina L.A.* Photodynamic therapy and cervical intraepithelial neoplasia: current achievements and development prospects. Obstetrics, Gynecology and Reproduction. 2022;16(5):600-610. (In Russ.) https://doi.org/10.17749/2313-7347/ob.gyn.rep.2022.287 )

15. *Kogure K., Tanaka T., Ogawa K.* et al. Clinical trial of photodynamic therapy for HPV-related cervical intraepithelial neoplasia: Results of a phase 2 study. *Cancer Treatment and Research*. 2017;179:207-217.

16. *Kotopoulis S., Prabhu A., Smith D.* et al. Photodynamic therapy as an emerging treatment for HPV-associated cervical lesions. *Gynecologic Oncology Reports*. 2019;28:91-95.

17. *Kralova J.* et al. A comparison of photodynamic therapy and surgical excision in the treatment of cervical intraepithelial neoplasia. *European Journal of Obstetrics & Gynecology and Reproductive Biology*. 2019;238:113-119.

18. *Lee H., Jung E., Park Y.* et al. Efficacy of photodynamic therapy in the management of HPV-related cervical cancer. *Journal of Cancer Therapy*. 2020;11(2):106-113.

19. *Lee Y., Woo K., Shin M.* et al. The use of photodynamic therapy in the treatment of HPV-induced cervical lesions: A multicenter study. *Clinical Gynecology and Obstetrics*. 2018;29(3):229-235.

20. *Liu H., Hu Z., Liu Q.* et al. Role of photodynamic therapy in the treatment of HPV-related cervical precancerous lesions. *Photochemistry and Photobiology*. 2018;94(6):1046-1054.

21. *Park J., Choi D., Ryu Y.* et al. Photodynamic therapy: A safe and effective alternative to traditional treatments for cervical neoplasia. *Cervical Cancer Journal*. 2019;12(1):45-52.

22. *Prakash S.* et al. Review of photodynamic therapy as a treatment modality for cervical dysplasia. *Journal of Photomedicine and Laser Surgery*. 2020.38(5):295-304.

23. *Sharma R., Gupta A., Khurana P.* et al. Photodynamic therapy for the treatment of cervical dysplasia: A review of clinical trials. *Journal of Photochemistry and Photobiology B: Biology*. 2020.212:111998.

24. *Sharma R., Ghosh D., Roy A.* et al. Advances in photodynamic therapy for HPV-associated cervical lesions. *Clinical Microbiology and Infection*. 2023. Vol. 29, №12. С.1521–1529. URL: https://www.sciencedirect.com/science/article/pii/S157210002300652X (дата обращения: 22.05.2025).

25. *Singh A., Sharma S., Jha R.* et al. Efficacy of photodynamic therapy in patients with persistent HPV-induced cervical dysplasia. *Journal of Clinical and Experimental Oncology*. 2021;2(1):102-110.

26. *Tao X.H., Guan Y., Shao D., et al.* Efficacy and safety of photodynamic therapy for cervical intraepithelial neoplasia: a systemic review // Photodiagnosis Photodyn Ther. 2014 Jun. 11(2):104-12

27. *Van der Zee J., González D., van der Voort van Zyp J.R.N.* et al. Successful treatment of cervical intraepithelial neoplasia with topical photodynamic therapy // *Gynecologic Oncology*. – 2005. – Vol. 97, №2. – С. 523–529. – URL: https://pubmed.ncbi.nlm.nih.gov/16118506/ (дата обращения: 22.05.2025).

28. *Wang S., Yang L., Li R.* et al. Photodynamic therapy in the treatment of cervical intraepithelial neoplasia: A systematic review. *Photodiagnosis and Photodynamic Therapy*. 2018.22:55-61.

29. *Wenjia Zhang, Aijia Zhang, et al.* Efficacy and safety of photodynamic therapy for cervical intraepithelial neoplasia and human papilloma virus infection: A systematic review and meta-analysis of randomized clinical trials // Medicine (Baltimore). 2018 May. 97(21).

30. *Xiang L., Li J., Yang W.* et al. Conization using an electrosurgical knife for cervical intraepithelial neoplasia and microinvasive carcinoma. PLoS One. 2015;10(7):e0131790. https://doi.org/10.1371/journal.pone.0131790

31. *Zepeda M., Villanueva O., Romero D.* et al. The role of photodynamic therapy in the treatment of cervical precancerous lesions: A systematic review. *Journal of Clinical Medicine*. 2019;8(5):723.

32. *Zhou C., Tuong Z.K., Frazer I.H.* Papillomavirus immune evasion strategies target the infected cell and the local immune system // Front Oncol. 2019. 9:682. DOI: 10.3389/fonc.2019.00682.

***References:***

1. Shanazarov N.A., Kisikova S.D., Albayev R.K., Afanasyev M.S., Khamidullina Z.G., Grishacheva T.G., Khangeldi A.Ye. Primenenie fotodinamicheskoi terapii u zhenshchin s VPCh-assotsirovannym predopukholevym zabolevaniem sheiki matki. Obzor literatury [The use of photodynamic therapy in women with HPV-associated precancerous cervical disease. Literature review]. *Nauka i Zdravookhranenie*, [Science and Healthcare], 2023, Vol. 25, No. 4, pp. 231-237. [in Russian]

**Information about the authors:**

**Akmaral Eskeldikyzy Khangeldi** – Obstetrician-Gynecologist, PhD student in Medicine, NCJSC «Astana Medical University», Phone: +7(707)712-00-93, E-mail: akhangeldi@mail.ru, ORCID: https://orcid.org/0000-0003-0603-1230, 49A Beibitshilik Avenue, Astana, Republic of Kazakhstan;

**Zaytuna Gadilovna Khamidullina -** PhD, Candidate of Medical Sciences, Head of the Department of Obstetrics and Gynecology No. 1, NCJSC "Astana Medical University", Phone: +7(777)153-65-84, E-mail: 59@gmail.com, ORCID: https://orcid.org/0000-0002-5324-8486, 9/4 Kabanbay Batyr Street, Astana, Republic of Kazakhstan;

**Nasrulla Abdullayevich Shanazarov** - Doctor of Medical Sciences, Professor, Chief Oncologist, RSE "Hospital of the Medical Center of the Administrative Department of the President of the Republic of Kazakhstan" on the right of economic management, Phone: +7(777)079-13-07, E-mail: nasrulla@inbox.ru, ORCID: https://orcid.org/0000-0002-2976-259X, 2 Y495 Street, Astana, Republic of Kazakhstan;

**Maxim Stanislavovich Afanasyev -** Doctor of Medical Sciences, Professor of the Department of Clinical Immunology and Allergology, N.V. Sklifosovsky Institute of Clinical Medicine, Sechenov First Moscow State Medical University of the Ministry of Health of the Russian Federation (Sechenov University), Phone: +7(913)685-52-38, E-mail: maxim.afanasyev78@gmail.com, ORCID: https://orcid.org/0000-0002-5860-4152, 3 Bolshaya Sukharevskaya Square, Moscow, Russian Federation;

**Tatyana Georgievna Grishacheva -** PhD (Biology), Senior Researcher, Center for Laser Medicine, Pavlov First Saint Petersburg State Medical University, Phone: +7(911)220-38-90, E-mail: grishatanchik82@gmail.com, ORCID: https://orcid.org/0000-0002-9515-914X, 6/8 Lva Tolstogo Street, St. Petersburg, Russian Federation;

**Nagima Nurlanovna Akkazhiyeva** - Obstetrician-Gynecologist, Municipal State Enterprise on the Right of Economic Management "City Multidisciplinary Hospital No. 2", Phone: +7(701)609-73-27, E-mail: Akk.n.n@mail.ru, ORCID: https://orcid.org/0000-0003-1571-6960, 8 Ryskulov Street, Astana, Republic of Kazakhstan;

**Tanysheva Gulyash Altyngazinovna -** Candidate of Medical Sciences, Head of the Department of Obstetrics and Gynecology, NCJSC «Semey Medical University», phone 8(777)153-53-57, email gulyash1965@mail.ru, https://orcid.org/0000-0001-9531-5950, 103 Abay Street, Semey, Kazakhstan.

**Corresponding author:**

**Akmaral Eskeldikyzy Khangeldi** – Obstetrician-Gynecologist, PhD student in Medicine, Non-profit Joint-Stock Company «Astana Medical University», Astana, Republic of Kazakhstan;

**Post address:** 49a Beibitshilik St., Astana 010000, Republic of Kazakhstan;

**E-mail:** akhangeldi@mail.ru

**Phone:** +7 (707) 712-00-93

Получена: 07 Февраля 2025 / Принята: 14 Июня 2025 / Опубликована online: 30 Июня 2025

***DOI 10.34689/SH.2025.27.3.007***

***УДК 614.2:241.12(574.5)***

This work is licensed under a Creative Commons Attribution 4.0 International License

# DOMESTIC VIOLENCE AS A PUBLIC HEALTH CHALLENGE: RESULTS OF A MASS SOCIOLOGICAL STUDY IN TURKISTAN REGION

**Saltanat S. Kyrykbayeva*[1], https://orcid.org/0000-0001-6151-6025**

**Aynash E. Oshibaeva[1], https://orcid.org/0000-0002-5655-5465**

**Gulnaz O. Nuskabayeva[1], https://orcid.org/0000-0003-2139-3221**

**Maiya V. Goremykina[2], https://orcid.org/0000-0002-5433-7771**

**Nailya M. Urazalina[2], https://orcid.org/0000-0003-0200-1763**

**[1] Akhmet Yassawi International Kazakh-Turkish University, Turkestan, Republic of Kazakhstan;**
**[2] NCJSC «Semey Medical University», Semey, Republic of Kazakhstan.**

**Abstract**

**Introduction:** Domestic violence is a significant public health concern, particularly in regions with persistent gender norms. In Kazakhstan, up-to-date regional data on the prevalence and perception of violence remain scarce.

**Objective:** To assess the prevalence, forms, and risk factors of domestic violence, levels of help-seeking behavior, and awareness of support services among the adult population in the Turkestan region.

**Materials and methods:** A cross-sectional study was conducted via an anonymous online survey with 24,621 adult participants. The questionnaire included sections on demographics, personal or family experience of violence, help-seeking behavior, awareness of legislation, and trust in institutional support. Data were analyzed using descriptive and comparative statistics ($\chi^2$, $p < 0.05$).

**Results:** A total of 693 respondents (2.8%) reported domestic violence, mostly physical (48.2%) and psychological (43.7%). Only 1.1% contacted police services. Key barriers included fear (58.4%), shame (46.9%), and distrust in the system (34.1%). Women and rural residents were less likely to seek help. Nearly 95% of respondents supported prevention efforts.

Conclusions: Domestic violence remains highly underreported. Lack of institutional trust and cultural normalization of violence reduce help-seeking behavior. Locally tailored information, protection, and support programs are needed.

***Keywords:*** *domestic violence, public health, help-seeking, gender differences, Kazakhstan prevention.*

***For citation:***

Kyrykbayeva S.S., Oshibaeva A.E., Nuskabayeva G.O., Goremykina M.V., Urazalina N.M. Domestic Violence as a Public Health Challenge: Results of a Mass Sociological Study in Turkistan Region // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 64-69. *doi 10.34689/SH.2025.27.3.007*

**Резюме**

# ДОМАШНЕЕ НАСИЛИЕ КАК ВЫЗОВ ОБЩЕСТВЕННОМУ ЗДРАВООХРАНЕНИЮ: РЕЗУЛЬТАТЫ МАССОВОГО СОЦИОЛОГИЧЕСКОГО ИССЛЕДОВАНИЯ В ТУРКЕСТАНСКОЙ ОБЛАСТИ

**Салтанат С. Кырыкбаева*[1], https://orcid.org/0000-0001-6151-6025**

**Айнаш Е. Ошибаева[1], https://orcid.org/0000-0002-5655-5465**

**Гульназ О. Нускабаева[1], https://orcid.org/0000-0003-2139-3221**

**Майя В. Горемыкина[2], https://orcid.org/0000-0002-5433-7771**

**Найля М. Уразалина[2], https://orcid.org/0000-0003-0200-1763**

**[1] Международный Казахско-Турецкий университет имени Ходжи Ахмеда Ясави, г. Туркестан, Республика Казахстан;**
**[2] НАО «Медицинский университет Астаны», г. Астана, Республика Казахстан.**

**Введение:** Домашнее насилие представляет собой значимую проблему общественного здравоохранения, особенно в регионах с традиционными гендерными установками. В Республике Казахстан отсутствуют актуальные данные о распространенности и восприятии насилия на региональном уровне.

**Цель исследования:** Оценить распространенность, формы и факторы риска домашнего насилия, уровень обращения за помощью и осведомлённости о службах поддержки среди взрослого населения Туркестанской области.

**Материалы и методы:** Проведено поперечное исследование методом онлайн-анкетирования. В выборку вошли 24 621 респондент в возрасте от 18 лет. Анкета включала блоки по демографическим данным, опыту насилия, обращению за помощью, знанию законодательства и доверию к государственным структурам. Статистическая обработка включала описательную и сравнительную аналитику ($\chi^2$, $p < 0.05$).

**Результаты:** О личном или семейном опыте насилия сообщили 693 человека (2,8 %), при этом физическое (48,2 %) и психологическое (43,7 %) насилие преобладали. Только 1,1 % пострадавших обращались в полицию. Основные барьеры — страх (58,4 %), стыд (46,9 %) и недоверие к системе (34,1 %). Женщины и сельские жители реже обращались за помощью. Почти 95 % респондентов поддерживают профилактику.

**Выводы:** Домашнее насилие остаётся глубоко латентным. Недостаток доверия к государственным структурам и нормализация насилия препятствуют обращению за помощью. Требуется развитие локальных программ информирования, защиты и поддержки жертв.

***Ключевые слова:*** *домашнее насилие, общественное здравоохранение, обращение за помощью, гендерные различия, Казахстан, профилактика.*

***Для цитирования:***

*Кырыкбаева С.С., Ошибаева А.Е., Нускабаева Г.О., Горемыкина М.В., Уразалина Н.М.* Домашнее насилие как вызов общественному здравоохранению: результаты массового социологического исследования в Туркестанской области // Наука и Здравоохранение. 2025. Vol.27 (3), С.64-69. *doi 10.34689/SH.2025.27.3.007*

**Түйіндеме**

# ТҮРКІСТАН ОБЛЫСЫНДАҒЫ ЖАППАЙ СОЦИОЛОГИЯЛЫҚ ЗЕРТТЕУ НӘТИЖЕЛЕРІ: ОТБАСЫЛЫҚ ЗОРЛЫҚ-ЗОМБЫЛЫҚ – ҚОҒАМДЫҚ ДЕНСАУЛЫҚ САҚТАУ ЖҮЙЕСІ ҮШІН МАҢЫЗДЫ ШАҚЫРУ

**Салтанат С. Кырыкбаева*[1], https://orcid.org/0000-0001-6151-6025**

**Айнаш Е. Ошибаева[1], https://orcid.org/0000-0002-5655-5465**

**Гульназ О. Нускабаева[1], https://orcid.org/0000-0003-2139-3221**

**Майя В. Горемыкина[2], https://orcid.org/0000-0002-5433-7771**

**Найля М. Уразалина[2], https://orcid.org/0000-0003-0200-1763**

**[1] Қожа Ахмет Ясауи атындағы Халықаралық қазақ-түрік университеті, Түркістан қ., Қазақстан Республикасы;**
**[2] «Семей медицина университеті» КеАҚ, Семей қ., Қазақстан Республикасы.**

**Кіріспе:** Отбасылық зорлық-зомбылық — дәстүрлі гендерлік көзқарастар басым өңірлерде қоғамдық денсаулық сақтау саласындағы маңызды мәселе болып табылады. Қазақстанда өңірлік деңгейдегі нақты деректердің жетіспеушілігі байқалады.

**Зерттеу мақсаты:** Түркістан облысы тұрғындары арасында отбасылық зорлық-зомбылықтың таралуын, түрлерін, қауіп факторларын, көмекке жүгіну деңгейін және ақпараттану деңгейін бағалау.

**Материалдар мен Әдістері:** 18 жастан асқан 24 621 респондент арасында онлайн-анонимді сауалнама жүргізілді. Сауалнамада демографиялық мәліметтер, зорлық-зомбылық тәжірибесі, көмекке жүгіну, заңнамалық және әлеуметтік институттарға сенім мәселелері қарастырылды. Деректер $\chi^2$ және $p < 0.05$ деңгейіндегі статистикалық талдау арқылы өңделді.

**Нәтижелер:** Респонденттердің 2,8 %-ы (693 адам) отбасылық зорлық-зомбылық тәжірибесі туралы хабарлады. Ең жиі кездескен түрлері — физикалық (48,2 %) және психологиялық (43,7 %) зорлық. Тек 1,1 %-ы полицияға жүгінген. Қиындықтар — қорқыныш (58,4 %), ұят (46,9 %) және жүйеге сенімсіздік (34,1 %). Әйелдер мен ауыл тұрғындары сирек көмек сұраған. 95 %-ға жуығы профилактикалық шараларды қолдайды.

**Қорытынды:** Зорлық-зомбылықтың жасырын сипаты сақталуда. Мемлекеттік органдарға сенімсіздік пен зорлықты қалыпты құбылыс ретінде қабылдау көмек сұрауға кедергі келтіреді. Аймақтық қолдау және ақпараттандыру бағдарламаларын дамыту қажет.

***Түйінді сөздер:*** *отбасылық зорлық-зомбылық, қоғамдық денсаулық сақтау, көмекке жүгіну, гендерлік айырмашылықтар, Қазақстан, алдын алу.*

***Дәйексөз үшін:***

*Кырыкбаева С.С., Ошибаева А.Е., Нускабаева Г.О., Горемыкина М.В., Уразалина Н.М.* Түркістан облысындағы жаппай социологиялық зерттеу нәтижелері: отбасылық зорлық-зомбылық – қоғамдық денсаулық сақтау жүйесі үшін маңызды шақыру // Ғылым және Денсаулық сақтау. 2025. Vol.27 (3), Б. 64-69. *doi 10.34689/SH.20254.27.3.007*

**Introduction**

Domestic violence remains one of the most pressing social issues, impacting human rights, public health, and community resilience. According to the World Health Organization, one in three women worldwide has experienced physical or sexual violence by an intimate partner [22]. In countries with patriarchal norms, such as Kazakhstan, the scale of the problem may be even greater but often remains hidden due to underreporting, stigma, and weak institutional response [6, 8, 9].

According to the Ministry of Internal Affairs of the Republic of Kazakhstan, more than 100,000 reports related to domestic violence were filed in 2023, the majority of them from women [5]. In early 2024, over 28,000 new complaints were registered [3]. However, international organizations estimate that many victims do not seek help due to fear of social condemnation and a lack of trust in the effectiveness of the system [4, 6, 17].

Research by UN Women and the OECD shows that Central Asia still lacks effective monitoring mechanisms, and traditional gender norms hinder recognition of the issue [8, 9, 14].

Turkistan Region is a densely populated area with a young demographic and strong cultural traditions. Cases of domestic violence are more frequently recorded here, particularly in rural areas [2]. Since 2021, pilot projects have been implemented in the region, including mobile response teams, trust centers, and awareness campaigns supported by governmental and international organizations [4, 12].

In some local communities, residents have initiated restrictions on alcohol sales — one of the recognized triggers of violence — which has led to a reduction in domestic conflicts [1]. This aligns with the international approach that integrates legal, social, and educational prevention measures [11, 13].

Nevertheless, there is still a lack of large-scale field studies reflecting public opinion on domestic violence—its forms, perceived acceptability, reasons for silence, and trust in support services. Such data are essential not only for understanding the current situation but also for designing effective, evidence-based solutions [20, 21].

The Council of Europe emphasizes that sustainable change is only possible through public engagement and continuous monitoring of societal attitudes [7]. Kazakhstan is currently considering ratification of the Istanbul Convention, but its implementation requires sensitivity to the cultural context and the expectations of the population.

Another important area of prevention is the involvement of men and boys as partners in the fight against violence. UNFPA and the United Nations identify this as one of the most promising approaches, particularly in countries with deeply rooted gender stereotypes [10, 19].

**The aim of this study** is to assess the prevalence and forms of domestic violence, the level of help-seeking behavior, and awareness of support services among the adult population of the Turkistan Region.

**Research objectives:**

1. To determine the prevalence of various forms of domestic violence (physical, psychological, economic, etc.) in the region.
2. To identify the sociodemographic characteristics of respondents affected by violence.
3. To analyze victims' help-seeking behavior and identify key barriers to accessing support.
4. To assess the level of trust in protective institutions and awareness of available resources.
5. To develop practical recommendations for the prevention of domestic violence, taking into account regional specificities.

**Methods**

**Study design.**

This was a descriptive cross-sectional study conducted through an anonymous online survey. The purpose was to assess the prevalence, forms, and public perceptions of domestic violence, as well as the level of awareness about support services among the adult population.

**Sample.** A total of **24,621 residents** of Turkistan Region aged 18 years and older participated in the survey. The sample was formed through voluntary participation. The questionnaire was distributed via social media platforms, messaging apps, and local NGOs.

**Inclusion criteria** were: age 18 or older, residence in Turkistan Region, and informed voluntary consent to participate.

**Instrument.** A structured questionnaire was used, developed based on UNFPA and WHO survey tools, adapted to the regional context. The questionnaire was designed with input from experts in psychology, sociology, and public health. It included six sections:

1. Sociodemographic characteristics
2. Experience of violence and its forms
3. Frequency and recurrence of incidents
4. Help-seeking behavior and perceived barriers
5. Awareness of legal protection mechanisms
6. Subjective perceptions of causes and prevention strategies

The questionnaire underwent expert review for content relevance but was not formally psychometrically validated, as the study was descriptive in nature.

**Ethical considerations.** Ethical committee approval was not required, as the study involved no interventions and did not collect personal identifying information. Participation was voluntary and anonymous, in accordance with the principles of sociological and humanities research ethics.

**Statistical analysis.** Data were processed using Microsoft Excel and SPSS version 26. Descriptive statistics (frequencies and percentages) were calculated, and the chi-square test ($\chi^2$) was applied to assess differences between subgroups (by gender, age, and place of residence). The significance level was set at $p < 0.05$.

Responses to open-ended questions were analyzed qualitatively, with key themes identified and manually coded.

**Results**

A total of 24,621 respondents from Turkistan Region participated in the study. The majority of the sample were women — 20,190 individuals (82%), while 4,431 (18%) were men. The most represented age groups were 31–40 years (7,140; 29%) and 41–50 years (5,663; 23%).

More than half of the participants lived in rural areas - 14,336 individuals (58.2%), while the remainder resided in urban areas (10,285; 41.8%) (see Table 1).

Table 1. **Sociodemographic profile of respondents (n = 24,621)**

| Characteristic | Absolute number | Percentage (%) |
|---|---|---|
| Gender | | |
| Women | 20,190 | 82.0% |
| Men | 4,431 | 18.0% |
| Age group | | |
| 18–30 years | 5,168 | 21.0% |
| 31–40 years | 7,140 | 29.0% |
| 41–50 years | 5,663 | 23.0% |
| 51–60 years | 3,447 | 14.0% |
| Over 60 years | 3,203 | 13.0% |
| Place of residence | | |
| Rural areas | 14,336 | 58.2% |
| Urban areas | 10,285 | 41.8% |

**Prevalence of Domestic Violence.** Out of all participants, 693 individuals (2.8%) reported having personal or family experience with domestic violence. The most commonly reported types were physical violence — 334 cases (48.2%) and psychological violence - 303 cases (43.7%). Reports of economic and sexual violence were significantly less frequent (see Table 2).

*Table 2.* **Experience of domestic violence among respondents (n = 693).**

| Type of violence | Absolute number | Percentage of victims (%) |
|---|---|---|
| Physical | 334 | 48.2% |
| Psychological | 303 | 43.7% |
| Sexual | 21 | 3.0% |
| Economic | 17 | 2.5% |
| Repeated episodes reported | 46 | 6.7% |

The majority of victims experienced repeated or systematic violence. Only 46 individuals (1.1% of those affected) sought help from the police, while 39 people (<1%) accessed medical assistance. A significant portion of respondents preferred to turn to relatives or friends for support (see Table 3).

*Table 3.* **Help-seeking behavior in response to domestic violence (n = 693).**

| Behavior / Response | Abs. number | Percentage (%) |
|---|---|---|
| Reported to the police | 46 | 6.6% |
| Sought medical assistance | 39 | 5.6% |
| Turned to relatives | 286 | ~41.2% |
| Turned to friends | 158 | ~22.8% |
| Did not seek any help | 250 | ~36.1% |
| Reasons for not seeking help | | |
| Fear | 405 | 58.4% |
| Shame | 325 | 46.9% |
| Distrust in the system | 236 | 34.1% |

**Causes of Violence and Attitudes Toward Prevention.** Respondents identified the primary causes of domestic violence as stemming mainly from individual and family-related factors (see Table 4).

Nearly 23,374 respondents, representing 95% of the total sample, expressed support for strengthening domestic violence prevention measures. Notably, 78% of respondents believed that mandatory education on this topic should be introduced in schools and universities.

*Table 4.* **Perceived causes of domestic violence (according to all respondents, n = 24,621).**

| Cause | Absolute number | Percentage (%) |
|---|---|---|
| Aggression, lack of mutual respect | 5,221 | 21.2% |
| Patriarchal norms, family culture | 4,583 | 18.6% |
| Poverty, financial instability | 3,915 | 15.9% |
| Alcohol abuse (from open-ended responses) | ~1,100 | — |

**Gender Differences.** The analysis revealed a significant correlation between gender and the likelihood of experiencing domestic violence. Women were nearly three times more likely than men to report such experiences ($\chi^2 = 16.4$; $p < 0.001$), and more frequently mentioned repeated episodes and pronounced emotional consequences, such as anxiety, guilt, and a sense of vulnerability. These findings are consistent with international data and highlight the need for gender-sensitive prevention strategies.

**Age.** The most vulnerable group was individuals aged 31–50, likely due to the combined burden of family, financial, and emotional stressors. Younger (18–30) and older (60+) respondents reported domestic violence less frequently. However, help-seeking behavior did not increase with age, indicating that barriers to seeking support are universal ($\chi^2 = 10.7$; $p = 0.005$).

**Urban vs. Rural.** Rural respondents were significantly less informed about available support services and exhibited lower levels of trust in the police and social services ($\chi^2 = 12.1$; $p = 0.001$). Fear, shame, and stigma were more commonly cited in rural areas. Even among those who were aware of support options, actual willingness to seek help remained extremely low ($\chi^2 = 8.6$; $p = 0.003$), indicating deep-rooted cultural and behavioral barriers that cannot be overcome by information alone.

**Discussion.** The study revealed a concerning paradox: despite reaching over 24,000 respondents, only 2.8% reported having personal or family experience with domestic violence. This figure is significantly lower than WHO estimates (27–33% among women [22]) and national statistics from Kazakhstan (at least 14–16% [5, 3]).

This discrepancy can be explained by high latency — the reluctance to speak about violence and the lack of recognition of violence as a problem. In rural areas, domestic violence is often perceived as a "private family matter", which aligns with international observations in patriarchal societies [4, 6].

A particularly striking finding is the extremely low rate of help-seeking - fewer than 1% of victims sought help from the police or medical professionals. Meanwhile, 6.7% of respondents reported repeated episodes of abuse. More than half were unaware of available support services, and among those who were informed, less than 10% were willing to use them. This points to a disconnect between the formal availability of services and public trust in them [1, 4].

According to Amnesty International and UN Women, the key barriers include fear of judgment, feelings of guilt, distrust in the system, and fear of secondary victimization [6, 17]. Even in urban settings, women often doubt that

seeking help will lead to actual protection**,** fearing instead that it may worsen their situation**.**

These perceptions are shaped by prevailing social norms. According to the SIGI Index (OECD), Kazakhstan continues to exhibit a high level of institutional gender discrimination, which limits the legal protection available to women [9]. This hinders the recognition of emotional, economic, and sexual violence as socially significant problems and slows the development of effective support mechanisms.

The analysis of subgroup differences revealed that women experience violence 2–3 times more often than men and are more likely to report anxiety and guilt. The 31–50 age group was identified as the most vulnerable, yet help-seeking did not increase with age, indicating persistent structural and psychological barriers. Rural residents were found to be less informed about services and less trusting of law enforcement — a trend also confirmed by regional reports [2, 18].

Encouragingly, there is a strong public demand for prevention: 95% of respondents consider domestic violence a serious issue, and 78% support introducing education on the topic in schools and universities. This presents a valuable window of opportunity for implementing awareness and prevention programs.

International experience shows that successful initiatives require the involvement of not only professionals, but also community members, religious leaders, and especially men themselves [10, 19]. The importance of "men's clubs" and dialogue platforms has been particularly emphasized, as they promote the re-evaluation of gender roles and encourage nonviolent behavior models [10, 11].

The Council of Europe also stresses the value of a comprehensive, intersectoral approach, which includes not only legal sanctions but also education, support services, and rehabilitation efforts [7]. According to the UN Women's Women Count initiative, systemic change is impossible without regular, reliable statistics that reflect the perspectives of citizens — not just administrative reports [20].

The study highlights three key problems:

1. Cultural latency — violence is not perceived as a deviation from the norm.
2. Institutional mistrust — services exist but are not perceived as a usable resource.
3. Social inequality in access — especially pronounced in rural areas.

Nevertheless, the strong support for prevention expressed by the population creates opportunities for the development of locally adapted strategies aimed at reducing stigma, increasing awareness, and strengthening trust in the support system.

Practical Recommendations

– In light of the identified trends, there is a need for systemic preventive measures tailored to the social context of the region and feasible for implementation in practice:

– It is necessary to expand legal education by including the topic of nonviolence in educational programs, outreach lectures, and local media, especially in rural areas.

– It is important to engage religious and community leaders in promoting zero tolerance toward violence within communities.

– Men's dialogue platforms should be supported to foster the rethinking of gender roles and the development of a culture of nonviolent behavior.

– It is recommended to provide anonymous and accessible digital channels for seeking help — hotlines, chatbots, and mobile applications.

– Regular public opinion monitoring should be conducted to evaluate the effectiveness of measures and adapt them to the needs of the population.

**Conclusions**

The study demonstrated that domestic violence in the Turkistan Region remains highly latent: only 2.8% of respondents reported having experienced violence, despite evidence of repeated episodes. The most common forms were physical and psychological violence, while sexual and economic violence was the least recognized and rarely disclosed.

Help-seeking behavior was extremely low (less than 1%), limited by fear, shame, lack of trust in services, and low awareness. The most vulnerable groups were women, rural residents, and middle-aged respondents.

The findings underscore the urgent need for regionally adapted prevention strategies that include enhancing legal literacy, reducing stigma, and developing intersectoral cooperation.

***Study Limitations:*** *The single-center nature of the study may limit its generalizability, and the absence of long-term follow-up data restricts the assessment of post-discharge outcomes.*

***Author Contributions****: All authors contributed equally to the writing of this manuscript.*

***Conflict of Interest:*** *The authors declare no conflicts of interest. This material has not been submitted to other journals and is not under consideration elsewhere.*

***Funding:*** *No funding was received for this study.*

***Acknowledgements:*** *The authors express their gratitude to the Representative Office of the Commissioner for Human Rights in the Republic of Kazakhstan for Turkistan Region for their support in organizing and conducting the study.*

***Literature:***

1. Agency for Public Development of the Republic of Kazakhstan. *Local Community Initiatives for Domestic Violence Prevention: Collection of Practices.* – Astana: APDRK, 2024. Available at: https://eljastary.kz/ru/methodics/17358?yearr=81 https://qamqor.gov.kz (accessed 03.12.2024)

2. Analytical Report. *Domestic Violence: A Study of the Problem and Solutions in Turkistan Region.* – Turkistan, 2025. – 42 p.

3. Committee on Legal Statistics and Special Records of the General Prosecutor's Office of the Republic of Kazakhstan. *Unified Register of Offenses* [Electronic resource]. Available at: https://qamqor.gov.kz (accessed 03.12.2024)

4. Ministry of Information and Social Development of the Republic of Kazakhstan. *Pilot Project on Domestic Violence Response. Press Release.* – Astana: MISDRK, 2021. Available at: https://www.gov.kz/memleket/entities/aqmola-bulandy/press/article/details/12267?lang=ru https://qamqor.gov.kz (accessed 06.09.2024)

5. Ministry of Internal Affairs of the Republic of Kazakhstan. Statistical Bulletin on Domestic Violence for 2023. – Astana: MIA RK, 2024.

6. Amnesty International. Kazakhstan: The Invisible Scars – Domestic Violence and Impunity. – London: Amnesty International, 2021. https://www.amnesty.org/en/documents/eur57/3259/2021/en (accessed 06.09.2024)

7. Council of Europe. Istanbul Convention: Action Against Violence Against Women and Domestic Violence. – *Strasbourg:* Council of Europe, 2011. https://www.coe.int/en/web/istanbul-convention (accessed 06.09.2024)

8. *Garcia-Moreno C., Jansen H.A.F.M., Ellsberg M., Heise L., Watts C.H. WHO Multi-country Study on Women's Health and Domestic Violence Against Women: Initial Results on Prevalence, Health Outcomes and Women's Responses.* – Geneva: WHO, 2005. https://www.who.int/publications-detail-redirect/who-multi-country-study-on-women-s-health-and-domestic-violence-against-women (accessed 06.09.2024)

9. OECD Development Centre. *Social Institutions and Gender Index (SIGI) 2023 Global Report.* – Paris: OECD, 2023. https://www.oecd.org/en/publications/sigi-2023-global-report_4607b7c7-en.html

10. UNFPA. *Engaging Men and Boys in Gender Equality and Health: A Global Toolkit for Action.* – New York: UNFPA, 2010. https://www.unfpa.org/publications/engaging-men-and-boys-gender-equality-and-health (accessed 06.09.2024)

11. UNFPA EECA Regional Office. Community Mobilization to Prevent Domestic Violence in Rural Areas. – Almaty: UNFPA, 2022.

12. UNFPA. Rapid Gender Assessment for the COVID-19 Situation in the Republic of Kazakhstan. – Nur-Sultan: UNFPA, 2021. https://kazakhstan.unfpa.org/sites/default/files/pub-pdf/rga_eng_.pdf (accessed 06.09.2024)

13. UNODC. *Global Study on Homicide: Gender-Related Killing of Women and Girls.* – Vienna: UNODC, 2019. https://www.unodc.org/documents/data-and-analysis/gsh/Booklet_5.pdf (accessed 08.11.2024)

14. UN Women. Ending Violence Against Women in Central Asia: Legal and Policy Review. – Almaty: UN Women, 2023. https://eca.unwomen.org/en/stories/press-release/2025/02/united-to-advance-the-2030-agenda-central-asia-countries-pledge-to-act-for-gender-equality-in-the-region (accessed 08.11.2024)

15. UN Women. Gender Equality in Times of Crisis: SIGI 2023 Global Report. – Paris: OECD, 2023. https://www.oecd-ilibrary.org/development/sigi-2023-global-report_939a6819-en

16. UN Women. Progress of the World's Women 2019–2020: Families in a Changing World. – New York: UN Women, 2020. https://www.unwomen.org/en/digital-library/publications/2019/06/progress-of-the-worlds-women-2019-2020 (accessed 08.11.2024)

17. UN Women. *Research and Data: Ending Violence Against Women.* – New York: UN Women, 2023. Available at: https://www.unwomen.org/en/what-we-do/ending-violence-against-women/research-and-data (accessed 08.11.2024)

18. UN Women. *The Dark Side of Digitalization: Technology-Facilitated Gender-Based Violence in Central Asia.* – Almaty: UN Women, 2024. Available at: https://eca.unwomen.org/sites/default/files/2024-01/research-tf-vaw_full-report_24-january2.pdf (accessed 08.11.2024)

19. UN Women. Uniting for Progress: Launch of the Central Asian Alliance to End Gender-Based Violence. – New York: UN Women, 2023. Available at: https://open.unwomen.org/en/our-reach/KZ/XM-DAC-41146-KAZ_D_1.1 (accessed 22.12.2024)

20. UN Women. *Women Count: Europe and Central Asia.* – New York: UN Women, 2024. Available at: https://data.unwomen.org/sites/default/files/documents/Women%20Count/Women_Count_Europe_and_Central_Asia.pdf (accessed 10.09.2024)

21. UN Women. *Women Count: The State of Gender Data in Europe and Central Asia.* – New York: UN Women, 2022. https://data.unwomen.org/publications/state-gender-data-europe-central-asia (accessed 08.11.2024)

World Health Organization. *Violence Against Women: Prevalence Estimates, 2018.* – Geneva: WHO, 2021. https://www.who.int/publications/i/item/9789240022256 (accessed 03.10.2024)

**Information about the authors:**

**Oshibaeva Ainash Esimbekovna -** Vice-Rector of Science and Strategic Development of the International Kazakh-Turkish University named after Khoja Ahmet Yasavi, Turkestan, tel: +7-701-717-06-34 e-mail: ainash.oshibayeva@ayu.edu.kz, https://orcid.org/0000-0002-5655-5465

**Nuskabayeva Gulnaz Orazbekovna -** Candidate of medical sciences, associate professor, Dean of the Faculty of Medicine Department of "Special Clinical Disciplines", Faculty of Medicine Khoja Akhmet Yassawi International kazakh-turkish University, Turkestan city, Republic of Kazakhstan; email - nuskabaeva.gulnaz@ayu.edu.kz; Phone: +77052853131; https://orcid.org/0000-0003-2139-3221

**Goremykina Maiya Valentinovna -** Candidate of Medical Sciences, Associate Professor, Department of Internal Medicine and Rheumatology, NCJSC «Semey Medical University», 103 Abay Street, Semey, 071400, Kazakhstan; Email: maya.goremykina@smu.edu.kz; phone number: +7 (777) 390 8234; https://orcid.org/0000-0002-5433-7771

**Urazalina Nailya Muratkhanovna** - Candidate of Medical Sciences, Associate Professor of the Department of physiological disciplines named after honored scientist of the republic of Kazakhstan, professor T.A. Nazarova, NJSC "Semey Medical University", Semey, Kazakhstan; phone: 8 777 907 55 89, e-mail: hakim_15@mail.ru, https://orcid.org/0000-0003-0200-1763

**Corresponding author:**

*** Kyrykbayeva Saltanat Sayatovna** - MD, PhD, Head of the Center for Strategic Development, Rating and Quality of the International Kazakh-Turkish University named after Khoja Ahmet Yasawi; https://orcid.org/0000-0001-6151-6025

**Postal code:** X41A4E4, Bekzat Sattarhanov Street No:29 Turkestan/ Kazakhstan

**E-mail:** kyrykbayeva.s@gmail.com

**Phone:** +7 775 537 97 57

Received: 24 January 2025 / Accepted: 14 May 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2025.27.3.008***

***UDC 579.842.16:615.33.***

This work is licensed under a Creative Commons Attribution 4.0 International License

# ASSESSMENT OF DEPRESSION, FATIGUE, AND PSYCHOLOGICAL WELL-BEING IN PATIENTS AFTER STROKE: RESULTS OF A CROSS-SECTIONAL STUDY USING THE BECK, FAS, AND MHC-SF SCALES

**Akgul O. Bayzullina[1], https://orcid.org/0000-0002-3992-1419**

**Lazzat M. Zhamaliyeva[1], https://orcid.org/0000-0003-3625-3651**

**Aigul P. Ermagambetova[1], https://orcid.org/0000-0002-3230-0433**

**[1] Marat Ospanov West Kazakhstan Medical University, Aktobe, Republic of Kazakhstan.**

**Abstract**

**Relevance:** Stroke represents a substantial challenge in contemporary medicine. In addition to the neurological deficits arising from cerebrovascular damage, this condition significantly influences the psychological state and overall quality of life of affected individuals. The provision of psychological support and timely emotional intervention during the acute phase of a cerebral hemorrhage is essential for facilitating optimal motor recovery. The early identification and treatment of psycho-emotional disorders are particularly critical for enhancing recovery prospects following a stroke.

This study **aims** to evaluate the levels of depression, fatigue, and psychological well-being among stroke survivors utilizing validated assessment tools, specifically the Beck Depression Inventory (BDI), Fatigue Assessment Scale (FAS), and Mental Health Continuum-Short Form (MHC-SF).

**Materials and Methods:** Cross-sectional study conducted across two multidisciplinary hospitals in Aktobe from February to July 2024, the study encompassed 150 inpatients at designated stroke centers. Assessment of depression, fatigue, and psychological well-being was performed via the BDI, FAS, and MHC-SF scales.

**Results:** Among the 150 participants, a majority were female (58.7%). Ischemic strokes accounted for 55.3% of cases. Fatigue was reported by 54.7% of participants, with a mean FAS score of 35.68±9.28. The mean BDI score of 10.74±8.03 indicated the presence of mild depression, while the average MHC-SF score of 79.19±17.797 suggested a moderately high level of subjective psychological well-being.

**Conclusion:** The results underscore the necessity of adopting a comprehensive approach to post-stroke rehabilitation, which emphasizes not only the importance of physical recovery but also the reduction of fatigue, enhancement of psychological well-being, and timely diagnosis of depressive states. The emotional resources preserved by numerous patients can be utilized to elevate their quality of life and rehabilitation outcomes.

***Keywords:*** *stroke, depression, fatigue, psychological well-being.*

***For citation:***

*Bayzullina A.O., Zhamaliyeva L.M., Ermagambetova A.P.* Assessment of depression, fatigue, and psychological well-being in patients after stroke: results of a cross-sectional study using the BECK, FAS, and MHC-SF scales // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 70-78. *doi 10.34689/SH.2025.27.3.008*

**Резюме**

# ОЦЕНКА ВЫРАЖЕННОСТИ ДЕПРЕССИИ, УСТАЛОСТИ И УРОВНЯ ПСИХОЛОГИЧЕСКОГО БЛАГОПОЛУЧИЯ У ПАЦИЕНТОВ ПОСЛЕ ИНСУЛЬТА: РЕЗУЛЬТАТЫ ПОПЕРЕЧНОГО ИССЛЕДОВАНИЯ С ПРИМЕНЕНИЕМ ШКАЛ *BECK, FAS* И *MHC-SF*

**Акгуль О. Байзуллина [1], https://orcid.org/0000-0002-3992-1419**

**Лаззат М. Жамалиева [1], https://orcid.org/0000-0003-3625-3651**

**Айгуль П. Ермагамбетова [1], https://orcid.org/0000-0002-3230-0433**

**[1] Западно-Казахстанский медицинский университет имени Марата Оспанова, г. Актобе, Республика Казахстан.**

**Актуальность.** Инсульты являются одной из глобальных проблем современной медицины. Помимо нейрологических дефицитов, которые возникают в результате поражения головного мозга, данное заболевание существенно влияет на психологическое состояние и качество жизни пациентов. Психологическая поддержка и своевременная коррекция эмоционального фона при остром кровоизлиянии в мозг играют важную роль для успешного восстановления моторной активности. Для повышения шансов на благоприятное течение восстановления после инсульта особенно важно на ранних этапах выявлять и корректировать психоэмоциональные расстройства.

**Цель:** оценка уровня депрессии, усталости и психологического благополучия у пациентов, перенесших инсульт, с использованием валидированных шкал Beck Depression Inventory (BDI), Fatigue Assessment Scale (FAS) и Mental Health Continuum-Short Form (MHC-SF).

**Материалы и методы.** Поперечное исследование было инициировано в двух многопрофильных стационарах г. Актобе. С февраля 2024 года по июль 2024 года мы набирали участников, находящихся на стационарном лечении в инсультных центрах в этих клиниках. В исследовании приняли участие 150 человек. Проведены оценки усталости, депрессии и психологического благополучия с использованием различных инструментов – шкала депрессии Beck, FAS и MHC-SF.

**Результаты.** Мы включили в исследование 150 пациентов. Женщин было больше (58,7%, 95%ДИ 31,3- 46,9). Подавляющее большинство включенных в исследование (n=83; 55,3%) были с ишемическими поражениями. Усталость присутствовала у 82 участников исследования (54,7%). Среднее значение FAS 35,68±9,28 (ДИ 41,3-57,3). Шкала BDI (оценка депрессии)**:** среднее значение (10,74±8,03) указывает на легкий уровень депрессии в выборке. Шкала FAS (оценка усталости)**:** среднее значение (35,68±9,28) указывает на наличие усталости. По результатам опроса с использованием шкалы MHC-SF, среднее значение составило 79,19±17,797, что свидетельствует о умеренно высоком уровне субъективного психологического благополучия среди участников.

**Заключение.** Результаты исследования подчеркивают значимость многоаспектного подхода к восстановлению пациентов после инсульта, предполагающего не только физическую реабилитацию, но и внимание к снижению уровня усталости, укреплению психологического благополучия, а также своевременной диагностике депрессивных состояний. Эмоциональные ресурсы, сохраняющиеся у многих пациентов, могут быть использованы для улучшения их качества жизни и повышения эффективности реабилитационных программ.

***Ключевые слова:*** *инсульт, депрессия, усталость, психологическое благополучие.*

***Для цитирования:***

*Байзуллина А.О., Жамалиева Л.М., Ермагамбетова А.П.* Оценка выраженности депрессии, усталости и уровня психологического благополучия у пациентов после инсульта: результаты поперечного исследования с применением шкал *BECK, FAS* и *MHC-SF* // Наука и Здравоохранение. 2025. Т.27 (3), С. 70-78. doi: 10.34689/SH.2025.27.3.008

**Түйіндеме**

# ИНСУЛЬТТАН КЕЙІНГІ НАУҚАСТАРДА ДЕПРЕССИЯНЫҢ, ШАРШАУДЫҢ ЖӘНЕ ПСИХОЛОГИЯЛЫҚ ӘЛ-АУҚАТ ДЕҢГЕЙІН АУЫРЛЫҒЫН БАҒАЛАУ: BECK, FAS ЖӘНЕ MHC-SF ШКАЛАЛАРЫН ҚОЛДАНА ОТЫРЫП, КӨЛДЕНЕҢ ЗЕРТТЕУ НӘТИЖЕЛЕРІ

**Акгуль О. Байзуллина [1], https://orcid.org/0000-0002-3992-1419**

**Лаззат М. Жамалиева [1], https://orcid.org/0000-0003-3625-3651**

**Айгуль П. Ермагамбетова [1], https://orcid.org/0000-0002-3230-0433**

**[1] Марат Оспанов атындағы Батыс Қазақстан медицина университеті**
**Ақтөбе қ., Қазақстан Республикасы.**

**Кіріспе.** Инсульт-қазіргі заманғы медицинаның жаһандық проблемаларының бірі. Мидың зақымдануы нәтижесінде пайда болатын неврологиялық тапшылықтардан басқа, бұл ауру пациенттердің психологиялық жағдайы мен өмір сапасына айтарлықтай әсер етеді. Жедел ми қан кетуіндегі психологиялық қолдау және эмоционалды фонды уақтылы түзету мотор белсенділігін сәтті қалпына келтіру үшін маңызды рөл атқарады. Инсульттан кейін қалпына келтірудің қолайлы ағымының мүмкіндігін арттыру үшін психоэмоционалды бұзылуларды ерте кезеңде анықтау және түзету өте маңызды.

**Зерттеу мақсаты**. Beck Depression Inventory (BDI), Fatigue Assessment Scale (FAS) және Mental Health Continuum-Short Form (MHC-SF) валидацияланған шкалаларын пайдалана отырып, инсультпен ауыратын науқастардағы депрессия, шаршау және психологиялық әл-ауқат деңгейін бағалау.

**Материалдар мен тәсілдер.** Көлденең зерттеу Ақтөбе қаласындағы екі көпсалалы стационарда басталды. 2024 жылдың ақпанынан 2024 жылдың шілдесіне дейін біз осы клиникалардағы инсульт орталықтарында стационарлық емдеуге қатысушыларды жинадық. Зерттеуге 150 адам қатысты. Шаршауды, депрессияны және психологиялық әл – ауқатты бағалау әртүрлі құралдарды-Beck, FAS және MHC-SF депрессия шкаласын қолдана отырып жүргізілді.

**Нәтижелер.** Біз зерттеуге 150 пациентті қостық. Әйелдер көп болды (58,7%, 95% CI 31,3 - 46,9). Зерттеуге қатысқандардың басым көпшілігі (N=83; 55,3%) ишемиялық зақымданулармен болды. Шаршау зерттеуге 82 қатысушыда болды (54,7%). FAS орташа мәні 35,68±9,28 (CI 41,3-57,3). BDI шкаласы (депрессияны бағалау): орташа мән (10,74±8,03) үлгідегі депрессияның жеңіл деңгейін көрсетеді. FAS шкаласы (шаршауды бағалау): орташа (35,68±9,28) шаршаудың болуын көрсетеді. MHC-SF шкаласын қолдана отырып жүргізілген сауалнама нәтижелері бойынша орташа көрсеткіш 79,19±17,797 құрады, бұл қатысушылар арасында субъективті психологиялық әл-ауқаттың орташа жоғары деңгейін көрсетеді.

**Қорытынды:** Зерттеу нәтижелері физикалық оңалтуды ғана емес, сонымен қатар шаршау деңгейін төмендетуге, психологиялық әл-ауқатты нығайтуға, сондай-ақ депрессиялық жағдайларды уақтылы диагностикалауға назар аударуды қамтитын инсульттан кейін пациенттерді қалпына келтіруге көп қырлы көзқарастың маңыздылығын көрсетеді. Көптеген пациенттерде сақталатын эмоционалды ресурстарды олардың өмір сүру сапасын жақсарту және оңалту бағдарламаларының тиімділігін арттыру үшін пайдалануға болады.

***Түйінді сөздер**: инсульт, депрессия, шаршау, психологиялық әл-ауқат.*

***Дәйексөз үшін:***

*Байзуллина А.О., Жамалиева Л.М., Ермагамбетова А.П.* Инсульттан кейінгі науқастарда депрессияның, шаршаудың және психологиялық әл-ауқат деңгейін ауырлығын бағалау: BECK, FAS және MHC-SF шкалаларын қолдана отырып, көлденең зерттеу нәтижелері // Ғылым және Денсаулық. 2025. Т.27 (3), Б. 70–77. doi: 10.34689/SH.2025.27.3.008

**Relevance**

Strokes represent a significant global challenge within contemporary medicine, predominantly affecting individuals of advanced age, though there is an observable trend towards occurrence in younger populations. The World Health Organization identifies stroke as the second leading cause of death and disability worldwide, with a prevalence estimated at 6.67 per 100,000 individuals. In addition to the neurological deficits resulting from cerebral damage, stroke notably impacts the psychological well-being and quality of life of affected individuals. Neuropsychiatric changes frequently accompany stroke, leading to an increased likelihood of developing anxious-depressive syndromes, depressive states, hypochondriacal disorders, apathy, diminished self-esteem and outlook regarding the future, as well as social maladjustment. These factors substantially hinder the effective implementation of rehabilitation strategies. Timely psychological support and appropriate modification of the emotional landscape following acute cerebral hemorrhage are critical for the successful restoration of motor function. Furthermore, the active engagement of patients in their treatment process, coupled with a positive mindset, plays a crucial role in the adequate recovery of functional abilities and mitigation of residual effects of the illness. Post-stroke rehabilitation continues to be a primary objective in modern medical practice, as the ramifications of a stroke impose significant burdens not only on the individual experiencing emotional distress and suffering but also on society, due to diminished levels of social and professional integration. The efficacy of recovery is heavily influenced by the motivation of the patient, their family members, and healthcare professionals to restore previously lost functions. Nevertheless, the presence of depressive symptoms, which often co-occur with anxiety, phobic, and obsessive disorders, as well as reduced motivation, can severely hinder the attainment of favorable outcomes. Studies indicate that the prevalence of depressive disorders subsequent to a stroke ranges from 30% to 60%. Moreover, it has been documented that over 50% of patients experiencing an acute cerebrovascular event exhibit depressive disorders. Post-stroke depression typically manifests during the early recovery phase, although symptoms may arise as early as within the first week post-stroke, predominantly between days 7 and 10. This complication, frequently remaining undiagnosed, adversely impacts the recovery trajectory, potentially delaying the restoration of motor abilities, exacerbating cognitive impairments, increasing mortality risk, and significantly diminishing the patient's quality of life and willingness to engage in rehabilitation activities. To enhance the likelihood of a favorable recovery post-stroke, early identification and intervention for psycho-emotional disturbances are paramount. The effectiveness and pace of rehabilitation are greatly influenced by the prompt initiation of psychological support interventions, including addressing the manifestations of post-stroke depression. Evaluating psychological well-being and identifying contributors to deterioration in condition constitute critical phases in providing support to stroke survivors. Tools such as the Beck Depression Inventory (BDI), the Fatigue Assessment Scale (FAS), and the Mental Health Survey-Short Form (MHC-SF) are commonly employed to assess psychological and emotional status.

**Objective of the study** – to assess the levels of depression, fatigue, and psychological well-being in patients who have suffered a stroke, using validated scales: the Beck Depression Inventory (BDI), the Fatigue Assessment Scale (FAS), and the Mental Health Continuum-Short Form (MHC-SF).

**Materials and Methods of the Study.**

This study was initiated in two multidisciplinary hospitals in the city of Aktobe. From February 2024 to July 2024, we recruited participants undergoing inpatient treatment in the stroke centers of these clinics. The institutions where the research was conducted were informed about the progress of the research. There are no objections to the publication of the results in the open press. The study included 150 patients, among whom were 62 men (41.3%) and 88 women (58.7%), aged between 38 and 79 years. Participants were selected based on predefined inclusion and exclusion criteria. All participants were thoroughly informed about the objectives and conditions of the study and provided written consent to participate. After obtaining consent, demographic and clinical data were collected, including age, gender, education level, smoking and alcohol habits, presence of diabetes, heart diseases, and blood pressure level, stroke type, and lesion location. Data collection was conducted in a calm environment. After that, fatigue, depression, and psychological well-being assessments were conducted using the Beck Depression Inventory, FAS, and MHC-SF scales.

The obtained data were processed using SPSS software version 26.0. Results are presented as means and standard deviations. The chi-squared test ($\chi^2$) was used to analyze binary variables, and the Mann-Whitney non-parametric test was used for comparing categorical indicators. To assess correlations between depression levels, fatigue, and indicators of psychological well-being, Spearman's rank correlation coefficient was applied.

**Study Design** – cross-sectional study.

**Study Participants**

The study included patients aged 18 years and older who had experienced ischemic or hemorrhagic stroke (either first-time or recurrent), with cognitive impairments confirmed by MoCA scores ≤ 22.

***Exclusion criteria*** included severe speech disorders (severe aphasia or dysarthria) or significant cognitive impairments hindering independent completion of diagnostic questionnaires. Also excluded were patients with unstable somatic conditions deemed clinically unsuitable for participation, individuals with previously undiagnosed psychiatric or severe neurological disorders, participants under 18 years of age, and patients who scored less than 23 points on the Mini Mental State Evaluation (MMSE) scale.

**Instruments**

All patients were surveyed using structured questionnaires. To identify patients with depression, the Beck Depression Inventory-II (BDI-II) was used. Fatigue was assessed using the Fatigue Assessment Scale (FAS), and psychological well-being was evaluated with the Mental Health Continuum-Short Form (MHC-SF). All measurements for each participant were completed on the same day.

Depression was assessed using the Beck Depression Inventory (BDI), which has been validated for stroke patients. The BDI is a self-report scale developed as a questionnaire to quantify the severity of depressive symptoms. It consists of 21 items covering symptoms such as sadness, pessimism, past failures, loss of pleasure, guilt, punishment feelings, self-dislike, self-criticism, suicidal thoughts, crying, irritability, loss of interest, indecisiveness, worthlessness, loss of energy, sleep changes, fatigue, appetite changes, weight loss, agitation, and loss of interest in sex. Each item is rated on a 4-point scale (0 = not at all; 3 = very severe). The total BDI score ranges from 0 to 63. A score of 14–19 indicates mild depression, 20–28 moderate depression, and 29–63 severe depression.

Fatigue was measured using the Fatigue Assessment Scale (FAS), a reliable and validated tool for assessing fatigue in stroke patients. The questionnaire includes 10 statements, five reflecting mental fatigue and five physical fatigue. Each item is rated on a 5-point scale from 1 (never) to 5 (always), indicating symptom frequency. Scores are summed to produce a total score; for items 4 and 10, responses are reverse-coded (from 5 to 1). The total score ranges from 10 to 50, with higher values indicating greater fatigue. A score of 22 or above is considered a diagnostic criterion for pathological fatigue syndrome.

The Mental Health Continuum-Short Form (MHC-SF) is one of the most widely recognized self-assessment tools internationally for comprehensively measuring psychological well-being. It covers three core aspects of mental health: emotional well-being, social well-being, and psychological well-being. Emotional well-being is assessed with 3 items, social with 5 items, and psychological with 6 items. The total score is interpreted to determine the level of subjective psychological well-being:

63 and above – very high,
49–62 – significantly above average,
36–48 – moderately above average,
23–35 – moderately below average,
9–22 – significantly below average,
8 and below – extremely low well-being.

The structure and methods of the study were approved by the Ethics Committee of the West Kazakhstan Medical University in 2017. (Protocol No.6/25, June 17, 2021).

**Results**

We included 150 patients in the study. The majority were women (58.7%, 95% CI: 31.3–46.9). Most of the participants (n = 83; 55.3%) had ischemic strokes. The remaining participants were diagnosed with hemorrhagic stroke (n = 14; 9.3%), transient ischemic attack (n = 52; 34.7%), and subarachnoid hemorrhage (n = 1; 0.7%). The stroke was the first occurrence in 127 cases (84.7%) and recurrent in 23 cases (15.3%).

Tables 1 and 2 present the demographic and clinical characteristics of the patients (mean age: 60.44 years, standard deviation: 9.42 years).

Fatigue was present in 82 study participants (54.7%). The mean FAS score was 35.68±9.28 (95% CI: 41.3–57.3).

Table 2 presents statistical data for the BDI (Beck Depression Inventory), FAS (Fatigue Assessment Scale), and MHC-SF (Mental Health Continuum-Short Form) scales.

- **BDI (Depression Assessment):** The mean score (10.74±8.03) indicates a mild level of depression in the sample.
- **FAS (Fatigue Assessment):** The mean score (35.68±9.28) confirms the presence of fatigue**.**
- **MHC-SF (Mental Health Assessment):** The average score was 79.19±17.797**,** reflecting a moderately high level of subjective psychological well-being among participants.

The data also indicate moderate expression of depressive symptoms and fatigue**,** while the overall psycho-emotional condition of the respondents can be characterized as stable, with a predominance of positive components of well-being**.** The wide range of BDI scores highlights the heterogeneity of depressive symptoms**,** emphasizing the need for an individualized approach to diagnosis and treatment**.** The presence of fatigue confirms its significance as a clinical symptom in stroke patients**.** The average level of psychological well-being indicates that many patients retain emotional resources**,** which can be utilized in rehabilitation programs.

*Table 1.*

**Clinical and demographic characteristics of patients classified by the presence of post-stroke depression.**

| Characteristics | Patients with depression (BDI >9) (n = 75) | Patients without depression ( BDI < 9) (n = 75) | Total (n =150) | p -value |
|---|---|---|---|---|
| Age | 62.92 ± 8.61 | 59.89±9.59 | 60.44±9.42 | 0,001 |
| BMI | 28.54±5.73 | 28.21±5.52 | 28.38±5.61 | 0.708 |
| glucose ( mmol /l) | 7.70±3.07 | 7.69±3.91 | 7.69±3.49 | 0.628 |
| cholesterol ( mmol /l) | 5.47±1.46 | 5.27±1.32 | 5.37±1.39 | 0.265 |
| HDL ( mmol /l) | 1.59±0.68 | 3.17±11.18 | 2.39±8.00 | 0.707 |
| LDL ( mmol /l) | 3.10±1.28 | 4.67±10.13 | 3.92±7.38 | 0.505 |
| triglycerides ( mmol /l) | 1.61±1.09 | 1.67±1.07 | 1.63±1.08 | 0.424 |
| Creatinine ( μmol ) | 80.42±24.37 | 84.13±25.95 | 82.21±25.11 | 0.346 |
| SBP (mmHg ) st ) | 149.08±23.21 | 154.60±25.87 | 151.80±24.63 | 0.201 |
| DBP (mmHg ) st ) | 87.63±10.94 | 89.59±12.46 | 88.60±11.72 | 0.544 |
| SCF (ml/min/1.73 sq m) CKD - EPI | 85.96±19.41 | 87.09±20.69 | 86.5±19.96 | 0.626 |
| Floor | 0.5±0.50 | 0.68±0.47 | 0.59±0.49 | 0.032 |
| Social status | 3.80±1.50 | 3.14±1.71 | 3.47±1.64 | 0.036 |
| Education | 4.92±0.99 | 5.11±0.80 | 5.01±0.90 | 0.529 |
| Main diagnosis | 1.75±0.93 | 1.86±0.97 | 1.81±0.95 | 0.717 |
| Event | 1.22±0.42 | 1.08±0.27 | 1.15±0.36 | 0.022 |
| Localization | 1.38±0.49 | 1.3±0.46 | 1.34±0.48 | 0,071 |
| Smoking | 0.54±0.79 | 0.64±0.79 | 0.59±0.79 | 0.627 |
| Alcohol | 0.34±0.64 | 0.41±0.70 | 0.37±0.67 | 0.832 |
| Arterial hypertension | 1.23±0.61 | 1.39±0.74 | 1.31±0.68 | 0.497 |
| Diabetes mellitus | 0.30±0.46 | 0.18±0.38 | 0.24±0.43 | 0.182 |

*Table 2.*

**Characteristics of the results of the BDI, FAS, and MHC-SF scales of patients classified by the presence of post-stroke depression.**

| Characteristics | Patients with depression (BDI >9) ( n =75) | Patients without depression (BDI < 9 ) ( n = 75) | Total ( n =150) | p -value |
|---|---|---|---|---|
| BDI scale | 16.70±6.95 | 6.51±3.82 | 10.74±8.03 | |
| FAS scale | 39.89 ± 9.80 | 31.35 ± 6.29 | 35.68±9.28 | 0,000 |
| MHC-SF scale | 72.78 ± 16.61 | 85.77 ± 16.62 | 79.19±17.79 | 0,000 |

Table 3 presents the distribution of patients by degrees of depression, as assessed using the BDI (Beck Depression Inventory).

*Table 3.*

**Descriptive statistics for the BDI depression scores.**

| Degree of depression | Abs. | % | DI |
|---|---|---|---|
| Absence of depressive symptoms | 74 | 49.3 | 41.3-57.3 |
| Mild depression | 47 | 31.3 | 23.9-38.8 |
| Moderate depression | 10 | 6.7 | 2.7-10.7 |
| Severe depression | 16 | 10.7 | 5.7-15.6 |
| Severe depression | 3 | 2.0 | -0.2-4.2 |

The analysis includes absolute numbers, percentages, and confidence intervals (CI). Absence of depressive symptoms: The largest proportion of patients (N = 74, 49.3%, CI: 41.3–57.3) showed no depressive symptoms. Nearly half of the study sample was in a normal emotional state, suggesting a low prevalence of depression in the group. Mild depression was observed in 31.3% (N = 47, CI: 23. Moderate depression was noted in 6.7% (N = 10, CI: 2.7–10.7). Marked depression was present in 10.7% (N = 16, CI: 5.7–15.6). Severe depression was identified in 2% (N = 3, CI: -0.2–4.2) ] About half of the sample showed no symptoms of depression, while 50.7% of patients displayed various degrees of depression (ranging from mild to severe). Mild and marked depression comprised the majority among those with symptoms, highlighting the need for monitoring and early intervention.

Table 4 presenting descriptive statistics, shows the mean values (μ), standard deviations (SD), and confidence intervals (CI) for each item of the Beck Depression Inventory (BDI). The data allow for an assessment of the intensity of various aspects of depression in the studied group.

**Items with the highest mean values:**

- *Loss of interest in sex* (1.45±0.12, CI: 1.22–1.69) had the highest score, indicating the prevalence of this symptom among patients. This may be associated with physiological and psycho-emotional changes caused by stroke.
- *Fatigue* (0.77 ± 0.07, CI: 0.62–0.91) and *sleep disturbance* (0.72 ± 0.09, CI: 0.55–0.89) also showed high mean values, confirming their significance as components of depressive states in this patient group.
- *Irritability* (0.70 ± 0.06, CI: 0.57–0.83) and *loss of energy* (0.66 ± 0.08, CI: 0.51–0.81) were also notably pronounced among participants.

**Items with low mean values:**

• *Suicidal thoughts* (0.13±0.20, CI: 0.07–0.20) and *appetite changes* (0.21 ± 0.05, CI: 0.12–0.31) had the lowest scores, suggesting these aspects of depression were less prominent in this sample.

• *Past failures* (0.19 ± 0.05, CI: 0.09–0.29) and *self-dislike* (0.23 ± 0.05, CI: 0.12–0.33) were also relatively infrequent.

*Table 4.*

**Descriptive statistics of the Beck Depression Inventory.**

| Points | μ | SD | DI |
|---|---|---|---|
| Sadness | 0.53 | 0.06 | 0.42-0.64 |
| Pessimism | 0.62 | 0.05 | 0.51-0.73 |
| Failures in the past | 0.19 | 0.05 | 0.09-0.29 |
| Loss of pleasure | 0.41 | 0.06 | 0.30-0.52 |
| Guilt | 0.42 | 0.06 | 0.30-0.54 |
| Feeling of Punishment | 0.27 | 0.07 | 0.14-0.41 |
| Self-loathing | 0.23 | 0.05 | 0.12-0.33 |
| Self-criticism | 0.56 | 0.08 | 0.41-0.71 |
| Thoughts of suicide | 0.13 | 0.20 | 0.07-0.20 |
| Cry | 0.40 | 0.05 | 0.30-0.50 |
| Irritability | 0.70 | 0.06 | 0.57-0.83 |
| Loss of interest | 0.43 | 0.07 | 0.30-0.56 |
| Indecision | 0.68 | 0.09 | 0.50-0.86 |
| Uselessness | 0.40 | 0.07 | 0.27-0.53 |
| Loss of energy | 0.66 | 0.08 | 0.51-0.81 |
| Change of sleep | 0.72 | 0.09 | 0.55-0.89 |
| Fatigue | 0.77 | 0.07 | 0.62-0.91 |
| Change in appetite | 0.21 | 0.05 | 0.12-0.31 |
| Weight loss | 0.42 | 0.08 | 0.27-0.57 |
| Anxiety | 0.57 | 0.08 | 0.42-0.71 |
| Loss of interest in sex | 1.45 | 0.12 | 1.22-1.69 |

The high scores for fatigue, sleep changes, and energy loss confirm the importance of the physical aspects of depression in stroke patients.

***Descriptive statistics of the Beck Depression Inventory***

The physical and mental fatigue scores were compared using the Mann–Whitney U test in stroke patients with and without depressive symptoms. A p value < 0.05 was considered statistically significant. Stroke survivors with depressive symptoms had significantly higher FAS, physical, and mental scores than those without symptoms (Table 5).

*Table 5.*

**Comparison of fatigue scores with and without depressive symptoms.**

| | Me (IQR) | U Mann-Whitney | Z | p |
|---|---|---|---|---|
| General<br>With depression<br>No depression | <br>39 (32-46)<br>30 (27-35) | 1207,5 | -6,040 | 0,001 |
| Physical fatigue<br>With depression<br>No depression | <br>13 (11-16)<br>10 (9-12) | 1504.5 | -4,944 | 0,001 |
| Mental fatigue<br>With depression<br>No depression | <br>13 (10-16)<br>10 (9-11) | 1339,0 | -5,587 | 0,001 |

Correlation analysis showed significant positive relationships between all three categories of well-being: emotional and social well-being: r = 0.415** (p < 0.01), emotional and psychological well-being: r = 0.461** (p < 0.01), social and psychological well-being: r = 0.576** (p < 0.01). These results confirm that higher levels of one type of well-being are associated with higher levels of other types of well-being. Thus, emotional, social and psychological well-being are interrelated aspects of overall well-being reflected in the MHC-SF (Table 6).

*Table 6.*

**Descriptive statistics and Spearman's correlation coefficients subscales MHC – SF.**

| | Emotional well-being | Social welfare | Psychological well-being | MHC-SF total |
|---|---|---|---|---|
| M (SD) | 14.09 ( 0.29 ) | 13.92 ( 0.40 ) | 23.17 ( 0.40 ) | 51,80 (10,12) |
| Emotional well-being | - | 0.415 ** | 0.461 ** | |
| Social welfare | 0.415 ** | - | 0.576 ** | |
| Psychological well-being | 0.461 ** | 0.576 ** | - | |

** - the correlation is significant at the 0.01 level

The relationships between the FAS fatigue scale, the MHC-SF psychological well-being scale and the Beck scale were assessed. The results are presented as correlation coefficients: the Beck scale and the psychological well-being scale (MHC-SF) correlate positively (r = 0.579**), indicating a significant relationship between low levels of depression (according to the Beck scale) and high levels of psychological well-being, the Beck scale and the FAS fatigue scale correlate negatively (r = -0.375**), indicating that higher levels of depression are associated with increased levels of fatigue, the FAS fatigue scale and the psychological well-being scale (MHC-SF) correlate negatively (r = -0.192**), indicating that high levels of fatigue are associated with lower levels of psychological well-being (Table 7).

*Table 7.*

**Spearman Correlation Coefficients of Beck Depression Inventory, FAS Fatigue, and MHC - SF Psychological Well-Being.**

| | Fatigue Scale (FAS) | MHC - SF Psychological Well-Being Scale |
|---|---|---|
| Beck scale | 0.579 ** | -0.375 ** |
| Fatigue Scale (FAS) | | -0.192 ** |

** *Correlation is significant at the 0.01 level*

* *Correlation is significant at the 0.05 level*

**Discussion**

This study analyzed the clinical and demographic indicators of stroke survivors, with a focus on identifying the presence of post-stroke depression (PSD). The results revealed a statistically significant association between participants' age and the manifestation of depressive symptoms. The average age of patients with PSD was 62.92±8.61 years, which is higher than that of the group without signs of depression (59.89±9.59 years; p=0.001). This finding suggests that the likelihood of developing depression after a stroke increases with age, a trend supported by previously published studies. Specifically, according to literature, the average age of patients with PSD is about 68.3 years, while among those without depression it is around 63.1 years. Additional support for this trend comes from a study by *Monika Sadlonova and colleagues,* which found a higher frequency of depressive symptoms in individuals over the age of 60, aligning with the findings of this analysis.

When comparing clinical-laboratory parameters (including body mass index, blood glucose levels, total cholesterol, lipoproteins, triglycerides, creatinine, and glomerular filtration rate), no significant differences were found between patients with and without post-stroke depression. These data suggest that metabolic and vascular factors did not play a leading role in the development of depressive symptoms in the examined group. However, other studies point to the potential significance of certain biomarkers. For example, according to a meta-analysis by *Yiwen Wang and colleagues,* elevated blood glucose levels during the acute phase of stroke may increase the risk of developing PSD. A study led by *Yagiang Li* found an association between low levels of low-density lipoproteins (LDL) and the onset of PSD in cases of mild stroke, as well as between a high monocyte-to-high-density lipoprotein cholesterol (HDL) ratio and the risk of depression. Additionally, *Shiming Li and colleagues* demonstrated that a higher body mass index is associated with a greater risk of developing PSD (OR=2.46). However, these findings remain contradictory, as other studies have not confirmed a significant association between BMI and depressive symptoms after stroke. Regarding creatinine levels and glomerular filtration rate, the available literature provides very limited data on their connection to PSD, and no direct relationship has been established thus far.

**Gender and social status** demonstrated a significant impact on the likelihood of developing post-stroke depression (PSD). In particular, women were statistically more frequently represented among patients diagnosed with depression (p=0.032), which confirms data from previous studies highlighting the greater vulnerability of the female population to affective disorders. These findings align with the results of a meta-analysis conducted by Matthias Volz and co-authors. It was also found that patients with PSD had a lower social status compared to those without depressive symptoms (p=0.036). This suggests that socio-economic conditions may play a substantial role in the development of depressive manifestations in the post-stroke period. The influence of social status is likely mediated not only through profession or societal standing but also through factors such as the level of social support, economic stability, the severity of functional limitations, and the possibility of returning to customary social and occupational activities.

**Fatigue** was recorded in 54.7% of the examined patients, with a mean FAS score of 35.68±9.28, indicating the prevalence of this condition among the post-stroke population. Group comparisons revealed that patients with depressive symptoms exhibited a significantly higher level of fatigue (39.89±9.80) compared to those without depression (31.35±6.29; p<0.001), suggesting a close link between depression and subjectively experienced fatigue. PSD is one of the key factors contributing to pronounced fatigue following a stroke. Such patients experience fatigue more frequently and more intensely than those without depressive symptoms.

It should be noted that, despite their close association, **fatigue and depression can exist independently**: fatigue may persist even when depressive symptoms decrease. Moreover, a significant portion of patients without clinically apparent depression also experience fatigue at various points post-stroke — reported in 43% to 51% of cases according to the literature. In these patients, fatigue is associated with reduced physical activity, limited mobility, impaired daily functioning, and decreased overall quality of life. In PSD patients, fatigue is often accompanied by additional symptoms such as sleep disturbances, cognitive deficits (including slower information processing and memory impairment), and a greater degree of disability.

Given the clinical relevance of both the physical and psychological components of fatigue in patients diagnosed with depression, this symptom should be considered an important marker deserving special attention during screening, diagnosis, and in the planning of comprehensive PSD therapy.

**Analysis of the data obtained using the MHC-SF scale** showed that patients with pronounced depressive symptoms had a significantly lower level of psychological well-being (72.78±16.61) compared to participants without signs of depression (85.77±16.62; $p < 0.001$). These differences underscore the substantial impact of depression on the overall psycho-emotional state of stroke survivors. The results confirm that the presence of depressive symptoms in post-stroke patients is associated with a more marked decline in subjective well-being.

According to the literature, about one-third of stroke patients experience depression, which negatively affects all aspects of quality of life—physical health, emotional state, and social activity. Depression can also hinder successful rehabilitation and increase the risk of mortality. Research indicates that depression is one of the most significant predictors of reduced psychological well-being, as measured by tools like the MHC-SF and similar scales.

**The conducted correlation analysis** revealed significant associations between the severity of depression, levels of fatigue, and psychological well-being. A higher level of depressive symptoms was associated with a lower level of subjective well-being ($r = 0.579$; $p < 0.01$) and with more pronounced fatigue ($r = -0.375$; $p < 0.01$). These findings emphasize the need for a comprehensive approach to evaluating the psycho-emotional state of stroke patients, including assessments of depression, fatigue, and psychological well-being, since these factors are closely

interconnected and may mutually reinforce each other's negative effects.

**The analysis of the severity of depressive symptoms** showed that 50.7% of participants exhibited signs of depression of varying severity. The most common was mild depression, diagnosed in 31.3% of participants, highlighting the importance of early detection of emotional disturbances and timely initiation of psychotherapeutic support. According to previous studies, mild depression is found in approximately 13–15% of stroke patients, while severe forms occur in 17–18% of cases. Additionally, the sample showed a high prevalence of individual depression symptoms, such as fatigue, sleep disturbances, and reduced libido. These clinical manifestations deserve special attention as they can significantly reduce patients' quality of life.

Independent studies also confirm that the most typical depressive symptoms after a stroke include fatigue, insomnia, and loss of interest in sex. These conditions often persist over time and hinder successful recovery. Notably, decreased libido may remain under-recognized in clinical practice due to the sensitive nature of the topic and patients' reluctance to discuss sexual health with medical professionals.

In conclusion, the data indicate a high prevalence of depressive symptoms among stroke survivors and their association with factors such as age, gender, social environment, and fatigue levels. Incorporating a comprehensive assessment of depression and fatigue into standard rehabilitation care could contribute to a more complete recovery of the psycho-emotional state and positively impact the overall quality of life for these patients.

**Conclusion**

The results of the study highlight the importance of a multifaceted approach to stroke patient recovery, which should include not only physical rehabilitation but also efforts to reduce fatigue, enhance psychological well-being, and ensure timely diagnosis of depressive states. The emotional resources retained by many patients can be leveraged to improve their quality of life and increase the effectiveness of rehabilitation programs.

***Conflict of interest.*** *No conflicts of interest have been declared.*

***Authors' Contributions.*** *All authors participated equally in the writing of this article. This material has not been previously submitted for publication in other publications and is not under consideration by other publishers.*

***Funding.*** *No funding was provided. There was no third-party funding or medical representation in the conduct of this work.*

***Literature:***

1. *Virani S.S., Alonso A., Aparicio H.J., Benjamin E.J., Bittencourt M.S., Callaway C.W.* et al. Heart Disease and Stroke Statistics-2021 Update: A Report From the American Heart Association. *Circulation*. February 23, 2021; 143(8):e254–743.

2. Post-stroke depression: scientifically substantiated approaches to choosing therapy | Starchina | *Neurology, Neuropsychiatry, Psychosomatics* [Internet]. [Accessed January 27, 2025]. Available from: https://nnp.ima-press.net/nnp/article/view/344

3. Post-stroke depression - PubMed [Internet]. [Accessed January 27, 2025]. Available from: https://pubmed.ncbi.nlm.nih.gov/18088202/

4. «Pharmateka» Post-stroke depression [Internet]. [Accessed January 27, 2025]. Available from: https://pharmateca.ru/ru/archive/article/8293

5. Post-stroke depression: scientifically substantiated approaches to therapy – read the full research article for free in the CyberLeninka electronic library [Internet]. [Accessed January 27, 2025]. Available from: https://cyberleninka.ru/article/n/postinsultnaya-depressiya-nauchno-obosnovannye-podhody-k-vyboru-terapii

6. Post-stroke depression: prevalence, pathogenesis, diagnosis, and treatment – read the research article for free in the CyberLeninka electronic library [Internet]. [Accessed January 27, 2025]. Available from: https://cyberleninka.ru/article/n/postinsultnaya-depressiya-rasprostranennost-patogenez-diagnostika-i-lechenie

7. Validity of the Beck Depression Inventory, Hospital Anxiety and Depression Scale, SCL-90, and Hamilton Depression Rating Scale as screening instruments for depression in stroke patients - PubMed [Internet]. [Accessed January 27, 2025]. Available from: https://pubmed.ncbi.nlm.nih.gov/12297607/

8. *Mead G., Lynch J., Greig C., Young A., Lewis S., Sharpe M.* Evaluation of fatigue scales in stroke patients. *Stroke*. July 2007; 38(7):2090–5.

9.*Jaiswal V., Ang S.P., Suresh V., Nasir Y., Joshi A., Kumar D.* et al. Abstract TP24: C-Reactive Protein, and Homocysteine as Predictors of Post-Stroke Depression Among Stroke Patients: A Meta-Analysis and Meta Regression. *Stroke*. February 2024; 55(Suppl_1):ATP24–ATP24.

10. *Sadlonova M., Wasser K., Nagel J., Weber-Krüger M., Gröschel S., Uphaus T.* et al. Health-related quality of life, anxiety and depression up to 12 months post-stroke: Influence of sex, age, stroke severity and atrial fibrillation – A longitudinal subanalysis of the Find-AFRANDOMISED trial. *Journal of Psychosomatic Research*. March 1, 2021; 142:110353.

11. *Wang Y., Zhu L., Tan X., Cheng Y., Wang X., Fang S.* Higher levels of peripheral blood glucose in the acute stage of stroke increase the risk of post-stroke depression: A systematic review and meta-analysis. *Neuroscience & Biobehavioral Reviews*. November 1, 2022; 142:104829.

12. *Li Y., Zhang M., Xue M., Liu D., Sun J.* Elevated monocyte-to-HDL cholesterol ratio predicts post-stroke depression. *Front Psychiatry* [Internet]. July 22, 2022 [Accessed May 31, 2025];13. Available from: https://www.frontiersin.org/journals/psychiatry/articles/10.3389/fpsyt.2022.902022/full

13. *Li S., Guo B., Yang Q., Yin J., Tian L., Zhu H.* et al. Evaluation of depression status and its influencing factors in convalescent elderly patients with first-episode stroke. *Asian Journal of Psychiatry* [Internet]. 2022 [Accessed May 31, 2025]. 77. Available from: https://consensus.app/papers/evaluation-of-depression-status-and-its-influencing-li-guo/3ac6e651dfcf59fe980e334bf2b0d9af/

14. The effect of metabolic factors on post-stroke depression in ischemic stroke patients. 2019. Available

from: https://consensus.app/papers/the-effect-of-metabolic-factors-on-the-poststroke/081273bbfce855a7b4ae77766ca4f3f8/ [Accessed May 31, 2025];

15. *Volz M., Ladwig S., Werheid K.* Gender differences in post-stroke depression: A longitudinal analysis of prevalence, persistence, and predictive value of known risk factors. *Neuropsychological Rehabilitation*. January 2, 2021; 31(1):1–17.

16. *Nguyen T.T.P., Nguyen T.X., Nguyen T.C., Nguyen H.T.T., Nguyen T.N., Nguyen T.T.H.,* et al. Post-stroke depression in Vietnamese patients is associated with decreased sleep quality and increased fatigue: a one-institution cross-sectional analysis. *Sleep Breath*. August 1, 2023; 27(4):1629–37.

17. *Zhang S., Cheng S., Zhang Z., Wang C., Wang A., Zhu W.* Related risk factors associated with post-stroke fatigue: a systematic review and meta-analysis. *Neurological Sciences*. April 1, 2021; 42(4):1463–71.

18. *Dong Y., Tang L., Badrin S., Badrin S., Wu J.* Factors associated with post-stroke fatigue among stroke survivors: a cross-sectional study. *PeerJ*. March 6, 2025; 13:e19052.

19. *Kirchberger I., Wallner F., Linseisen J., Zickler P., Ertl M., Naumann M.* et al. Factors Associated With Early and Late Post-stroke Fatigue in Patients With Mild Impairment. Results From the Stroke Cohort Study Augsburg. *Frontiers in Neurology* [Internet]. March 14, 2022 [Accessed May 31, 2025];13. Available from: https://www.frontiersin.org/journals/neurology/articles/10.3389/fneur.2022.852486/full

20. *Lee Y.J., Jung W.S., Kwon S., Jin C., Cho S.Y, Park S.U.* et al. An Analysis of Characteristics of Post-Stroke Fatigue in Patients without Depression: A Retrospective Chart Review. *Brain Sciences*. December 2021; 11(12):1642.

21. *Fischer S., Linseisen J., Kirchberger I., Zickler P., Ertl M., Naumann M.* et al. Association of post-stroke depression and health-related quality of life three months after the stroke event. Results from the Stroke Cohort Augsburg (SCHANA) study. *Psychology, Health & Medicine*. May 28, 2023; 28(5):1148–59.

22. *Curatoli C., Marcassoli A., Guastafierro E., Leonardi M., Bersano A, Boncoraglio G.* et al. An observational, cross-sectional and monocentric study assessing psychological and cognitive features as main predictors of psychological well-being in stroke survivors. *International Journal of Rehabilitation Research*. December 2023; 46(4):355.

23. *Chen H., Sun Y., Song Z., Lin Z., Sang Y., Fu X.* et al. Association of depressive symptom severity and suicidal ideation with health-related quality of life among stroke survivors, NHANES 2005–2018. *Psychiatry Research*. June 1, 2024; 336:115891.

24. *Liu L., Xu M., Marshall I.J., Wolfe C.D., Wang Y., O'Connell M.D.* Prevalence and natural history of depression after stroke: A systematic review and meta-analysis of observational studies. *PLOS Medicine*. 2023; 20(3):e1004200.

25. *Medeiros G.C., Roy D., Kontos N., Beach S.R.* Post-stroke depression: A 2020 updated review. *General Hospital Psychiatry*. September 1, 2020; 66:70–80.

**Information about the authors:**

**Baizullina Akgul Ospanovna** – Master of Medical Sciences, West Kazakhstan Marat Ospanov Medical University, Aktobe, Kazakhstan, phone 8 777 800 72 72, email: baizullinaakgul@gmail.com https://orcid.org/0000-0002-3992-1419;

**Zhamaliyeva Lazzat Manbetzhanovna -** Candidate of medical sciences, associate professor, West Kazakhstan Marat Ospanov Medical University, Aktobe, Kazakhstan, phone 8 701 213 0862; email: lzhamalieva@mail.ru, https://orcid.org/0000-0003-3625-3651;

**Yermagambetova Aigul Pazylbekovna** Candidate of medical sciences, associate professor, West Kazakhstan Marat Ospanov Medical University, Aktobe, Kazakhstan, phone phone +7 747 219 3323; email: aiguler72@mail.ru https://orcid.org/0000-0002-3230-0433;

**Corresponding author:**

**Baizullina Akgul Ospanovna** - Master of Medical Sciences, West Kazakhstan Marat Ospanov Medical University, Aktobe, Kazakhstan,

**Postal code:** Republic of Kazakhstan, 030019, Aktobe city, Maresyev Street 68.

**E-mail:** baizullinaakgul@gmail.com

**Phone:** +7 777 800 72 72

Received: 12 February 2025 / Accepted: 14 May 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2025.27.3.009***

***UDC 316.728:316.344.273.4(574)***

This work is licensed under a Creative Commons Attribution 4.0 International License

# SOCIAL DETERMINANTS OF HEALTH AMONG UNEMPLOYED YOUTH IN KAZAKHSTAN: HOW ECONOMIC DISPARITY AFFECTS QUALITY OF LIFE

**Samal Duisekova[1]**, **https://orcid.org/0000-0001-7644-145X**
**Mereilim Gaisina [2],** **https://orcid.org/0009-0002-5829-4008**
**Kamila M. Akhmetova[1],** **https://orcid.org/0009-0009-6257-4337**
**Margulan Uazhanov[1],** **https://orcid.org/0000-0002-7075-3716**
**Raushan K. Sekenova[1],** **https://orcid.org/0000-0001-7533-160X**
**Gaukhar Sh. Dauletova[1],** **https://orcid.org/0000-0002-1621-8149**

**[1] NJSC "Astana Medical University", Astana, Republic of Kazakhstan;**
**[2] Nazarbayev University School of Medicine, Astana, Republic of Kazakhstan.**

**Abstract**

**Objectives.** Both globally and in Kazakhstan, youth unemployment remains a problem contributing to social, economic and health inequalities. This study **aimed** to assess the social determinants of health among unemployed youth in Kazakhstan, with a specific focus on how economic inequality influences their quality of life. **Materials and methods.** A cross-sectional study design was employed using the Quality of Life, Enjoyment, and Satisfaction Questionnaire (Q-LES-Q) among unemployed and employed youth aged 18–29. Statistical analyses, including the Mann-Whitney test and multiple regression, were conducted. **Results.** Unemployed youth reported significantly lower overall quality of life compared to employed youth (U=36878.5, Z=-3.472, p=0.001). Key determinants of quality of life included financial well-being, marital status, and perceived governmental support. Regression analysis revealed that financial well-being, marital status, and perceived governmental support were significant predictors of quality of life, with the model explaining 58% of the variance ($R^2$=0.582). **Conclusion.** Youth unemployment in Kazakhstan is strongly associated with reduced quality of life, which is affected by economic inequality and limited social support. Addressing financial insecurity and strengthening state and community support systems are important for improving the well-being of unemployed youth.

***Keywords:*** *quality of life, unemployment, NEET, Self-rated health, youth health, social determinants.*

***For citation:***

Duisekova S., Gaisina M., Akhmetova K., Uazhanov M., Sekenova R.K., Dauletova G.Sh. Social Determinants of Health Among Unemployed Youth in Kazakhstan: How Economic Disparity Affects Quality of Life // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 79-87. *doi 10.34689/SH.2025.27.3.009*

**Резюме**

# СОЦИАЛЬНЫЕ ДЕТЕРМИНАНТЫ ЗДОРОВЬЯ СРЕДИ БЕЗРАБОТНОЙ МОЛОДЕЖИ В КАЗАХСТАНЕ: КАК ЭКОНОМИЧЕСКОЕ РАЗЛИЧИЕ ВЛИЯЕТ НА КАЧЕСТВО ЖИЗНИ

**Самал Б. Дуйсекова[1],** **https://orcid.org/0000-0001-7644-145X**
**Мерейлим М. Гайсина[2],** **https://orcid.org/0009-0002-5829-4008**
**Камила М. Ахметова[1],** **https://orcid.org/0009-0009-6257-4337**
**Маргулан Уажанов[1],** **https://orcid.org/0000-0002-7075-3716**
**Раушан К. Секенова[1],** **https://orcid.org/0000-0001-7533-160X**
**Гаухар Ш. Даулетова[1],** **https://orcid.org/0000-0002-1621-8149**

**[1] НАО «Медицинский университет Астана», г. Астана, Республика Казахстан;**
**[2] Школа медицины Назарбаев Университета, г. Астана, Республика Казахстан**

**Цели.** Как в мире, так и в Казахстане, безработица среди молодежи остается проблемой, способствующей социальным, экономическим и здравоохранительным неравенствам. **Цель исследования** была направлена на оценку социальных детерминант здоровья среди безработной молодежи в Казахстане, с особым акцентом на то, как экономическое неравенство влияет на качество их жизни. **Материалы и методы.** Была использована поперечная

структура исследования с применением Опросника качества жизни, удовольствия и удовлетворения (Q-LES-Q) среди безработной и работающей молодежи в возрасте 18–29 лет. Проводился статистический анализ, включая критерий Манна-Уитни и множественную регрессию. **Результаты.** У безработной молодежи было зафиксировано значительно более низкое общее качество жизни по сравнению с работающей молодежью (U=36878.5, Z=-3.472, p=0.001). Ключевыми детерминантами качества жизни были финансовое благополучие, семейное положение и воспринимаемая молодежью государственная поддержка. Регрессионный анализ показал, что финансовое благополучие, семейное положение и воспринимаемая государственная поддержка являются значимыми предикторами качества жизни, при этом модель объясняет 58% дисперсии ($R^2$=0.582). **Выводы.** Безработица среди молодежи в Казахстане тесно связана со снижением качества жизни, на которое влияют экономическое неравенство и ограниченная социальная поддержка. Устранение финансовой нестабильности и укрепление систем поддержки со стороны государства и общества важны для повышения благополучия безработной молодежи.

***Ключевые слова:*** *качество жизни, безработица, NEET, самооценка здоровья, здоровье молодежи, социальные детерминанты.*

***Для цитирования:***

*Дуйсекова С., Гайсина М., Ахметова К.М., Уажанов М., Секенова Р.К., Даулетова Г.Ш.* Социальные детерминанты здоровья среди безработной молодежи в Казахстане: как экономическое различие влияет на качество жизни // Наука и Здравоохранение. 2025. Т.27 (3), С. 79-87. doi: 10.34689/SH.2025.27.3.009

**Түйіндеме**

# ҚАЗАҚСТАНДАҒЫ ЖҰМЫССЫЗ ЖАСТАРДЫҢ ДЕНСАУЛЫҚТЫҢ ӘЛЕУМЕТТІК АНЫҚТАУЫШТАРЫ: ЭКОНОМИКАЛЫҚ ЕРЕКШЕЛІКТЕРДІҢ ӨМІР САПАСЫНА ӘСЕРІ

**Самал Б. Дуйсекова[1], https://orcid.org/0000-0001-7644-145X**
**Мерейлим М. Гайсина[2], https://orcid.org/0009-0002-5829-4008**
**Камила М. Ахметова[1], https://orcid.org/0009-0009-6257-4337**
**Маргулан Уажанов[1], https://orcid.org/0000-0002-7075-3716**
**Раушан К. Секенова[1], https://orcid.org/0000-0001-7533-160X**
**Гаухар Ш. Даулетова[1], https://orcid.org/0000-0002-1621-8149**

**[1] «Астана медицина университеті» КеАҚ, Астана қ., Қазақстан Республикасы;**
**[2] Назарбаев Университетінің Медицина мектебі, Астана қ., Қазақстан Республикасы.**

**Мақсаты.** Әлемдегі трендттермен қатар Қазақстанда жастар арасындағы жұмыссыздық әлеуметтік, экономикалық және денсаулық теңсіздіктеріне ықпал ететін мәселе болып қала береді. Бұл зерттеу Қазақстандағы жұмыссыз жастардың денсаулық әлеуметтік анықтауыштарын, әсіресе экономикалық теңсіздіктің өмір сапасына әсерін бағалауға бағытталды. **Әдістері.** Зерттеуде көлденең зерттеу дизайны қолданылды, жұмыссыз және жұмыспен қамтылған 18–29 жас аралығындағы жастар арасында Өмір Сапасы, Ризашылық және Қанағаттану Сауалнамасы (Q-LES-Q) пайдаланылды. Статистикалық талдаулар, соның ішінде Манн-Уитни тесті және көптік регрессия жүргізілді. **Нәтижелері.** Жұмыссыз жастардың өмір сапасы жұмыспен қамтылған жастарға қарағанда едәуір төмен екені анықталды (U=36878.5, Z=-3.472, p=0.001). Өмір сапасының негізгі анықтағыштары қаржылық жағдай, ерлі-зайыптылық және үкіметтік қолдаудың қабылдануы болып табылды. Регрессия талдауы өмір сапасының айтарлықтай болжаушылары ретінде қаржылық жайт, отбасылық жағдай және үкіметтік қолдауды анықтады, модель өзгеріс көрсеткішінің 58%-ын түсіндірді ($R^2$=0.582). **Қорытынды.** Қазақстандағы жастар арасындағы жұмыссыздық олардың өмір сапасының төмендеуімен тығыз байланысты, оған экономикалық теңсіздік пен шектеулі әлеуметтік қолдау әсер етеді. Қаржылық тұрақсыздықты азайту және мемлекет пен қауымдастықтың қолдау жүйелерін күшейту жұмыссыз жастардың әл-ауқатын жақсарту үшін маңызды болып табылады.

***Түйінді сөздер:*** *өмір сапасы, жұмыссыздық, NEET, денсаулықтың өзін-өзі бағалау, жастар денсаулығы, әлеуметтік анықтағыштар.*

***Дәйексөз үшін:***

*Дуйсекова С., Гайсина М., Ахметова К.М., Уажанов М., Секенова Р.К., Даулетова Г.Ш.* Қазақстандағы жұмыссыз жастардың денсаулықтың әлеуметтік анықтауыштары: Экономикалық ерекшеліктердің өмір сапасына әсері // Ғылым және Денсаулық. 2025. Т.27 (3), Б. 79–87. doi: 10.34689/SH.2025.27.3.009

**Introduction**

One of the sharpest problems all over the world is the growth of unemployment. As we know, the high level of economic crisis increases social and political instability in society. Moreover, socio-economic inequality and poverty influence various aspects of youth life, including access to healthcare, nutrition, physical and mental health [1, 2, 3].

According to research conducted by the ILO, the rate of temporary employment among young people is twice as high as among adults, young people are more likely to be employed in irregular paid work without a contract [4]. Today in Kazakhstan the problems of the market are: mismatch of qualification and professional structure of demand and supply of labour force; mismatch of personnel training to the needs of the economy; difficulty of employment of certain groups of population (women, young people, people of pre-retirement age, disabled people) [5, 6]. Reducing the loss of health of the population cannot be assigned to only one link of assistance to unemployed youth. Often young people belong to vulnerable groups in the labour market. A number of such factors contribute to this: lack of a certain level of qualification and practical work experience, etc. [7]. As an emerging subject of social relations, young people are in the stage of forming their status and motivation - needs, interests, values, motives, attitudes, ideals [8, 9].

According to the WHO, the NEET rate, together with the unemployment rate, is an important indicator that determines the situation of young people [10]. Modern science also increasingly uses the concept of 'NEET generation' (English: Not in Education, Employment or Training) or 'ni ni generation' (Spanish: ni estudia, ni trabaja). The World Bank emphasizes that a high NEET rate, even in the presence of a low youth unemployment rate, may indicate significant discouragement among young people, reflecting their disengagement from both employment and educational opportunities [11]. According to the International Labour Organization (ILO) report, the persistently high levels of NEET in the world are a growing concern among today's young people: the youth unemployment rate in 2023 was 13 per cent (64.9 million people) [12]. In Kazakhstan in 2001 it was revealed that every fifth young person has this status. It should be noted that in our country this index is considered in a wider diapason: for in the Republic of Kazakhstan youth are citizens of the country from 14 to 25 (29) years old [13].

Historically, unemployment has been associated with various physical and psychological consequences, such as rising, alcohol and cigarette use, low self-esteem and life satisfaction. In addition to mental health, unemployment also has adverse effects on the physical health of young people [14]. Youth unemployment as a chronic disease has a number of complications [15] which are exacerbated by lifestyle factors of the unemployed young person, including irregular routines and diet, and increased stressful environment. Among the consequences of low youth employment, social, emotional and health problems can be singled out separately; moreover, this segment of the population is exposed to low levels of well-being. And, as we know, protecting the health of the young population is one of the most important tasks for the state.

Despite the growing recognition of youth unemployment as a critical issue, limited research has been conducted in Kazakhstan to examine the social determinants of health among unemployed youth. This study aimed to identify key social determinants influencing health of unemployed youth in Kazakhstan, focusing on assessing how economic inequality affects their quality of life. Existing studies often overlook the multidimensional impact of unemployment on physical, mental, and social well-being, and few have utilized comprehensive tools like Q-LES-Q to assess quality of life in this demographic. The study seeks to understand the interplay between economic inequality and health outcomes among this vulnerable population.

To achieve the expected goal, it is important to work out the following objectives:

1. Conducting a literature review on unemployment and its impact on general well-being
2. To analyse the impact of socio-economic inequality on the quality of life of unemployed youth using the Quality of Life, Enjoyment, and Satisfaction Questionnaire (Q-LES-Q).
3. To identify specific predictors of life satisfaction among unemployed youth, including physical and mental health of young people
4. To compare the quality-of-life indicators between Kazakhstani employed and unemployed youth.

**Methodology**

Quantitative study with elements of qualitative analysis was conducted to provide a deeper understanding of social determinants of health among unemployed youth.

*Data Collection and Sample*

Published international and national literature was reviewed, mainly devoted to the association of unemployment with the health and quality of life of the youth population, as well as to the organisation of health care for this contingent and some other issues. The search was carried out using the scientific international library systems such as PubMed, Springer, Elseiver, Web of Science, and Cochrane. A systematic keyword-based evidence search was conducted, using the PICO (TICO) methodology.

As part of a cross-sectional investigation, survey administered to unemployed youth to gather information on healthcare access, nutrition quality, and levels of physical and mental health. The standardised questionnaire Q-LES-Q (quality of life, enjoyment and satisfaction) was used. An integral index of quality of life was measured, which ranged from 14 to 70, where 14 was the worst value.

At the planning stage, the sample size was calculated using Lehr's formula. Purposive sampling of 669 participants aged 18 to 29 was performed, covering both urban and rural unemployed youth living in Kazakhstan in 2021. Of these: 184 (27.7%) unorganised respondents participated and 485 (72.3%) employed (working/student) respondents were enrolled as the control group. Participants were recruited through various communication channels, including employment centres, youth policy department, parties, NGOs, online forums and messengers.

The questionnaires were completed online - 651, in person - 18. A t-test was conducted to determine if there was a significant difference between the in-person or virtual responses and it was found that there was no difference in these responses. Therefore, it was decided to review the

data together. Sex, age, place of residence, education level of the respondent and his/her parents, and previous health status were used as covariates in the analyses. The survey consisted of 42 questions of which 17 were of general description, 25 aimed to study the impact of unemployment on the health of young people. Questions address income, education level, healthcare access, and daily habits.

*Ethical Considerations.*

The questionnaire was approved by the Local Ethical Commission. Participant confidentiality and voluntary participation in the study were ensured by study authors by obtaining hard-copy informed consent.

*Data Analysis Methods*

The methods of descriptive and analytical statistics were used. Statistical analysis of survey results was conducted using IBM SPSS Statistics 22 version software to identify correlations between socio-economic status and access to healthcare. Multiple regression was applied to assess relationships. The dependent variable was the quantitative variable 'Integral index of quality of life (according to Q-LES-Q)', the predictors were personal data of respondents and some other characteristics.

It should be noted that the investigation had several limitations including the subjectivity of the participants and the lack of long-term data.

**Results**

The Quality of Life, Enjoyment and Satisfaction Questionnaire (Q-LES-Q) is a self-report instrument designed to enable researchers to easily obtain sensitive measures of the degree of enjoyment and satisfaction experienced by subjects in various domains of daily activities.

According to the analysis, unemployed youth rated 53% "fair", 12 units higher than employed youth, who rated more than 9 % higher on the 'good' scale. The value of 'very poor' is the same in both cases.

Figure 1 shows the response options to the question 'How would you rate your overall satisfaction with your life in the last week?' among 18-29 years old unemployed and employed youth.

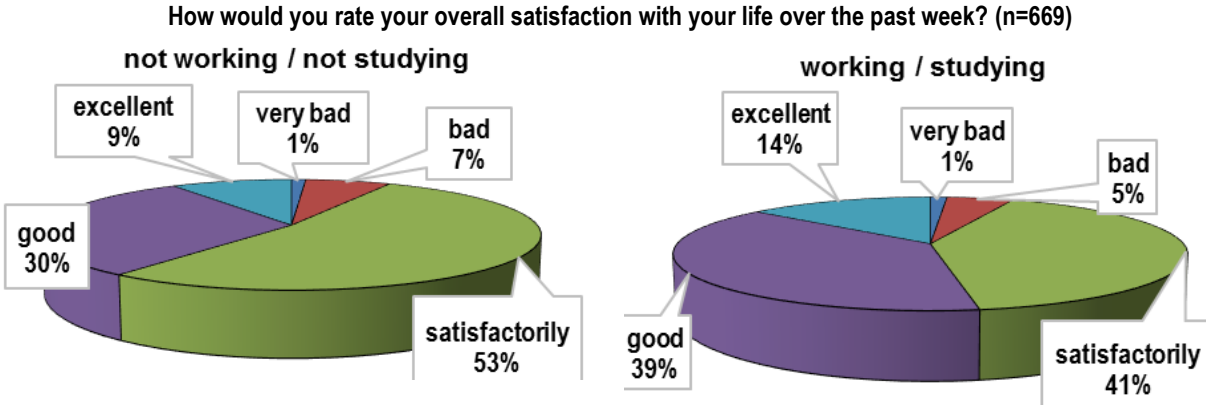



**Figure 1. Respondents' assessment of overall life satisfaction.**

From interviews conducted, employed young people feel more stable, which allows them not to worry about several daily activities. In contrast, the unemployed have a more marked concern, which is accompanied by an emotional impact. At the same time, the deterioration in overall quality of life is found more frequently in unemployed young people than in employed young people.

Figures 2 and 3 show the distribution of respondents' answers. According to the rules of interpretation of the Q-LES-Q scale, the scores are distributed from 14 to 70, where 14 is the worst score. As a result of evaluation of respondents' answers, the worst satisfaction indicators are present in the questions concerning the quality of "housing situation, physical health, economic condition", and vice versa, higher satisfaction results were shown in the sections "household affairs and social relations".

Table 1 presents descriptive statistics for the integral indicator of quality of life (according to Q-LES-Q).

The Mann-Whitney criterion was used to assess the differences between the average quality of life indicators in the groups of employed and unemployed young people: the difference is statistically significant (U=36878.5, Z=-3.472, p=0.001).

Multiple regression analysis was used to assess correlations. The dependent variable was the quantitative variable 'Integral indicator of quality of life (according to Q-LES-Q)'.

The following expected predictors of interest were analysed, which, in our belief, can affect the quality of life of unemployed youth: 'Gender', "Age", "Marital status", "Region of residence", "Place of residence", "Time of unemployment", "Education", "Mother's education", "Father's education", "Satisfaction with their education", "Occupation", "Sleep duration", "Time using social media", "Physical activity", "Financial well-being, after job loss/absence", 'Positioning with socioeconomic class', "COVID-19 disease fact", "Feeling supported by the government", "Feeling supported by family-parents", "Feeling supported by friends", "Assessment of one's (current) financial status", "Health problems in the last year", "Presence of chronic diseases", "Hospitalisation fact in the last year", "Smoking fact", "Alcohol consumption fact".

A stepwise inclusion method was used, in which the variables were entered into the model one at a time, until the regression equation was satisfactory, and the model was correct. A total of 7 steps were needed to select predictors that make a statistically significant contribution to the predictive ability of the model. The R-square measure was 0.582, which indicates that predictor variables can explain about 58% of the variation in the frequency of the dependent variable (quality of life of unemployed youth). The variables were tested for 'strong' relationship: there is no multicollinearity. The Durbin-Watson value was 1.858, with no autocorrelation.

According to the results of regression analysis, the model includes such predictors as 'Financial well-being, after job loss/absence (b=1.670, p=0.079)', 'Alcohol consumption (b=2.861, p=0.063)', 'Region of residence b=0. 379, p=0.009', "Feeling supported by the state b=-5.309, p=0.009", "Assessment of one's (current) financial situation b=2.127, p=0.012", "Marital status b=4.624 p=0.003" and "Occupation b=-1.115, p=0.049" (Figure 4). The other predictors were excluded, according to the results of the analysis, due to their insignificance. Thus, when assessing the quality of life of unemployed youth, reliable predictors of the level of satisfaction with the quality of life were the level of government support, financial well-being, and satisfaction with the quality of medical care.

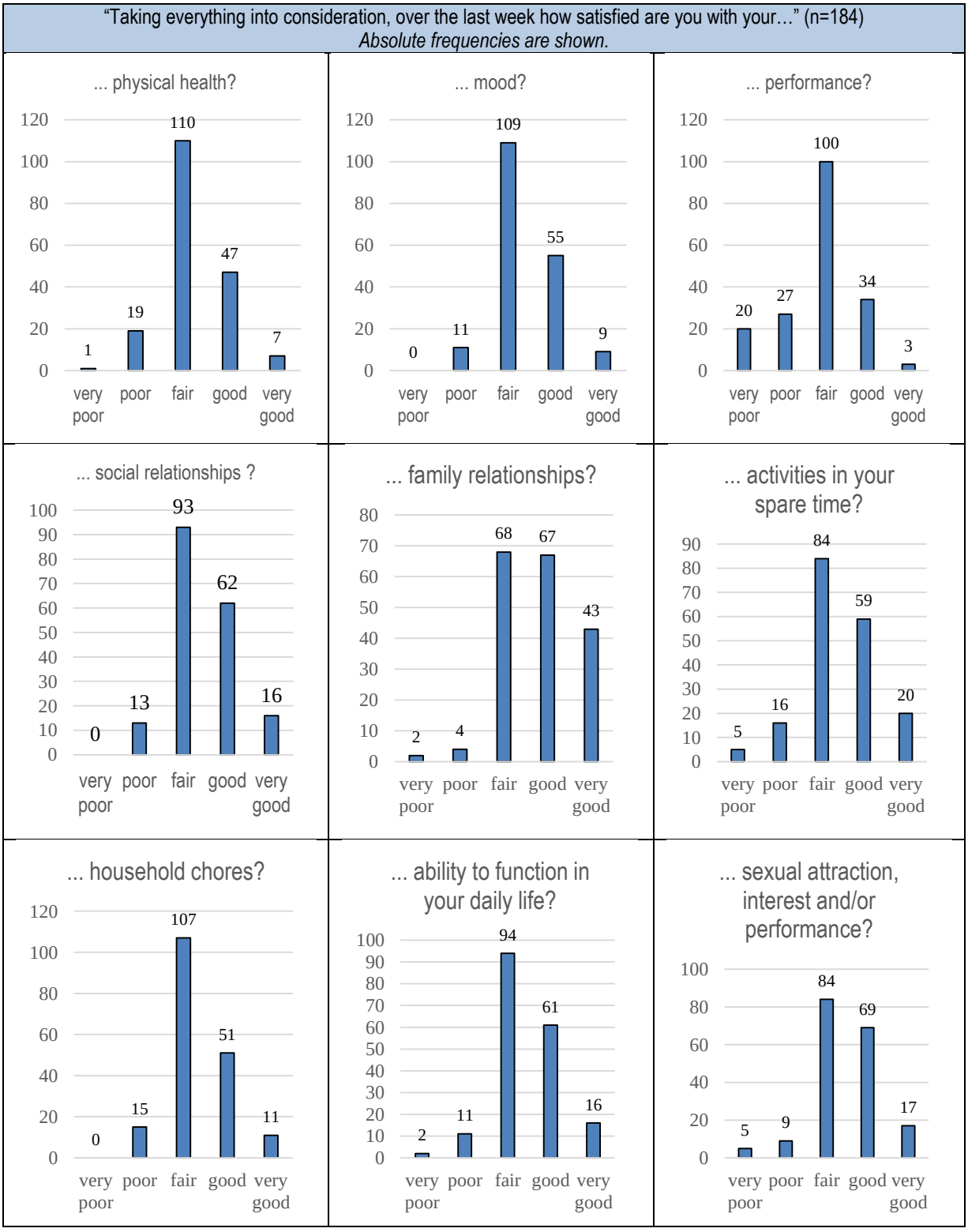



**Figure 2. Distribution of respondents' satisfaction with life aspects over the past week. Absolute frequencies.**

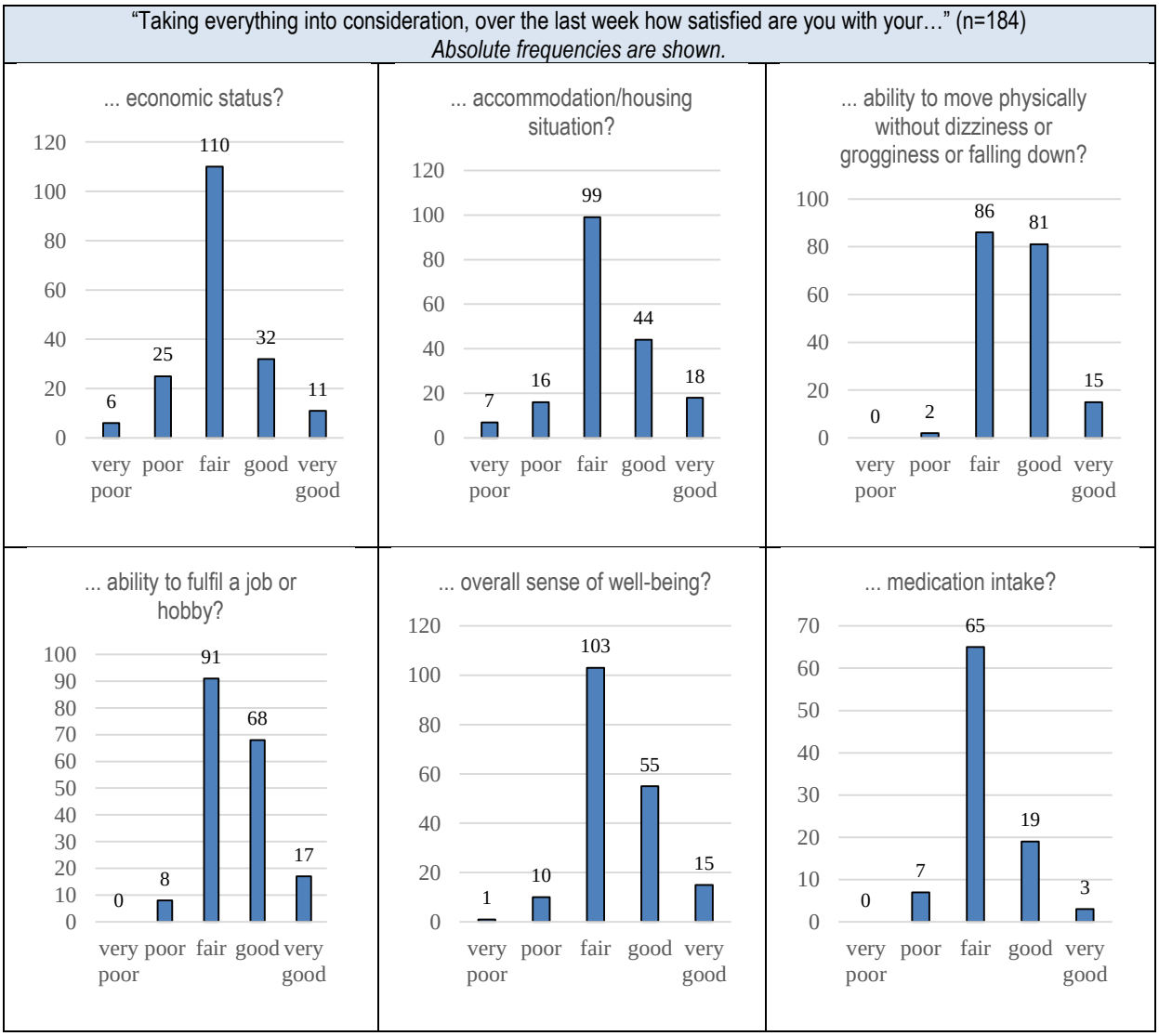



**Figure 3 - Distribution of respondents' satisfaction with life aspects over the past week. Absolute frequencies (cont'd).**

*Table 1.*

**Descriptive statistics for the integral indicator of quality of life (according to Q-LES-Q).**

| Statistical indicator | | Social status | |
|---|---|---|---|
| | | working / studying | not working / not studying |
| Mean | | 49,40 | 47,09 |
| Standard error of the mean | | 0,405 | 0,544 |
| Median | | 49,0 | 45,0 |
| Mode | | 42 | 42 |
| Dispersion | | 79,531 | 54,521 |
| Minimum | | 16 | 31 |
| Maximum | | 70 | 70 |
| Percentiles | 25 | 43,0 | 42,0 |
| | 50 | 49,0 | 45,0 |
| | 75 | 56,0 | 52,0 |

**Discussion**

The findings of our investigation using the Quality of Life, Enjoyment and Satisfaction Questionnaire (Q-LES-Q) underscore indicate significant disparities between employed and unemployed youth in various fields of daily life satisfaction.

In general, the quality of life of Kazakhstani youth is slightly above the threshold level (above 50%). Meanwhile, in the cohort of unemployed youth, the quality of life is significantly lower by 12% compared to employed youth (differences in average quality of life indicators are significant at the level of p=0.001). Despite this finding, a deeper analysis depicts that employed (working/studying) young people scored 9% higher on the 'good' scale and reported greater stability in daily activities, suggesting a more balanced sense of well-being. This moment is corroborated with existing studies reporting that unemployed people are likely to have heightened concerns and emotional stress, and poorer health related quality of life than employed people [16, 17].

In previous studies, such socio-demographic components as age gender, education level, marital status, household income, geographic location, and social network and support most used in statistical models and in the reporting of stratified assessments [18, 19]. An analogous pattern was obtained in our investigation demonstrating that the quality of life of unemployed youth is associated with such predictors as: 'Financial well-being', "Region of residence", "Marital status" and "Occupation".

The analysis on quality of life of unemployed young people emphasized the lowest satisfaction scores in such factors as “housing situation, physical health, and economic condition”, aligning with literature that highlight inadequate housing and overall economic strain as critical predictors [20].

**Model Summary**

| Model | R | R Square | Adjusted R Square | Std.Error of Estimate |
|---|---|---|---|---|
| 1 | .492 | .242 | .231 | 7053 |
| 2 | .595 | .354 | .335 | 6558 |
| 3 | .656 | .430 | .405 | 6205 |
| 4 | .692 | .479 | .447 | 5983 |
| 5 | .717 | .514 | .476 | 5824 |
| 6 | .745 | .555 | .513 | 5613 |
| 7 | .763 | .582 | .535 | 5483 |

**Coefficients**

| Model | | Unstandardized Coefficients | | Standardized Coefficients | | |
|---|---|---|---|---|---|---|
| | | B | Std.Error | Beta | t | Sig. |
| 1 | (Constant) | 41.380 | 1.737 | | 23.829 | .000 |
| | **Financial well-being, after job loss/absence** | 4.587 | .984 | .492 | 4.661 | .000 |
| 2 | (Constant) | 33.172 | 2.897 | | 11.451 | .000 |
| | **Financial well-being, after job loss/absence** | 4.082 | .927 | .438 | 4.404 | .000 |
| | **Alcohol consumption fact** | 5.567 | 1.631 | .339 | 3.413 | .001 |
| 3 | (Constant) | 30.246 | 2.912 | | 10.386 | .000 |
| | **Financial well-being, after job loss/absence** | 3.353 | .911 | .360 | 3.682 | .000 |
| | **Alcohol consumption fact** | 5.123 | 1.551 | .312 | 3.304 | .002 |
| | **Region of residence** | .449 | .151 | .289 | 2.973 | .004 |
| 4 | (Constant) | 41.745 | 5.475 | | 7.624 | .000 |
| | **Financial well-being, after job loss/absence** | 2.555 | .937 | .274 | 2.728 | .008 |
| | **Alcohol consumption fact** | 4.618 | 1.509 | .282 | 3.060 | .003 |
| | **Region of residence** | .465 | .146 | .300 | 3.190 | .002 |
| | **Feeling supported by the government** | -5.222 | 2.134 | -.238 | -2.447 | .017 |
| 5 | (Constant) | 37.174 | 5.74 | | 6.476 | .000 |
| | **Financial well-being, after job loss/absence** | 1.765 | .983 | .189 | 1.795 | .077 |
| | **Alcohol consumption fact** | 4.103 | 1.489 | .25 | 2.756 | .008 |
| | **Region of residence** | .444 | .142 | .287 | 3.127 | .003 |
| | **Feeling supported by the government** | -5.081 | 2.079 | -.232 | -2.444 | .017 |
| | **Assessment of one's (current) financial status** | 1.849 | .862 | .213 | 2.144 | .036 |
| 6 | (Constant) | 29.763 | 6.315 | | 4.713 | .000 |
| | **Financial well-being, after job loss/absence** | 1.918 | .950 | .206 | 2.019 | .048 |
| | **Alcohol consumption fact** | 3.988 | 1.435 | .243 | 2.778 | .007 |
| | **Region of residence** | .467 | .137 | .302 | 3.406 | .001 |
| | **Feeling supported by the government** | -4.751 | 2.088 | -.217 | -2.367 | .021 |
| | **Assessment of one's (current) financial status** | 2.210 | .844 | .255 | 2.618 | .011 |
| | **Marital status** | 3.386 | 1.392 | .211 | 2.432 | .018 |
| 7 | (Constant) | 35.309 | 6.761 | | 5.223 | .000 |
| | **Financial well-being, after job loss/absence** | 1.670 | .936 | .179 | 1.785 | .079 |
| | **Alcohol consumption fact** | 2.861 | 1.511 | .174 | 1.894 | .063 |
| | **Region of residence** | .379 | .141 | .245 | 2.687 | .009 |
| | **Feeling supported by the government** | -5.309 | 1.981 | -.242 | -2.68 | .009 |
| | **Assessment of one's (current) financial status** | 2.127 | .826 | .245 | 2.576 | .012 |
| | **Marital status** | 4.624 | 1.493 | .288 | 3.096 | .003 |

**Figure 4 - Dependence of the quality of life of unemployed youth on some studied predictors (regression statistics).**

As can be seen from the survey results, greater satisfaction was noted in “household affairs and social relations,” reflecting the resilience of social connections that mitigate some of the negative effects of unemployment.

Our results cast a light on financial well-being, that appeared as an important determinant (β=1.670, p=0.079). This result ties well with previous studies wherein financial uncertainty exacerbates stress and decreases life

satisfaction among unemployed populations [21]. However, persistent economic inequalities may exacerbate inequalities, as expressed in lower rates of satisfaction with physical health and residential conditions.

Moreover, our results provide evidence to include indicators “Feeling supported by the government” and “Fact of alcohol consumption” among those affecting quality of life. Variables were tested for ‘strong’ association: no multicollinearity. The Durbin-Watson value was 1.858, which means there is no autocorrelation.

Alcohol use (β=2.861, p=0.063) and physical health problems had a negative impact on quality of life, which is consistent with previous research in the literature linking unemployment to higher levels of substance use and poor health outcomes [22]. Similar trends were highlighted by Jørgensen et al. (2019), which reveals that there is strong association between high alcohol consumption and likelihood of unemployment among employed individuals [23]. Consequently, chronic health problems and poor access to health care further exacerbated these problems, requiring targeted interventions to address health inequalities among unemployed youth.

Planned comparisons revealed that perceived lack of government support (β=-5.309, p=0.009) among participants notably predicted lower quality of life. This finding highlights the role of state interventions in mitigating unemployment’s impact. A similar conclusion was reached by other studies, pointing to the need for robust social protection systems to support vulnerable categories [24]. Others have shown that family and social support were interplayed with higher life satisfaction, in line with the defensive function of close relationships in coping with stress and economic hardship, even though it depends on gender [25].

The findings underscore the need for multi-sectoral approaches to address the social determinants of health among unemployed youth. The broad implication of the present research lies in a call for government intervention. Recommended policies should prioritise economic assistance, strengthening state and community support systems to increase resilience and social inclusion. In addition, improving access to health care will be fundamental to addressing chronic diseases and developing preventive care for socially vulnerable populations such as unemployed youth.

While this study provides valuable insights, it is limited by its cross-sectional design, which precludes causal inferences. Future research should explore longitudinal data to examine the long-term effects of unemployment on quality of life. Additionally, qualitative studies could deepen understanding of individual experiences and coping mechanisms.

**Conclusion**

In summary, this paper argued that unemployment has the most negative consequences for vulnerable groups, including young people. The study emphasises the significant impact of economic inequality and social determinants on the quality of life of unemployed youth in Kazakhstan. Findings show that unemployment leads to reduced satisfaction in key areas such as financial well-being, housing, and physical health, while increasing emotional stress and concerns about daily life. Reliable predictors of quality of life included financial well-being, government and social support, and satisfaction with medical care. The findings highlight the urgent need for targeted policies and interventions to reduce economic burdens, increase access to health care, and strengthen social safety nets. Addressing these challenges is essential to improve the well-being and resilience of unemployed youth. To further understand the complex relationship between youth unemployment and quality of life, future long-term studies are required.

***Conflicts of interest:*** *There are no conflicts of interest.*

***Financial support and sponsorship:*** *No sponsorship or financial support was provided for this study.*

***Authors' contributions:***

*Conceptualisation – S.D., M.G.; methodology - S.D. K.M.; verification - S.D. M.U.; formal analysis -M.G., S.D.; writing (original drafting) - S.D.; writing (review and editing) – M.G.*

*All authors have read, agreed to the final version of the manuscript and signed the copyright transfer form.*

***References:***

1. *Horvath T., Leoni T., Reschenhofer P., Spielauer, M.* Socio-economic inequality and healthcare costs over the life course - A dynamic microsimulation approach. Public health, 2023. 219, 124–130. https://doi.org/10.1016/j.puhe.2023.04.001

2. *Kumar R., Paswan B.* Changes in socio-economic inequality in nutritional status among children in EAG states, India. Public health nutrition, 2021. 24(6), 1304–1317. https://doi.org/10.1017/S1368980021000343

3. *Maleki A., Faghihzadeh E., Youseflu S., Barjasteh, S.Z.* Socio-economic inequalities in health-related quality of life among Iranian young people in the middle stage of adolescence: application of Health Equity Assessment Toolkit. BMC pediatrics, 2023. *23*(1), 16. https://doi.org/10.1186/s12887-022-03815-z

4. *Wanberg C.R.* (2012). The individual experience of unemployment. *Annual review of psychology*, *63*, 369–396. https://doi.org/10.1146/annurev-psych-120710-100500

5. OECD (2017), *Building Inclusive Labour Markets in Kazakhstan: A Focus on Youth, Older Workers and People with Disabilities*, OECD Publishing, Paris, https://doi.org/10.1787/9789264273023-en.

6. *Serikbayeva B.* Education-job mismatch in the labor market of Kazakhstan: implications for public policy. Nazarbayev University Graduate School of Public Policy. 2022. URL: https://nur.nu.edu.kz/handle/123456789/8231

7. *Von Wachter T.* The persistent effects of initial labor market conditions for young adults and their sources. Journal of Economic Perspectives. 2020. 34:168–194. doi: 10.1257/jep.34.4.168. [DOI]

8. *Vancea, M., Utzet, M.* How unemployment and precarious employment affect the health of young people: A scoping study on social determinants. Scandinavian journal of public health, 2017. 45(1), 73–84. https://doi.org/10.1177/1403494816679555

9. *Gajewski, P., & Zhukovska, K.* (2017). Short-run and long-run effects of unemployment on suicides: does welfare regime matter? *European journal of public health*, *27*(6), 1038–1042. https://doi.org/10.1093/eurpub/ckx180

10. World Health Organization. (n.d.). Proportion of young people aged 15–24 years not in education, employment, or training. URL:

https://www.who.int/data/gho/indicator-metadata-registry/imr-details/proportion-of-young-people-aged-15-24-years-not-in-education-employment-or-training

11. World Bank. (n.d.). World development indicators: Youth not in education, employment, or training (NEET). URL: https://databank.worldbank.org/metadataglossary/world-development-indicators/series/SL.UEM.NEET.FE.ZS

12. International Labour Organization. (2024). *Global employment trends for youth 2024*. International Labour Office. URL: https://www.ilo.org/publications/major-publications/global-employment-trends-youth-2024

13. Law of the Republic of Kazakhstan. On State Youth Policy: adopted on 9 February 2015, No. 285-V ZRK (as amended on 07.07.2020). https://adilet.zan.kz/rus/docs . 05.10.2020.

14. *Stauder J.* (2019). Unemployment, unemployment duration, and health: selection or causation? The European journal of health economics: HEPAC: health economics in prevention and care, 20(1), 59–73. https://doi.org/10.1007/s10198-018-0982-2

15. *Broomhall H.S., Winefield A.H.* A comparison of the affective well-being of young and middle-aged unemployed men matched for length of unemployment. The British journal of medical psychology, 1990. 63 (Pt 1), 43–52. https://doi.org/10.1111/j.2044-8341.1990.tb02855.x

16. *Norström F., Waenerlund A.K., Lindholm L., Nygren R., Sahlén K.G., Brydsten A.* Does unemployment contribute to poorer health-related quality of life among Swedish adults? BMC public health, 2019. 19(1), 457. https://doi.org/10.1186/s12889-019-6825-y

17. *Zhao Y., Zhou Z., Fan X., Nawaz R., Zhao D., Xu T., Su M., Cao D., Shen C., & Lai S.* Comparison of inequity in health-related quality of life among unemployed and employed individuals in China. BMC public health, 2021. 21(1), 52. https://doi.org/10.1186/s12889-020-10038-3

18. *Norström F., Virtanen P., Hammarström A., Gustafsson P.E., Janlert U.* How does unemployment affect self-assessed health? A systematic review focusing on subgroup effects. BMC public health, 2014. 14, 1310. https://doi.org/10.1186/1471-2458-14-1310

19. *Roos E., Lahelma, E., Saastamoinen P., & Elstad J.I.* The association of employment status and family status with health among women and men in four Nordic countries. Scandinavian journal of public health, 2005. 33(4), 250–260. https://doi.org/10.1080/14034940510005680

20. *Marc Hooghe, Bram Vanhoutte, Wim Hardyns, Tuba Bircan,* Unemployment, Inequality, Poverty and Crime: Spatial Distribution Patterns of Criminal Acts in Belgium, 2001–06, The British Journal of Criminology, Volume 51, Issue 1, January 2011, Pages 1–20, https://doi.org/10.1093/bjc/azq067

21. *Achdut N., Refaeli, T.* Unemployment and Psychological Distress among Young People during the COVID-19 Pandemic: Psychological Resources and Risk Factors. International journal of environmental research and public health, 2020. 17(19), 7163. https://doi.org/10.3390/ijerph17197163

22. *Nolte-Troha C., Roser P., Henkel D., Scherbaum, N., Koller G., Franke A.G.* Unemployment and Substance Use: An Updated Review of Studies from North America and Europe. Healthcare (Basel, Switzerland), 2023.11(8), 1182. https://doi.org/10.3390/healthcare11081182

23. *Jørgensen M.B., Pedersen J., Thygesen L.C., Lau.C.J., Christensen A.I., Becker U., Tolstrup, J.S.* Alcohol consumption and labour market participation: a prospective cohort study of transitions between work, unemployment, sickness absence, and social benefits. European journal of epidemiology, 2019. 34(4), 397–407. https://doi.org/10.1007/s10654-018-0476-7

24. *Yokobori Y., Kiyohara H., Mulati N., Lwin K.S., Bao T.Q.Q., Aung M.N., Yuasa.M., Fujita, M.* Roles of Social Protection to Promote Health Service Coverage among Vulnerable People toward Achieving Universal Health Coverage: A Literature Review of International Organizations. International journal of environmental research and public health, 2023. 20(9), 5754. https://doi.org/10.3390/ijerph20095754

25. *Artazcoz L., Benach J., Borrell C., Cortès I.* Unemployment and mental health: understanding the interactions among gender, family roles, and social class. American journal of public health, 2004. 94(1), 82–88. https://doi.org/10.2105/ajph.94.1.82

**Information about the authors:**

**Samal B. Duisekova** - PhD, associate research professor of the department of Public health and management, Astana Medical University, Astana, Kazakhstan. ORCID: https://orcid.org/0000-0001-7644-145X, duisekova.s@amu.kz

**Mereilim M. Gaisina** - Master of Public Health, Nazarbayev University School of Medicine, Astana, Kazakhstan https://orcid.org/0009-0002-5829-4008 mereilim.gaisina@nu.edu.kz

**Margulan U. Uazhanov** - PhD, Associate Professor of the Department of Public Health and Management, NJSC "Astana Medical University", Astana, Kazakhstan, ORCID: https://orcid.org/0000-0002-7075-3716 uazhanov.m@amu.kz

**Sekenova K. Raushana** - PhD, Associate Research Professor of the Department of Public Health and Management, NJSC "Astana Medical University", Astana, Kazakhstan, ORCID https://orcid.org/0000-0001-7533-160X sekenova.r@amu.kz

**Dauletova Sh. Gaukhar**- PhD, Associate Research Professor of the Department of Public Health and Management, NJSC "Astana Medical University", Astana, ORCID https://orcid.org/0000-0002-1621-8149 dauletova.g@amu.kz

**Corresponding author:**

**Kamila M. Akhmetova** Doctoral student of 1 year, Public Health Education Programme, NJSC "Astana Medical University", Astana, Republic of Kazakhstan

**Postal code:** Republic of Kazakhstan, 071400, Semey city, Abay Street 103.

**E-mail:** kamikhudaiberdina@gmail.com Akhmetova.km@amu.kz

**Phone:** +7 707 138 92 29

Received: 15 February 2025 / Accepted: 14 May 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2025.27.3.010***

***UDC 616-002.5***

This work is licensed under a Creative Commons Attribution 4.0 International License

# ANALYSIS OF SOCIO-DEMOGRAPHIC DETERMINANTS AND RISK FACTORS OF TUBERCULOSIS IN THE ABAI REGION DURING THE PERIOD 2014–2022

**Assylkhan B. Adilzhanov[1],**
**Maksat S. Adilgozhin[2],**
**Zhanara B. Ibrayeva[3],** https://orcid.org/0000-0001-7298-7869
**Nailya M. Urazalina[3],** https://orcid.org/0000-0003-0200-1763
**Dinara A. Mukanova[3],** https://orcid.org/0000-0001-5186-2346
**Natalya S. Zemlyanskaya[4],** https://orcid.org/0000-0003-1968-3246
**Elvira R. Aitenova[4],**
**Timur M. Shamshudinov[5],** https://orcid.org/0000-0001-5015-871X
**Laura T. Kassym[4],** https://orcid.org/0000-0003-4448-6455
**Assiya A. Kussainova[4],** https://orcid.org/0000-0002-5738-0804

**[1] Regional HIV Prevention Center, State Municipal Enterprise under the Health Department of the Abai Region, Semey, Republic of Kazakhstan;**
**2 Regional Center of Phthisiopulmonology, State Municipal Enterprise under the Right of Economic Management, Semey, Republic of Kazakhstan;**
**3 NCJSC «Semey Medical University», Semey, Republic of Kazakhstan;**
**4 NJSC "Astana Medical University", Astana, Republic of Kazakhstan;**
**5 «Medical and diagnostic Center of otorhinolaryngology» PRO-LOR, Almaty, Republic of Kazakhstan.**

**Abstract**

**Introduction:** Tuberculosis (TB) remains a major global health challenge, with over 7 million new cases reported in 2022 alone, partially due to pandemic-related disruptions. Despite global progress, drug-resistant forms and co-infections with HIV and diabetes continue to hinder TB control. In Kazakhstan, significant reductions in TB incidence and mortality have been achieved, yet multidrug-resistant TB and regional disparities persist. The Abai region, formed from the former East Kazakhstan area, has shown variable trends that warrant focused analysis.

The primary **objective** of this study was to assess the epidemiological situation of tuberculosis in the Abai region over the period from 2014 to 2022, with a particular focus on identifying key socio-demographic determinants and associated risk factors.

**Materials and Methods**: This retrospective epidemiological study was based on data from Form № TB-03/u of the National Tuberculosis Registry of Kazakhstan (NTR-TB RK) covering the period from 2014 to 2022. The registry includes detailed demographic, clinical, laboratory, and drug susceptibility data on all newly diagnosed and recurrent TB cases. Prior to analysis, the dataset was anonymized, standardized, and coded. Only complete records were included, while those with missing critical data were excluded. Statistical analysis involved incidence calculations, descriptive statistics, and appropriate comparative tests, with significance set at $p < 0.05$.

**Results:** A total of 3,555 TB cases were registered in the Abai region from 2014 to 2022, with a clear downward trend—from 752 cases in 2014 to 234 in 2022. Most patients were male (61.7%), and pulmonary TB predominated (85%), with infiltrative forms being the most common. Two-thirds of patients resided in urban areas, and nearly half (48.4%) were unemployed at diagnosis. Although no specific risk factors were identified in 84.8% of cases, alcohol abuse, diabetes, prior incarceration, and HIV infection were reported in a minority. Drug-resistant TB was detected in 29.3% of cases, and treatment success (cure or completion) was achieved in over 75% of patients.

**Conclusion:** To sustain and accelerate progress toward TB elimination, it is essential to integrate TB services into broader health and social care systems, with a focus on targeted support for high-risk groups and improved continuity of care across all stages of the treatment cascade.

***Keywords:*** *tuberculosis, epidemiology, risk factors, drug resistance, Kazakhstan*

***For citation:***

*Adilzhanov A.B., Adilgozhin M.S., Ibrayeva Zh.B., Urazalina N.M., Mukanova D.A., Zemlyanskaya N.S., Aitenova E.R., Shamshudinov T.M., Kassym L.T., Kussainova A.A.* Analysis of socio-demographic determinants and risk factors of tuberculosis in the Abai region during the period 2014–2022 // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 88-97. *doi 10.34689/SH.2025.27.3.010*

**Резюме**

# АНАЛИЗ СОЦИАЛЬНО-ДЕМОГРАФИЧЕСКИХ ДЕТЕРМИНАНТ И ФАКТОРОВ РИСКА ТУБЕРКУЛЁЗА В ОБЛАСТИ АБАЙ ЗА 2014–2022 ГОДЫ

**Асылхан Б. Адилжанов[1],**
**Максат С. Адильгожин[2],**
**Жанара Б. Ибраева[3], https://orcid.org/0000-0001-7298-7869**
**Найля М. Уразалина[3], https://orcid.org/0000-0003-0200-1763**
**Динара А. Муканова[3], https://orcid.org/0000-0001-5186-2346**
**Наталья С. Землянская[4], https://orcid.org/0000-0003-1968-3246**
**Эльвира Р. Айтенова[4],**
**Тимур М. Шамшудинов[5], https://orcid.org/0000-0001-5015-871X**
**Лаура Т. Касым[4], https://orcid.org/0000-0003-4448-6455**
**Асия А. Кусаинова[4], https://orcid.org/0000-0002-5738-0804**

**[1] КГП на ПХВ «Областной центр по профилактике ВИЧ-инфекции» УЗ области Абай, г. Семей, Республика Казахстан;**
**[2] КГП на ПХВ «Областной центр фтизиопульмонологии», УЗ области Абай, г. Семей, Республика Казахстан;**
**[3] НАО «Медицинский университет Семей», г. Семей, Республика Казахстан;**
**[4] НАО «Медицинский университет Астана», г. Астана, Республика Казахстан;**
**[5] «Лечебно-диагностический центр оториноларингологии» PRO-ЛОР, г. Алматы, Республика Казахстан.**

**Введение:** Туберкулёз (ТБ) остаётся одной из ведущих глобальных проблем здравоохранения: только в 2022 году было зарегистрировано более 7 миллионов новых случаев, что частично связано с последствиями пандемии. Несмотря на достигнутый прогресс, борьбу с туберкулёзом осложняют лекарственно-устойчивые формы заболевания, а также сочетанные инфекции с ВИЧ и сахарным диабетом. В Казахстане достигнуты значительные успехи в снижении заболеваемости и смертности от ТБ, однако сохраняется проблема мультирезистентного ТБ и выраженные региональные различия. Территория нынешнего Абайского региона, выделенного из Восточно-Казахстанской области, демонстрирует неоднородные эпидемиологические тенденции, требующие углублённого анализа.

**Целью** исследования являлась оценка эпидемиологической ситуации по туберкулёзу в области Абай в период с 2014 по 2022 год с акцентом на выявление ключевых социально-демографических детерминант и факторов риска.

**Материалы и методы:** Исследование выполнено в ретроспективном эпидемиологическом дизайне на основе данных формы № ТВ-03/у Национального регистра больных туберкулёзом Республики Казахстан (НРБ РК) за 2014–2022 годы. Регистр содержит подробную информацию о демографических характеристиках, клинических и лабораторных показателях, а также о лекарственной чувствительности возбудителя у всех впервые выявленных и рецидивирующих случаев ТБ. Перед началом анализа данные были обезличены, стандартизированы и закодированы. В выборку включались только полные записи; случаи с отсутствием ключевой информации исключались. Статистическая обработка включала расчёт заболеваемости, описательную статистику и методы сравнительного анализа с уровнем значимости $p < 0,05$.

**Результаты:** За период 2014–2022 годов в области Абай было зарегистрировано 3 555 случаев ТБ, при этом наблюдалась чёткая тенденция к снижению: с 752 случаев в 2014 году до 234 в 2022 году. Большинство пациентов составляли мужчины (61,7%), а преобладающей формой был лёгочный туберкулёз (85%), преимущественно инфильтративного типа. Две трети пациентов проживали в городах, при этом почти половина (48,4%) на момент постановки диагноза были безработными. Несмотря на то что в 84,8% случаев не были выявлены конкретные факторы риска, в части наблюдений отмечались злоупотребление алкоголем, наличие сахарного диабета, тюремное заключение в анамнезе и ВИЧ-инфекция. Лекарственно-устойчивые формы ТБ составили 29,3% случаев, при этом эффективность лечения (в виде выздоровления или завершения терапии) достигнута более чем у 75% пациентов.

**Заключение:** Для сохранения и ускорения достигнутого прогресса в ликвидации туберкулёза необходимо интегрировать услуги по ТБ в систему общего медицинского и социального обеспечения с особым вниманием к уязвимым группам населения и обеспечению преемственности медицинской помощи на всех этапах лечебного процесса.

***Ключевые слова:*** *туберкулез, эпидемиология, факторы риска, лекарственная устойчивость, Республика Казахстан.*

***Для цитирования:***

*Адилжанов А.Б., Адильгожин М.С., Ибраева Ж.Б., Уразалина Н.М., Муканова Д.А., Землянская Н.С., Айтенова Э.Р., Шамшудинов Т.М., Касым Л.Т., Кусаинова А.А.* Анализ социально-демографических детерминант и факторов риска туберкулёза в области Абай за 2014–2022 годы // Наука и Здравоохранение. 2025. Т.27 (3), С. 88-97. doi: 10.34689/SH.2025.27.3.010

**Түйіндеме**

# 2014–2022 ЖЫЛДАР АРАЛЫҒЫНДАҒЫ АБАЙ ОБЛЫСЫНДАҒЫ ТУБЕРКУЛЁЗДІҢ ӘЛЕУМЕТТІК-ДЕМОГРАФИЯЛЫҚ ДЕТЕРМИНАНТТАРЫ МЕН ҚАУІП ФАКТОРЛАРЫН ТАЛДАУ

**Асылхан Б. Адилжанов[1],**
**Максат С. Адильгожин[2],**
**Жанара Б. Ибраева[3],** https://orcid.org/0000-0001-7298-7869
**Найля М. Уразалина[3],** https://orcid.org/0000-0003-0200-1763
**Динара А. Муканова[3],** https://orcid.org/0000-0001-5186-2346
**Наталья С. Землянская[4],** https://orcid.org/0000-0003-1968-3246
**Эльвира Р. Айтенова[4],**
**Тимур М. Шамшудинов[5],** https://orcid.org/0000-0001-5015-871X
**Лаура Т. Касым[4],** https://orcid.org/0000-0003-4448-6455
**Асия А. Кусаинова[4],** https://orcid.org/0000-0002-5738-0804

[1] АО ДСБ «АИТВ инфекциясының алдын алу облыстық орталығы» ШЖҚ КМК, Семей қ., Қазақстан Республикасы;
[2] АО ДСБ «Фтизиопульмонология облыстық орталығы» ШЖҚ КМК, Семей қ., Қазақстан Республикасы;
[3] «Семей медицина университеті» КеАҚ, Семей қ., Қазақстан Республикасы;
[4] «Астана медицина университеті» КеАҚ, Астана қ., Қазақстан Республикасы;
[5] «Оториноларингологияның емдеу-диагностикалық орталығы» PRO-ЛОР, Алматы қ., Қазақстан Республикасы.

**Кіріспе:** Туберкулез (ТБ) — жаһандық денсаулық сақтау саласындағы өзекті мәселелердің бірі болып қала береді. 2022 жылының өзінде 7 миллионнан астам жаңа жағдай тіркеліп, бұл көрсеткіш пандемия салдарынан болған үзілістердің әсерін көрсетеді. Әлемдік деңгейде оң нәтижелерге қол жеткізілгенімен, дәріге төзімді формалар мен АИТВ және қант диабетімен қатар жүретін инфекциялар туберкулезге қарсы күресті қиындатуда. Қазақстанда туберкулездің аурушаңдығы мен өлім-жітімі айтарлықтай төмендегенімен, мультирезистентті формалар мен өңірлік айырмашылықтар сақталуда. Бұрынғы Шығыс Қазақстан облысының негізінде құрылған Абай өңірінде туберкулез бойынша әркелкі үрдістер байқалуда, бұл қосымша талдауды қажет етеді.

**Мақсат:** 2014–2022 жылдар аралығындағы Абай облысындағы туберкулездің эпидемиологиялық жағдайын бағалау, сондай-ақ негізгі әлеуметтік-демографиялық көрсеткіштер мен тәуекел факторларын анықтау болып табылады.

**Материалдар мен әдістер:** Зерттеу ретроспективті эпидемиологиялық сипатта жүргізіліп, 2014–2022 жылдар аралығындағы Қазақстан Республикасының Ұлттық туберкулез регистріндегі (НРБТ ҚР) № ТВ-03/у нысаны негізінде жүзеге асырылды. Бұл регистр жаңадан анықталған және қайталама ТБ жағдайлары туралы демографиялық, клиникалық, зертханалық және дәріге сезімталдық деректерін қамтиды. Деректер өңдеулер алдында анонимдендіріліп, стандартталып және кодталды. Зерттеуге тек толық толтырылған жазбалар енгізілді, ал маңызды өрістері жоқ жазбалар алынып тасталды. Статистикалық талдау аурушаңдық көрсеткіштерін есептеуді, сипаттамалық статистиканы және салыстырмалы сынақтарды қамтыды ($p < 0.05$).

**Нәтижелер:** 2014–2022 жылдар аралығында Абай облысында барлығы 3 555 туберкулез жағдайы тіркелді, бұл кезең ішінде анық төмендеу үрдісі байқалды: 2014 жылы 752 жағдай (21.2%) тіркелсе, 2022 жылы бұл көрсеткіш 234-ке (6.6%) дейін азайды. Науқастардың басым бөлігі ер адамдар (61.7%) болған, ал аурудың 85%-ы өкпелік формада тіркелген, олардың ішінде инфильтративті түрлері жиі кездескен. Екі науқастың бірі жұмыссыз болған (48.4%), ал тұрғындардың үштен екісі қалалық жерде өмір сүрген. Жағдайлардың 84.8%-ында нақты тәуекел факторлары анықталмағанымен, кейбір науқастарда алкогольге тәуелділік, қант диабеті, бас бостандығынан айырылу және АИТВ-инфекциясы кездескен. Дәріге төзімді ТБ 29.3% науқастарда анықталды, ал жалпы ем нәтижесі (жазылу немесе емді аяқтау) 75%-дан жоғары болды.

**Қорытынды:** Туберкулезбен күресте қол жеткізілген жетістіктерді сақтау және одан әрі ілгерілету үшін, ТБ қызметтерін жалпы денсаулық сақтау және әлеуметтік қолдау жүйелеріне біріктіру, жоғары тәуекел тобындағы тұлғаларға бағытталған көмекті күшейту және емдеу тізбегінің барлық кезеңдерінде үздіксіздікті қамтамасыз ету маңызды.

***Түйінді сөздер****: туберкулез, эпидемиология, қауіп факторлары, дәрілік тұрақтылық, Қазақстан Республикасы.*

***Дәйексөз үшін:***

*Адилжанов А.Б., Адильгожин М.С., Ибраева Ж.Б., Уразалина Н.М., Муканова Д.А., Землянская Н.С., Айтенова Э.Р., Шамшудинов Т.М., Касым Л.Т., Кусаинова А.А.* 2014–2022 жылдар аралығындағы Абай облысындағы туберкулёздің әлеуметтік-демографиялық детерминанттары мен қауіп факторларын талдау // Ғылым және Денсаулық. 2025. Т.27 (3), Б. 88-97. doi: 10.34689/SH.2025.27.3.010

**Background**

Tuberculosis (TB) continues to pose a critical challenge to global public health in the 21st century [22]. According to the World Health Organization (WHO), an estimated 2.5 billion people are infected with *Mycobacterium tuberculosis* (MBT), representing roughly a third of the global population [18]. Despite notable advancements in diagnosis, treatment, and prevention, the global burden of TB remains substantial, with millions of new cases reported annually [4]. TB continues to rank among the leading causes of death from infectious diseases, surpassing HIV/AIDS in mortality in several regions [21]. The growing incidence of drug-resistant TB and co-infections with HIV or diabetes further complicates control efforts [25]. Although the WHO's End TB Strategy—launched in 2014—sets ambitious targets for reducing incidence and mortality by 2025 and eliminating TB as a public health threat by 2035, progress has been inconsistent [27]. In 2022 alone, 7.5 million new TB cases were reported—the highest figure since global surveillance began—largely attributed to disruptions in health services caused by the COVID-19 pandemic [10].

In Kazakhstan, a middle-income country and the most economically developed state in Central Asia, TB continues to exert a significant public health burden [3]. Although the country was once listed among the top ten globally for new and recurrent TB cases, recent decades have seen encouraging improvements. Between 2000 and 2022, TB incidence declined from 171 to 78 cases per 100,000 population, while mortality from pulmonary TB fell from 7.4 to 1.5 per 100,000 [11, 23]. These advances reflect national efforts to modernize TB control programs, expand access to DOTS-based treatment, and implement advanced diagnostic technologies, such as GeneXpert [13]. Nevertheless, multidrug-resistant TB (MDR-TB) remains a major concern: in 2019, drug resistance was detected in 27% of newly diagnosed patients and 44% of previously treated cases [5]. Despite these challenges, Kazakhstan has maintained high treatment success rates, with over 85% of patients with drug-susceptible TB and over 80% of MDR-TB patients completing therapy successfully in 2021 [30].

At the subnational level, TB epidemiology in Kazakhstan demonstrates considerable variation. In 2019, the highest incidence rates were observed in Kyzylorda (115.0 per 100,000), followed by North Kazakhstan (88.9), and Aktobe (81.1) regions, whereas the lowest rates were recorded in Karaganda (55.0) [1]. In East Kazakhstan—currently divided into East Kazakhstan and Abai regions—TB incidence was 69.3 per 100,000 [1].

Key determinants of disease activation among the infected include HIV co-infection, diabetes, malnutrition, smoking, alcohol abuse, and exposure to indoor air pollutants [17, 24]. Social vulnerabilities—such as poverty, overcrowding, homelessness, incarceration, and limited access to healthcare—exacerbate transmission, while high-risk populations include children under five, the elderly, and migrants [19]. Men are statistically more affected, although postpartum and lactating women also exhibit increased susceptibility [20]. Studies confirm that the intensity and duration of contact with highly infectious individuals directly influence infection risk [9]. In Kazakhstan, while official reports have classified most TB cases as lacking identifiable risk factors, recent evidence highlights the disproportionate burden among migrant populations in regions with high internal mobility and poor access to healthcare [7].

Since 2003, Kazakhstan has maintained a centralized TB case registration system that records all newly diagnosed and recurrent cases. These data are systematically collected and entered into an electronic database, enabling the Ministry of Health and relevant stakeholders to monitor TB incidence and prevalence at the national level [2]. The compiled information serves as the basis for annual reporting at both national and international levels. However, there remains a significant gap in region-specific epidemiological analysis of pulmonary TB, particularly concerning treatment categories and determinants of treatment failure. A more granular assessment of these indicators is essential to identify local transmission drivers—especially in regions such as Abai—and to forecast disease trends in the population over the coming years.

Accordingly, the primary **objective** of this study was to assess the epidemiological situation of tuberculosis in the Abai region over the period from 2014 to 2022, with a particular focus on identifying key socio-demographic determinants and associated risk factors.

**Materials and Methods**

**Study Design.** This study employed a retrospective epidemiological design.

**Data Sources.** Empirical data were extracted from Form № TB-03/u, which is part of the National tuberculosis registry of the Republic of Kazakhstan (NTR-TB RK), an electronic component of the Unified National Health System (UNHS RK). This system facilitates the integration and digitalization of healthcare service data across the country. The registry captures individualized patient-level information on all newly diagnosed and recurrent TB cases, including both demographic and clinical-diagnostic indicators.

Form No. TB-03/u contains comprehensive patient-level data, including registration date and number, sex, age, affiliated primary healthcare provider, site of TB infection, history of TB disease, clinical diagnosis, treatment category, socio-demographic status, citizenship, country of origin, radiographic and laboratory findings, as well as microbiological and molecular genetic drug susceptibility test (DST) results. The DST methods include Löwenstein–Jensen, BACTEC, GeneXpert, Hain Test, and Bioneer. Data also cover HIV status and antiretroviral therapy (ART) receipt.

Prior to statistical analysis, the extracted Excel dataset was standardized, coded, and fully anonymized to ensure confidentiality.

*Inclusion criteria:* all patient records documented in the NTR-TB system from 2014 to 2022. *Exclusion criteria:* records with incomplete data (i.e., missing critical fields).

**Ethical Considerations**. The study protocol was approved by the Local Ethics Committee of the Non-Profit Joint Stock Company "Semey Medical University" (Protocol No. 16, dated October 25, 2024).

**Statistical Analysis**. Tuberculosis incidence analysis: TB incidence was calculated as the ratio of newly registered TB cases to the total population of Kazakhstan for each year, expressed per 100,000 population. Descriptive analysis: categorical variables were summarized using

absolute and relative frequencies (percentages), while continuous variables were described using medians with interquartile ranges (IQRs) or means with standard deviations (SDs), depending on distribution. Comparative tests: student's t-test or the Mann–Whitney U test was used for comparing continuous variables, based on the distribution normality. Fisher's exact test was employed to assess associations between categorical variables. Statistical significance was set at $p < 0.05$.

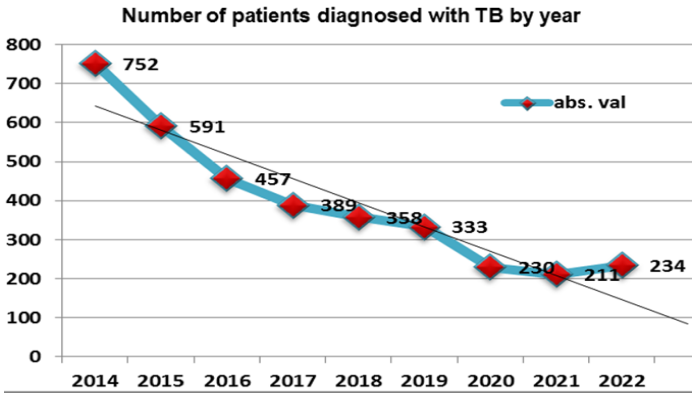



**Figure 1. The overall incidence of TB in the period from 2014 to 2022.**

The majority of respondents were male, comprising 61.7% (n=2,195), while females accounted for 38.3% (n=1,360). The mean age was 43.5 ± 16.2 years for men and 42.1 ± 16.0 years for women ($p$=0.026). (Table 1).

**Results**

A total of 3,555 individuals were registered in the study between 2014 and 2022.

Figure 1 shows that the highest number of registered TB cases was observed in 2014, accounting for 21.2% (n=752) of the total. A declining trend was noted thereafter, with the number of registered TB cases in the region dropping to 234 in 2022, representing 6.6% (n=234) of all cases studied.

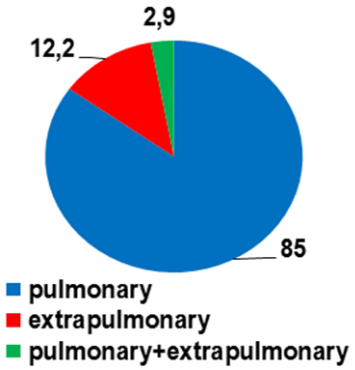



**Figure 2. The form of tuberculosis localization.**

With regard to the localization of TB, the majority of cases were pulmonary (85%, n=3,020), while extrapulmonary TB accounted for 12.2% (n=432). The remaining 2.9% (n=103) had both pulmonary and extrapulmonary TB. (Figure 2).

*Table 1.*

**Sex and age characteristics of the studied patients**

| | Gender | | Age | | *p* |
|---|---|---|---|---|---|
| | Frequency | Percent | Average value | Standard deviation | |
| male | 2195 | 61,7 | 43, 5 | 16,2 | 0,026 |
| female | 1360 | 38,3 | 42,1 | 16,0 | |
| Total | 3555 | 100,0 | | | |

A wide range of TB types was observed, with the most common being infiltrative pulmonary TB without bacterial excretion (39.7%, n=1,413) and infiltrative pulmonary TB with bacterial excretion (36%, n=1,280). Pulmonary tuberculoma without bacterial excretion was detected in 3.6% of patients (n=128), while bone and joint TB was also diagnosed in 3.6% (n=127). Tuberculous pleurisy (including empyema), either bacteriologically or histologically confirmed or unconfirmed, was found in 3.3% (n=118) and 3.0% (n=108) of cases, respectively. Focal pulmonary TB without bacterial excretion was noted in 2.0% (n=70) of cases. Other forms of TB were diagnosed in fewer than 2% of cases throughout the entire observation period (Table 2).

Over the entire observation period, approximately two-thirds of TB patients resided in urban areas, while one-third were from rural areas. This distribution remained consistent throughout the study period ($p$=0.002). (Table 3).

As illustrated in Figure 3, nearly half of the patients (48.4%, n=1,722) were unemployed at the time of TB diagnosis. Employed individuals constituted one-fifth of the cohort (n=710), retirees accounted for 16.4% (n=583), and students made up 4.1% (n=204). The employment status of 11.1% (n=394) of TB patients was undocumented.

In the majority of cases (84.8%, n=3,016), no specific risk factors for TB development were identified. A history of direct contact with a TB patient was reported by 3.8% (n=135) of the patients. Alcohol abuse was identified as a risk factor in 3.9% (n=138), diabetes mellitus in 3.0% (n=107), imprisonment in 1.3% (n=69), and drug addiction in 0.3% (n=9). Pregnancy was also reported as a risk factor in 1.3% of cases (n=47).

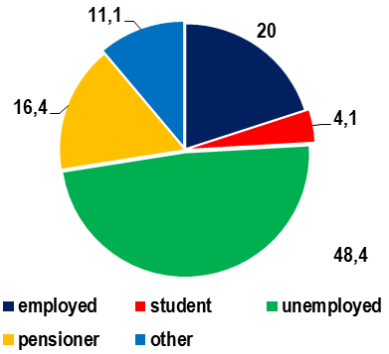



**Figure 3. Social status of TB patients.**

Statistically significant changes in risk factors were observed over the nine-year period ($p$<0.001). Diabetes mellitus peaked as a risk factor in 2018, reaching 6.7% (n=24). In contrast, incarceration as a risk factor showed a downward trend, declining to 0.9% (n=2) in 2022 compared to 3.2% (n=24) in 2014. The frequency of contact with TB patients also decreased over time, indicating improved TB control measures. (Table 4).

*Table 2.* **Prevalence of TB depending on diagnosis in the period from 2014 to 2022.**

| Diagnosis | Frequency | Percentage |
|---|---|---|
| Focal lung TB without bacterial excretion | 70 | 2,0 |
| Tuberculosis of the lungs without bacterial excretion | 128 | 3,6 |
| Infiltrative lung TB without bacterial excretion | 1413 | 39,7 |
| Infiltrative pulmonary TB with bacterial excretion | 1280 | 36,0 |
| Disseminated acute pulmonary TB without bacterial excretion | 25 | ,7 |
| Disseminated acute pulmonary TB with bacterial excretion | 19 | ,5 |
| Disseminated subacute pulmonary TB with bacterial excretion | 3 | ,1 |
| Disseminated chronic pulmonary TB with bacterial excretion | 1 | ,0 |
| Fibrous-cavernous lung TB without bacterial excretion | 5 | ,1 |
| Fibrous-cavernous pulmonary TB with bacterial excretion | 46 | 1,3 |
| Primary tuberculosis complex without bacterial excretion | 3 | ,1 |
| Generalized tuberculosis | 1 | ,0 |
| Tuberculous pleurisy (including empyema) not confirmed bacteriologically, histologically | 108 | 3,0 |
| TB of the bronchi, trachea of the upper respiratory tract, etc.(nose, mouth, pharynx) | 11 | ,3 |
| TB of intrathoracic lymph nodes without bacterial excretion | 31 | ,9 |
| TB of peripheral lymph nodes | 56 | 1,6 |
| TB of the intestine, peritoneum and mesenteric lymph nodes | 12 | ,3 |
| TB from other organs | 15 | ,4 |
| Tuberculous meningitis | 2 | ,1 |
| TB of bones and joints | 127 | 3,6 |
| TB of the genitourinary organs | 48 | 1,4 |
| Acute miliary TB of one specified localization | 5 | ,1 |
| Disseminated subacute pulmonary TB without bacterial excretion | 1 | ,0 |
| Tuberculous meningitis | 7 | ,2 |
| Cirrhotic lung TB without bacterial excretion | 1 | ,0 |
| Tuberculous pleurisy (including empyema) confirmed bacteriologically, histologically | 118 | 3,3 |
| Pulmonary tuberculosis with bacterial excretion | 1 | ,0 |
| Disseminated chronic pulmonary TB with bacterial excretion | 4 | ,1 |
| TB of skin | 3 | ,1 |
| Primary tuberculosis complex without bacterial excretion | 7 | ,2 |
| Generalized tuberculosis | 2 | ,1 |
| Cavernous pulmonary TB with bacterial excretion | 1 | ,0 |
| Acute miliary TB of multiple localization | 1 | ,0 |
| **Total** | **3555** | **100,0** |

*Table 3.* **The status of the place of residence of TB patients in the context from 2014 to 2022.**

| Year | | Resident city/village | | Total | *p* |
|---|---|---|---|---|---|
| | | city | village | | |
| 2014 | Frequency | 421 | 331 | 752 | 0,002 |
| | % per year | 56,0% | 44,0% | 100,0% | |
| 2015 | Frequency | 369 | 222 | 591 | |
| | % per year | 62,4% | 37,6% | 100,0% | |
| 2016 | Frequency | 283 | 174 | 457 | |
| | % per year | 61,9% | 38,1% | 100,0% | |
| 2017 | Frequency | 262 | 127 | 389 | |
| | % per year | 67,4% | 32,6% | 100,0% | |
| 2018 | Frequency | 235 | 123 | 358 | |
| | % per year | 65,6% | 34,4% | 100,0% | |
| 2019 | Frequency | 197 | 136 | 333 | |
| | % per year | 59,2% | 40,8% | 100,0% | |
| 2020 | Frequency | 154 | 76 | 230 | |
| | % per year | 67,0% | 33,0% | 100,0% | |
| 2021 | Frequency | 142 | 69 | 211 | |
| | % per year | 67,3% | 32,7% | 100,0% | |
| 2022 | Frequency | 141 | 93 | 234 | |
| | % per year | 60,3% | 39,7% | 100,0% | |
| **Total** | Frequency | 2204 | 1351 | 3555 | |
| | % per year | 62,0% | 38,0% | 100,0% | |

*Table 4.* **Risk factors for TB development in dynamics over 9 years.**

| Year | | | Risk factor | | | | | | | | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | unknown | contact with TB | diabetes mellitus | HIV | Alcoholism | Drug addiction | prisoners | pregnancy | more than one factor | |
| 2014 | Frequency | 630 | 43 | 15 | 2 | 28 | 3 | 24 | 7 | 0 | 752 |
| | % per year | 83,8% | 5,7% | 2,0% | 0,3% | 3,7% | 0,4% | 3,2% | 0,9% | 0,0% | 100,0% |
| 2015 | Frequency | 513 | 20 | 8 | 3 | 18 | 1 | 19 | 9 | 0 | 591 |
| | % per year | 86,8% | 3,4% | 1,4% | 0,5% | 3,0% | 0,2% | 3,2% | 1,5% | 0,0% | 100,0% |
| 2016 | Frequency | 386 | 18 | 10 | 0 | 23 | 0 | 12 | 8 | 0 | 457 |
| | % per year | 84,5% | 3,9% | 2,2% | 0,0% | 5,0% | 0,0% | 2,6% | 1,8% | 0,0% | 100,0% |
| 2017 | Frequency | 343 | 10 | 15 | 3 | 12 | 3 | 1 | 2 | 0 | 389 |
| | % per year | 88,2% | 2,6% | 3,9% | 0,8% | 3,1% | 0,8% | 0,3% | 0,5% | 0,0% | 100,0% |
| 2018 | Frequency | 285 | 20 | 24 | 3 | 14 | 0 | 5 | 7 | 0 | 358 |
| | % per year | 79,6% | 5,6% | 6,7% | 0,8% | 3,9% | 0,0% | 1,4% | 2,0% | 0,0% | 100,0% |
| 2019 | Frequency | 294 | 8 | 14 | 3 | 6 | 1 | 2 | 5 | 0 | 333 |
| | % per year | 88,3% | 2,4% | 4,2% | 0,9% | 1,8% | 0,3% | 0,6% | 1,5% | 0,0% | 100,0% |
| 2020 | Frequency | 193 | 10 | 8 | 6 | 10 | 1 | 1 | 1 | 0 | 230 |
| | % per year | 83,9% | 4,3% | 3,5% | 2,6% | 4,3% | 0,4% | 0,4% | 0,4% | 0,0% | 100,0% |
| 2021 | Frequency | 179 | 5 | 5 | 2 | 13 | 0 | 3 | 4 | 0 | 211 |
| | % per year | 84,8% | 2,4% | 2,4% | 0,9% | 6,2% | 0,0% | 1,4% | 1,9% | 0,0% | 100,0% |
| 2022 | Frequency | 193 | 1 | 8 | 1 | 14 | 0 | 2 | 4 | 11 | 234 |
| | % per year | 82,5% | 0,4% | 3,4% | 0,4% | 6,0% | 0,0% | 0,9% | 1,7% | 4,7% | 100,0% |
| **Total** | Frequency | 3016 | 135 | 107 | 23 | 138 | 9 | 69 | 47 | 11 | 3555 |
| | % per year | 84,8% | 3,8% | 3,0% | 0,6% | 3,9% | 0,3% | 1,9% | 1,3% | 0,3% | 100,0% |

The majority of TB patients (70.7%, n=2,514) had drug-sensitive TB, whereas 29.3% (n=1,041) had drug-resistant TB. Among all TB cases recorded in the database, 1.4% (n=49) were diagnosed with HIV, which is considered a major risk factor for both the development and severity of the disease. (Table 5).

*Table 5.* **Sensitivity to antibiotic therapy.**

| R sensitivity | Frequency | Percentage |
|---|---|---|
| TB+,R- | 2514 | 70,7 |
| TB+,R+ | 1041 | 29,3 |
| **Total** | 3555 | 100,0 |

Regarding treatment outcomes, treatment completion was achieved in 51.6% (n=1,834) of patients, while 25.2% (n=895) were documented as cured. A total of 12.3% (n=437) of patients were transferred to second-line anti-TB therapy. Ineffective treatment was reported in 2.7% (n=95) of cases. Death from non-TB-related causes occurred in 4.1% (n=146), while TB-related mortality in hospital was observed in 1.3% (n=47), and TB-related death outside the hospital was recorded in 8 cases. Furthermore, 1.0% (n=37) of patients were lost to follow-up, which may have contributed to a worsening of the TB epidemiological situation.

Regarding treatment outcomes, treatment completion was achieved in 51.6% (n=1,834) of patients, while 25.2% (n=895) were documented as cured. A total of 12.3% (n=437) of patients were transferred to second-line anti-TB therapy. Ineffective treatment was reported in 2.7% (n=95) of cases. Death from non-TB-related causes occurred in 4.1% (n=146), while TB-related mortality in hospital was observed in 1.3% (n=47), and TB-related death outside the hospital was recorded in 8 cases. Furthermore, 1.0% (n=37) of patients were lost to follow-up, which may have contributed to a worsening of the TB epidemiological situation. (Table 6).

*Table 6.* **Treatment outcomes in TB patients.**

| Treatment outcome | Frequency | Percentage |
|---|---|---|
| treatment completed | 1834 | 51,6 |
| cure | 895 | 25,2 |
| transferred to treatment of type II TB | 437 | 12,3 |
| death in hospital | 47 | 1,3 |
| ineffective treatment | 95 | 2,7 |
| loss for follow-up | 37 | 1,0 |
| death other causes | 146 | 4,1 |
| result not evaluated | 52 | 1,5 |
| death from TB not in hospital | 8 | ,2 |
| left for another country | 1 | ,0 |
| transferred to treatment of type II TB other causes | 3 | ,1 |
| Total | 3555 | 100,0 |

**Discussion**

The main finding of our study is that, between 2014 and 2022, the Abai region demonstrated a consistent decline in TB incidence. This trend may be attributed to improvements in early detection and treatment programs, as well as the implementation of modern therapeutic regimens, including those targeting drug-resistant TB forms. These findings are consistent with other national and international research. For example, *Kulmirzayeva D. et al.* (2025) similarly reported a sustained decline in TB incidence in Kazakhstan between 2000 and 2023, highlighting a significant reduction in the national incidence rate from 153.2 to 34.7 cases per 100,000 population [14]. On a global scale, a study conducted by *Lönnroth K. et al.* (2015) highlighted that several countries in Eastern Europe and Central Asia have experienced a gradual decrease in TB notification rates due to strengthened public health strategies, including active case finding, contact tracing, and scale-up of

directly observed therapy [15]. Furthermore, WHO reports indicate that between 2015 and 2021, global TB incidence declined by approximately 11%, reflecting the cumulative effect of global efforts under the End TB Strategy [29]. The observed decline in the Abai region thus aligns with broader trends, supporting the efficacy of integrated national TB control measures.

Pulmonary infiltrative tuberculosis remains the most prevalent clinical form of the disease, accounting for over 80% of all diagnosed TB cases. Treatment outcomes are strongly influenced by the clinical form and the presence of drug resistance. In our study, more than half of the patients successfully completed treatment; however, an appreciable proportion still experienced unfavorable outcomes, including mortality and loss to follow-up. These findings underscore the urgent need to strengthen patient management and monitoring at all stages of healthcare delivery. In Kazakhstan, *Urazayeva S. et al.* (2019) observed that infiltrative pulmonary TB accounted for the majority of cases, and the treatment success rate was compromised by multidrug-resistant TB (MDR-TB) and social determinants such as treatment interruptions and poor adherence [28]. In another study, *Sakko Y.* and colleagues (2023) reported that from 2014 to 2019, the incidence of tuberculosis declined significantly from 227 to 15.2 per 100,000 individuals, while all-cause mortality increased from 8.4 to 15.2 per 100,000 [23]. Internationally, *Lönnroth K. et al.* (2010) and *Glaziou P. et al.* (2018) have emphasized that unfavorable outcomes—particularly loss to follow-up and mortality-are frequently linked to late diagnosis, inadequate treatment monitoring, and drug resistance, especially in low- and middle-income countries [12, 16]. Furthermore, the WHO has identified that failure to retain patients throughout the treatment cascade remains a critical barrier to TB control globally [24]. Loss to follow-up is particularly concerning, as it contributes to ongoing transmission, acquired resistance, and worse long-term outcomes. According to *Toczek A. et al.* (2013), loss to follow-up is one of the main reasons for poor program performance in MDR-TB treatment cohorts [26].

Our study confirms that TB remains a socially significant disease, predominantly affecting unemployed individuals and the elderly (retirees). Additional risk factors of notable importance included prior contact with a TB patient, alcoholism, incarceration, and a history of diabetes mellitus. However, in nearly 84.8% of cases, it was not possible to determine the presence of specific risk factors. This underscores the urgent need to strengthen preventive measures among socially vulnerable populations and to integrate TB care into broader social support and geriatric healthcare programs. For example, In a study by *Davis A.* and colleagues (2017), participants who had ever smoked tobacco (aOR 1.73, 95% CI: 1.23–2.43, $P \leq 0.01$), consumed alcohol (aOR 1.41, 95% CI: 1.03–1.93, $P \leq 0.05$), were HIV-positive (aOR 36.37, 95% CI: 2.05–646.13, $P \leq 0.05$), or had diabetes mellitus (aOR 13.96, 95% CI: 6.37–30.56, $P \leq 0.01$) were significantly more likely to have tuberculosis [8]. Globally, comparable trends have been observed. According to *Lönnroth K. et al.* (2009), social determinants such as unemployment, poor living conditions, malnutrition, and substance abuse are consistently associated with a higher risk of TB infection and disease progression [16]. *Dara M. et al.* (2015) emphasize that vulnerable groups—including the homeless, migrants, prisoners, and the elderly—should be a primary target of TB control interventions in the WHO European Region [6].

The inability to identify risk factors in a majority of cases, as observed in our research, may reflect insufficient epidemiological investigation or the presence of latent, complex social vulnerabilities. This further strengthens the argument for the integration of TB control into multisectoral public health strategies, especially within programs addressing social welfare, elderly care, and chronic disease management.

**Conclusion**

To sustain and accelerate progress toward TB elimination, it is essential to integrate TB services into broader health and social care systems, with a focus on targeted support for high-risk groups and improved continuity of care across all stages of the treatment cascade. This includes strengthening collaborations between tuberculosis programs, primary healthcare, social protection services, and geriatric care to ensure a more holistic and patient-centered approach. Community-based interventions, such as mobile screening units, directly observed therapy (DOT) support, and patient education campaigns, should be scaled up to enhance early detection and adherence. Furthermore, addressing structural determinants—such as poverty, housing instability, and limited access to healthcare—will be critical to reducing both incidence and treatment failure. Investment in data-driven surveillance and follow-up systems can help identify gaps in care and allow for real-time intervention, especially in populations at risk of being lost to follow-up. Ultimately, a multisectoral strategy that incorporates medical, social, and economic dimensions is key to achieving sustained TB control and long-term disease elimination.

***Conflict of Interest.*** *The authors declare that they have no conflict of interest.*

***Contribution of authors.*** *All authors were equally involved in the writing of this article.*

***Funding:*** *No funding was provided.*

***Literature:***

*1. Арингазина А.М., Айтамбаева Н.Н., Назарова Л.З., Алимбекова Г.Т., Исмаилов Ш.Ш., Аденов М.М., Джазыбекова П.М., Мусабекова Г.А., Аликеева Э.А.* Уровень осведомленности в вопросах туберкулеза населения и ключевых групп Республики Казахстан. Наука и Здравоохранение. 2021. 5(Т.23). С. 67-77. doi 10.34689/SH.2021.23.5.008

2. Приказ Министра здравоохранения Республики Казахстан от 29 июля 2022 года № ҚР ДСМ-69 «О внесении изменений в приказ Министра здравоохранения Республики Казахстан от 24 марта 2022 года № ҚР-ДСМ-27 «Об утверждении Стандарта оказания медицинской помощи в стационарных условиях в Республике Казахстан»

*3. Akhmetova A., Bismilda V., Chingissova L., Filipenko M., Akilzhanova A., Kozhamkulov U.* Prevalence of Beijing Central Asian/Russian Cluster 94-32 among Multidrug-Resistant M. tuberculosis in Kazakhstan. Antibiotics (Basel). 2023. 13(1). 9. doi: 10.3390/antibiotics13010009.

*4. Chakaya J., Khan M., Ntoumi F., Aklillu E., Fatima R., Mwaba P., et al. Global* Tuberculosis Report 2020 -

Reflections on the Global TB burden, treatment and prevention efforts. Int J Infect Dis. 2021. 113 Suppl 1(Suppl 1). S7-S12. doi: 10.1016/j.ijid.2021.02.107.

*5. Daniyarov A., Molkenov A., Rakhimova S., Akhmetova A., et al.* Genomic Analysis of Multidrug-Resistant Mycobacterium tuberculosis Strains From Patients in Kazakhstan. Front Genet. 2021. 12. 683515. doi: 10.3389/fgene.2021.683515.

*6. Dara M., Acosta C.D., Melchers N.V.S., et al.* Tuberculosis control in prisons: current situation and research gaps. European Respiratory Journal. 2015. 45(3). 759–762.

*7. Darisheva M., Tracy M., Terlikbayeva A., Zhussupov B., Schluger N., McCrimmon T.* Knowledge and attitudes towards ambulatory treatment of tuberculosis in Kazakhstan. BMC Health Serv Res. 2020. 20(1). 563. doi: 10.1186/s12913-020-05413-0.

*8. Davis A., Terlikbayeva A., Aifah A., Hermosilla S., Zhumadilov Z., et al.* Risks for tuberculosis in Kazakhstan: implications for prevention. Int J Tuberc Lung Dis. 2017. 21(1). 86-92. doi: 10.5588/ijtld.15.0838.

*9. Escombe A., Ticona E., Chávez-Pérez V.* et al. Improving natural ventilation in hospital waiting and consulting rooms to reduce nosocomial tuberculosis transmission risk in a low resource setting. BMC Infect. 2019. 19. 88. https://doi.org/10.1186/s12879-019-3717-9

*10. Falzon D., Zignol M., Bastard M., Floyd K., Kasaeva T.* The impact of the COVID-19 pandemic on the global tuberculosis epidemic. Front Immunol. 2023. 14. 1234785. doi: 10.3389/fimmu.2023.1234785.

*11. Furin J., Cox H., Pai M.* Tuberculosis. Lancet. 2019. 393(10181). 1642-1656. doi: 10.1016/S0140-6736(19)30308-3.

*12. Glaziou, P., Floyd, K., Raviglione, M. C.* Global tuberculosis epidemic and progress in care, prevention, and research: an overview. The Lancet Respiratory Medicine. 2018. 6(4). 299–314. https://doi.org/10.1016/S2213-2600(18)30057-2

*13. Khanna A., Saha R., Ahmad N.* National TB elimination programme - What has changed. Indian J Med Microbiol. 2023. 42. 103-107. doi: 10.1016/j.ijmmb.2022.10.008.

*14. Kulmirzayeva D., Prabakaran I., Javaid M.* Retrospective analysis of tuberculosis incidence in Kazakhstan for 2000-2023. Journal of Health Development. 2025. №1. URL: https://cyberleninka.ru/article/n/retrospective-analysis-of-tuberculosis-incidence-in-kazakhstan-for-2000-2023

*15. Lönnroth, K., Castro,K.G., Chakaya J.M., Chauhan L.S., et al.* Tuberculosis control and elimination 2015–2035: cure, care and social development. The Lancet. 2015. 385(9979). 1814–1829. https://doi.org/10.1016/S0140-6736(15)60670-0

*16. Lönnroth K., Jaramillo E., Williams B.G., Dye, C., & Raviglione, M.* Drivers of tuberculosis epidemics: The role of risk factors and social determinants. Social Science & Medicine. 2009. 68(12). 2240–2246.

*17. Marrella V., Nicchiotti F., Cassani B.* Microbiota and Immunity during Respiratory Infections: Lung and Gut Affair. Int J Mol Sci. 2024. 25(7). 4051. doi: 10.3390/ijms25074051.

*18. Mbewana Ntshanka N.G., Msagati TAM.* Trends and Progress on Antibiotic-Resistant Mycobacterium tuberculosis and Genes in relation to Human Immunodeficiency Virus. Can J Infect Dis Med Microbiol. 2023. 6659212. doi: 10.1155/2023/6659212.

*19. Melsew Y.A., Doan T.N., Gambhir M., Cheng A.C., McBryde E., Trauer J.M.* Risk factors for infectiousness of patients with tuberculosis: a systematic review and meta-analysis. Epidemiol Infect. 2018. 146(3). 345-353. doi: 10.1017/S0950268817003041.

*20. Murphy M.E., Wills G.H., Murthy S., Louw C., Bateson AL.C, et al.* REMoxTB consortium. Gender differences in tuberculosis treatment outcomes: a post hoc analysis of the REMoxTB study. BMC Med. 2018. 16(1). 189. doi: 10.1186/s12916-018-1169-5.

*21. Qi CC., Xu LR., Zhao CJ.* et al. Prevalence and risk factors of tuberculosis among people living with HIV/AIDS in China: a systematic review and meta-analysis. BMC Infect Dis. 2023. 23. 584. https://doi.org/10.1186/s12879-023-08575-4

*22. Ristić L., Rancić M., Radović M.* Tuberculosis in the 21st century--challenges, endeavours and recommendations to doctors. Med Pregl. 2010. 63(11-12). 811-5. doi: 10.2298/mpns1012811r.

*23. Sakko Y., Madikenova M., Kim A., Syssoyev D., Mussina K., et al.* Epidemiology of tuberculosis in Kazakhstan: data from the Unified National Electronic Healthcare System 2014-2019. BMJ Open. 2023. 13(10). e074208. doi: 10.1136/bmjopen-2023-074208.

*24. Seth-Smith HMB., Imkamp F., Tagini F., Cuénod A., Hömke R., Jahn K., Tschacher A., et al.* Discovery and Characterization of Mycobacterium basiliense sp. nov., a Nontuberculous Mycobacterium Isolated From Human Lungs. Front. Microbiol. 2019. 9. 3184. doi: 10.3389/fmicb.2018.03184

*25. Singh A., Prasad R., Balasubramanian V., Gupta N.* Drug-Resistant Tuberculosis and HIV Infection: Current Perspectives. HIV AIDS (Auckl). 2020. 12. 9-31. doi: 10.2147/HIV.S193059.

*26. Toczek A., Cox H., Du Cros P., Cooke G., & Ford N.* Strategies for reducing treatment default in drug-resistant tuberculosis: systematic review and meta-analysis. PLOS ONE 2013. 8(8). e68300. https://doi.org/10.1371/journal.pone.0068300

*27. Uplekar M., Raviglione M.* WHO's End TB Strategy: From stopping to ending the global TB epidemic. Indian J Tuberc. 2015. 62(4). 196-9. doi: 10.1016/j.ijtb.2015.11.001.

*28. Urazayeva S.T., Turegaliyeva Z.T., Tussupkalieva K. Sh., et al.* Tuberculosis morbidity and mortality in the Aktobe province of Kazakhstan for the period 2008-2017. ROMJ. 2019. №1.

29. World Health Organization. Global tuberculosis report 2022. Geneva: World Health Organization. 2022. https://www.who.int/publications/i/item/9789240061729

*30. Yerezhepov D., Gabdulkayum A., Akhmetova A., et al.* Pulmonary tuberculosis epidemiology and genetics in Kazakhstan. Front Public Health. 2024. 12. 1340673. doi: 10.3389/fpubh.2024.1340673.

***References: [1-2]***

*1. Aringazina A.M., Ajtambaeva N.N., Nazarova L.Z., Alimbekova G.T., Ismailov Sh.Sh., Adenov M.M., Dzhazybekova P.M., Musabekova G.A., Alikeeva E.A.* Uroven' osvedomlennosti v voprosah tuberkuleza

naseleniya i klyuchevyh grupp Respubliki Kazahstan [The level of awareness of the population and key groups in tuberculosis issues in the Republic of Kazakhstan]. *Nauka i Zdravookhranenie* [Science and Healthcare]. 2021. 5(T.23). pp. 67-77. doi 10.34689/SH.2021.23.5.008 [in Russian]

2. Prikaz Ministra zdravoohraneniya Respubliki Kazahstan ot 29 iyulya 2022 goda № ҚR DSM-69 «O vnesenii izmenenij v prikaz Ministra zdravoohraneniya Respubliki Kazahstan ot 24 marta 2022 goda № ҚR-DSM-27 «Ob utverzhdenii Standarta okazaniya medicinskoj pomoshchi v stacionarnyh usloviyah v Respublike Kazahstan» [Order of the Minister of Health of the Republic of Kazakhstan dated July 29, 2022 No. ҚР ДСМ-69 "On Amendments to the Order of the Minister of Health of the Republic of Kazakhstan dated March 24, 2022 No. ҚР-ДСМ-27 "On Approval of the Standard for the Provision of Medical Care in Inpatient Settings in the Republic of Kazakhstan] [in Russian]

**Information about the authors:**

**Adilzhanov Assylkhan Bolatkhanovich** – Director of Regional HIV Prevention Center, State Municipal Enterprise under the Health Department of the Abai Region, phone: 8 707 721 06 85, e-mail: han_21.06.85@mail.ru, Semey, Republic of Kazakhstan;

**Adilgozhin Maksat Socialovich** - Candidate of Medical Sciences, Regional Center of Phthisiopulmonology, State Municipal Enterprise under the Right of Economic Management, phone: 8 708 260 42 31, e-mail: Adilgozhin@mail.ru, Semey, Republic of Kazakhstan;

**Ibrayeva Zhanara Beysengalievna** - PhD, Senior teacher, Department of Epidemiology and Biostatistics, NJSC "Semey Medical University", phone: 8 708 745 60 17, https://orcid.org/0000-0001-7298-7869, e-mail: zhanara.ibrayeva@smu.edu.kz, Semey, Republic of Kazakhstan;

**Urazalina Nailya Murathanovna** - Candidate of Medical Sciences, Associate Professor of the Department of physiological disciplines named after honored scientist of the republic of Kazakhstan, professor T.A. Nazarova, phone: 8 777 907 55 89, e-mail: hakim_15@mail.ru, https://orcid.org/0000-0003-0200-1763, Semey, Kazakhstan;

**Mukanova Dinara Adletovna** - Candidate of Medical Sciences, Associate Professor Department of simulation and educational technologies, NJSC "Semey Medical University", phone: 8 701 491 98 29, e-mail: mukanova.dinara@smu.edu.kz, https://orcid.org/0000-0001-5186-2346, Semey, Republic of Kazakhstan;

**Zemlyanskaya Natalya Sergeevna** - Master of Medicine, Assistant Department of General practice with a course of evidence-based medicine, NJSC "Astana Medical University", phone: 8 705 500 02 72, e-mail: zemlyanskaya.n@amu.kz, https://orcid.org/0000-0003-1968-3246, Astana, Republic of Kazakhstan;

**Aitenova Elvira Rustemovna** - Assistant Department of General practice with a course of evidence-based medicine, NJSC "Astana Medical University", phone: 8 775 313 08 05, e-mail: aitenova.e@amu.kz,

**Shamshudinov Timur Maratovich** – PhD, «Medical and diagnostic Center of otorhinolaryngology» PRO-ЛОР, phone: 8 701 204 10 70, e-mail: dr.shamshudinov@mail.ru, https://orcid.org/0000-0001-5015-871X, Almaty, Republic of Kazakhstan;

**Kassym Laura Talgatkyzy** – PhD, Associate Professor Department of General practice with a course of evidence-based medicine, NJSC "Astana Medical University", phone: 8 777 735 10 62, e-mail: laura.kassym@gmail.com, https://orcid.org/0000-0003-4448-6455, Astana, Republic of Kazakhstan.

**Kussainova Assiya Abikhasovna** - PhD, Acting Associate Professor Department of General practice with a course of evidence-based medicine, NJSC "Astana Medical University", phone: 8 707 498 73 48, e-mail: kuzilas@mail.ru, https://orcid.org/0000 0002-5738-0804, Astana, Republic of Kazakhstan;

**Corresponding author:**

**Kussainova Assiya Abikhasovna** - PhD, Acting Associate Professor Department of General practice with a course of evidence-based medicine, NJSC "Astana Medical University",

**Postal code:** Republic of Kazakhstan, 010000, Astana city, Abay Street 49.

**E-mail:** kuzilas@mail.ru

**Phone:** +7 707 498 73 48

Received: 09 February 2025 / Accepted: 10 May 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2025.27.3.011***

***UDC 579.842.16:615.33.***

This work is licensed under a Creative Commons Attribution 4.0 International License

# ANALYSIS OF ANTIBIOTIC SUSCEPTIBILITY AND RESISTANCE OF KLEBSIELLA PNEUMONIAE IN VARIOUS BIOLOGICAL MATERIALS

**Gulbarshyn D. Mukasheva[1], https://orcid.org/0000-0003-3490-5628**
**Saule B. Maukayeva[1], https://orcid.org/0000-0002-2679-6399**
**Nazym K. Kudaibergenova[1], https://orcid.org/0000-0002-6165-7677**
**Dariya M. Shabdarbayeva[1], https://orcid.org/0000–0001–9463–1935**
**Zhanargyl K. Smailova[1], https://orcid.org/0000-0002-4513-4614**
**Alma Z. Tokayeva[1], https://orcid.org/0000-0003-1238-9263**
**Yerbol M. Smail[1], https://orcid.org/0000-0003-3881-3747**
**Gulnara I. Nuralinova[1], https://orcid.org/0000-0002-0478-5154**
**Zhanar B. Issabekova[1], https://orcid.org/0000-0002-2744-0327**
**Saya S. Karimova[1]*, http://orcid.org/0000-0002-1167-5375**
**Dinara B. Kozubayeva[1], https://orcid.org/0000-0003-4937-708X**
**Maiya V. Goremykina[1], https://orcid.org/0000-0002-5433-7771**
**Nailya M. Urazalina[1], https://orcid.org/0000-0003-0200-1763**

**[1] NCJSC «Semey Medical University», Semey, Republic of Kazakhstan.**

**Abstract**

**Background:** Antibiotic resistance of Klebsiella pneumoniae remains one of the most pressing issues in clinical microbiology and healthcare. With the active spread of multidrug-resistant strains, especially in hospital settings, the need for local monitoring of antibiotic susceptibility is becoming increasingly urgent to ensure effective treatment selection.

**Objective:** To assess the susceptibility and resistance of K. pneumoniae isolated from various biological materials to a broad spectrum of antibiotics and to identify the most effective drugs for empirical therapy.

**Materials and Methods:** The study utilized retrospective laboratory data from 169 clinical isolates of Klebsiella pneumoniae, obtained from five types of biological materials: sputum (n=65), ENT samples (n=45), urine (n=45), cerebrospinal fluid (n=9), and wound exudate (n=5). The analysis included 15 antibiotics from different classes, including cephalosporins, carbapenems, fluoroquinolones, aminoglycosides, and others. Susceptibility and resistance percentages were calculated using standard formulas. Microsoft Excel was used for primary data processing, and IBM SPSS Statistics was employed for descriptive statistical analysis.

**Results:** The highest susceptibility rates were observed for Imipenem (84.5%), Minocycline (82.4%), and Amikacin (79.6%), with resistance levels remaining below 20%, confirming their high efficacy against K. pneumoniae. Moderate activity was shown by Piperacillin, Cefepime, and Meropenem (approximately 70% susceptibility). In contrast, Nitrofurantoin, Cefazolin, and Trimethoprim showed the lowest activity, with resistance reaching up to 60% in some sample types. Differences in susceptibility profiles were noted depending on the biological material, although overall trends were consistent.

**Conclusion:** The findings underscore the importance of systematic local monitoring of K. pneumoniae antibiotic susceptibility, particularly in the context of widespread resistant strains. Imipenem, Minocycline, and Amikacin may be considered first-line agents for empirical treatment of K. pneumoniae infections. The reduced efficacy of several traditional antibiotics also highlights the need for cautious use in clinical practice.

***Keywords:*** *Klebsiella pneumoniae, antibiotic resistance, susceptibility, resistance, biological materials.*

***For citation:***

Mukasheva G.D., Maukayeva S.B., Kudaibergenova N.K., Shabdarbayeva D.M., Smailova Zh.K., Tokayeva A.Z., Smail Y.M., Nuralinova G.I., Issabekova Zh.B., Karimova S.S., Kozubayeva D.B., Goremykina M.V., Urazalina N.M. Analysis of antibiotic susceptibility and resistance of Klebsiella Pneumoniae in various biological materials // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 98-107. *doi 10.34689/SH.2025.27.3.011*

**Резюме**

# АНАЛИЗ ЧУВСТВИТЕЛЬНОСТИ И УСТОЙЧИВОСТИ KLEBSIELLA PNEUMONIAE К АНТИБИОТИКАМ В РАЗЛИЧНЫХ БИОМАТЕРИАЛАХ

**Гүлбаршын Д. Мукашева[1],** https://orcid.org/0000-0003-3490-5628
**Сауле Б. Маукаева[1],** https://orcid.org/0000-0002-2679-6399
**Назым К. Кудайбергенова[1],** https://orcid.org/0000-0002-6165-7677
**Дария М. Шабдарбаева[1],** https://orcid.org/0000–0001–9463–1935
**Жанаргуль К. Смаилова[1],** http://orcid.org/0000-0002-4513-4614
**Алма З. Токаева[1],** https://orcid.org/0000-0003-1238-9263
**Ербол М. Смаил[1],** https://orcid.org/0000-0003-3881-3747
**Гульнара И. Нуралинова[1],** https://orcid.org/0000-0002-0478-5154
**Жанар Б. Исабекова[1],** https://orcid.org/0000-0002-2744-0327
**Сая С. Каримова*[1],** http://orcid.org/0000-0002-1167-5375
**Динара Б. Козубаева[1],** https://orcid.org/0000-0003-4937-708X
**Майя В. Горемыкина[1],** https://orcid.org/0000-0002-5433-7771
**Найля М. Уразалина[1],** https://orcid.org/0000-0003-0200-1763

**[1] НАО «Медицинский университет Семей», г. Семей, Республика Казахстан.**

**Введение:** Антибиотикорезистентность Klebsiella pneumoniae продолжает оставаться одной из наиболее актуальных проблем клинической микробиологии и здравоохранения. В условиях активного распространения мультирезистентных штаммов, особенно в стационарах, возрастает необходимость в локальном мониторинге чувствительности к антибактериальным препаратам для эффективного подбора терапии.

**Цель:** Оценить уровень чувствительности и устойчивости K. pneumoniae, выделенной из различных биологических материалов, к широкому спектру антибиотиков и определить наиболее эффективные препараты для эмпирического лечения.

**Материалы и методы:** В исследование включены ретроспективные лабораторные данные по 169 клиническим изолятам Klebsiella pneumoniae, полученным из пяти типов биоматериалов: мокрота (n=65), ЛОР-материалы (n=45), моча (n=45), церебральный канал (n=9), рана (n=5). Анализ включал 15 антибиотиков различных групп, в том числе цефалоспорины, карбапенемы, фторхинолоны, аминогликозиды и другие. Расчёт процентных показателей чувствительности и устойчивости проводился по стандартным формулам, с применением Microsoft Excel для первичной обработки данных и IBM SPSS Statistics — для статистического анализа.

**Результаты:** Максимальные уровни чувствительности выявлены у Imipenem (84,5%), Minocycline (82,4%) и Amikacin (79,6%), при минимальных показателях устойчивости (<20%), что подтверждает их высокую эффективность против K. pneumoniae. Умеренные показатели продемонстрировали Piperacillin, Cefepime и Meropenem (чувствительность около 70%). В то же время, наименьшая активность отмечена у Nitrofurantoin, Cefazolin и Trimethoprim, устойчивость к которым в отдельных материалах достигала 60%. Заметны отличия в профиле чувствительности в зависимости от биологического материала, однако общие тенденции сохраняются.

**Вывод:** Результаты подчёркивают необходимость систематического локального мониторинга антибиотикочувствительности K. pneumoniae, особенно в условиях высокой распространённости устойчивых штаммов. Imipenem, Minocycline и Amikacin могут рассматриваться в качестве препаратов первой линии при эмпирическом лечении инфекций, вызванных данным патогеном. Полученные данные также свидетельствуют о сниженной эффективности ряда традиционных препаратов, что требует осторожного подхода к их применению.

***Ключевые слова:*** *Klebsiella pneumoniae, антибиотикорезистентность, чувствительность, устойчивость, биоматериалы.*

***Для цитирования:***

*Мукашева Г.Д., Маукаева С.Б., Кудайбергенова Н.К., Шабдарбаева Д.М., Смаилова Ж.К., Токаева А.З., Смаил Е.М., Нуралинова Г.И., Исабекова Ж.Б., Каримова С.С., Козубаева Д.Б., Горемыкина М.В., Уразалина Н.М.* Анализ чувствительности и устойчивости Klebsiella Pneumoniae к антибиотикам в различных биоматериалах // Наука и Здравоохранение. 2025. Т.27 (3), С. 98-107. doi: 10.34689/SH.2025.27.3.011

**Түйіндеме**

# KLEBSIELLA PNEUMONIAE-НІҢ ӘРТҮРЛІ БИОЛОГИЯЛЫҚ МАТЕРИАЛДАРДАҒЫ АНТИБИОТИКТЕРГЕ СЕЗІМТАЛДЫҒЫ МЕН ТӨЗІМДІЛІГІН ТАЛДАУ

**Гүлбаршын Д. Мукашева[1], https://orcid.org/0000-0003-3490-5628**
**Сауле Б. Маукаева[1], https://orcid.org/0000-0002-2679-6399**
**Назым К. Кудайбергенова[1], https://orcid.org/0000-0002-6165-7677**
**Дария М. Шабдарбаева[1], https://orcid.org/0000–0001–9463–1935**
**Жанаргуль К. Смаилова[1], http://orcid.org/0000-0002-4513-4614**
**Алма З. Токаева[1], https://orcid.org/0000-0003-1238-9263**
**Ербол М. Смаил[1], https://orcid.org/0000-0003-3881-3747**
**Гульнара И. Нуралинова[1], https://orcid.org/0000-0002-0478-5154**
**Жанар Б. Исабекова[1], https://orcid.org/0000-0002-2744-0327**
**Сая С. Каримова[1], http://orcid.org/0000-0002-1167-5375**
**Динара Б. Козубаева[1], https://orcid.org/0000-0003-4937-708X**
**Майя В. Горемыкина[1], https://orcid.org/0000-0002-5433-7771**
**Найля М. Уразалина[1], https://orcid.org/0000-0003-0200-1763**

**[1] «Семей медицина университеті» КеАҚ,**
**Семей қ., Қазақстан Республикасы.**

**Кіріспе:** Klebsiella pneumoniae бактериясының антибиотиктерге төзімділігі клиникалық микробиология мен денсаулық сақтау саласындағы ең өзекті мәселелердің бірі болып қалып отыр. Ауруханаларда мультирезистентті штаммдардың кең таралуы тиімді емдеу әдістерін таңдауда жергілікті деңгейде антибиотиктерге сезімталдықты бақылаудың маңыздылығын арттырады.

**Мақсаты:** K. pneumoniae штаммдарының әртүрлі биологиялық материалдардан бөлініп алынған жағдайларында антибиотиктерге сезімталдық және төзімділік деңгейін бағалау, сондай-ақ эмпирикалық емдеу үшін ең тиімді препараттарды анықтау.

**Материалдар мен әдістер:** Зерттеу аясында 169 клиникалық Klebsiella pneumoniae изоляттарына қатысты ретроспективті зертханалық деректер пайдаланылды. Биоматериалдар мынадай бес топтан алынды: қақырық (n=65), ЛОР-мүшелерінен алынған материалдар (n=45), несеп (n=45), ми-жұлын сұйықтығы (n=9), жара іріңі (n=5). Зерттеу 15 антибиотикті қамтыды: цефалоспориндер, карбапенемдер, фторхинолондар, аминогликозидтер және басқа топтар. Антибиотикке сезімталдық пен төзімділіктің пайыздық көрсеткіштері стандартты формулалар бойынша есептелді. Деректер Microsoft Excel арқылы өңделіп, статистикалық талдау үшін IBM SPSS Statistics бағдарламасы қолданылды.

**Нәтижелер:** Ең жоғары сезімталдық Imipenem (84,5%), Minocycline (82,4%) және Amikacin (79,6%) антибиотиктерінде байқалды, ал төзімділік деңгейі 20%-дан төмен болды. Piperacillin, Cefepime және Meropenem препараттары орташа белсенділік көрсетті (шамамен 70%). Ал Nitrofurantoin, Cefazolin және Trimethoprim сияқты антибиотиктер төмен белсенділік көрсетті, кейбір материалдарда төзімділік деңгейі 60%-ға дейін жетті. Биоматериал түріне байланысты сезімталдық профилінде айырмашылықтар болғанымен, жалпы үрдістер сақталды.

**Қорытынды:** K. pneumoniae штаммдарының антибиотикке сезімталдығын жергілікті деңгейде жүйелі түрде бақылау аса маңызды, әсіресе резистентті штаммдардың таралуы жоғары болған жағдайда. Imipenem, Minocycline және Amikacin препараттары эмпирикалық емдеу үшін бірінші таңдаулы дәрілер ретінде қолдануға ұсынылады. Кейбір дәстүрлі антибиотиктердің тиімділігінің төмендеуі оларды қолдануда сақтықты талап етеді.

***Кілт сөздер:*** *Klebsiella pneumoniae, антибиотиктерге төзімділік, сезімталдық, биоматериалдар.*

***Дәйексөз үшін:***

*Мукашева Г.Д., Маукаева С.Б., Кудайбергенова Н.К., Шабдарбаева Д.М., Смаилова Ж.К., Токаева А.З., Смаил Е.М., Нуралинова Г.И., Исабекова Ж.Б., Каримова С.С., Козубаева Д.Б., Горемыкина М.В., Уразалина Н.М.* Klebsiella pneumoniae-нің әртүрлі биологиялық материалдардағы антибиотиктерге сезімталдығы мен төзімділігін талдау // Ғылым және Денсаулық. 2025. Т.27 (3), Б. 98–107. doi: 10.34689/SH.2025.27.3.011

**Introduction**

Klebsiella pneumoniae ranks among the leading causative agents of hospital-acquired infections and poses a serious threat to immunocompromised patients. In the context of the global rise in antibiotic resistance, the situation involving K. pneumoniae isolates resistant to carbapenems and third-generation cephalosporins is particularly alarming. These strains are increasingly detected in various types of biological materials such as blood, urine, sputum, and exudates, complicating the selection of effective empirical therapy [18].

An analysis of antibiotic susceptibility in strains isolated from different biological sources reveals significant variations in resistance profiles. For example, strains obtained from wounds and blood of patients with orthopedic infections often produce carbapenemases and exhibit multidrug resistance, including resistance to fluoroquinolones and aminoglycosides [4]. A similar situation is observed in dialysis and transplant facilities, where strains from urine and vascular catheters show high resistance to β-lactam antibiotics [10].

Particular attention should be given to strains isolated from children with cystic fibrosis: under constant colonization pressure from K. pneumoniae, unique mechanisms of adaptation and resistance to antimicrobial agents are formed [18]. In addition, patients with tuberculosis, who are frequently subjected to prolonged antibiotic therapy, demonstrate plasmid-mediated resistance mechanisms to broad-spectrum drugs [11].

Based on accumulated clinical data, it can be concluded that the resistance spectrum of K. pneumoniae is directly related to the infection site. For instance, strains isolated from bronchoalveolar lavage and lower respiratory tract aspirates often produce extended-spectrum β-lactamases, whereas those from urine tend to exhibit resistance to fluoroquinolones and nitrofurans [20]. Additional microbiological analysis of aspirates, punctates, and pleural exudates has shown a high frequency of isolation of multidrug-resistant strains with marked resistance to third-generation cephalosporins and carbapenems [17]. Particularly concerning data have been reported regarding oncohematological patients, in whom Klebsiella pneumoniae is found in virtually all types of biological materials from blood and aspirates to punctates and feces [5].

Modern approaches to assessing Klebsiella pneumoniae resistance involve not only phenotypic methods but also molecular-genetic characterization. For example, Gordinskaya and Boriskina demonstrated that isolates from different hospitals vary significantly in the presence of carbapenemase genes (e.g., KPC, NDM), as well as in resistance mechanisms to colistin, especially in aspirate and bronchoalveolar lavage samples [9].

Analysis of hypermucoid strains isolated from wound exudates revealed their increased resistance to cephalosporins and aminoglycosides, which may be related to capsular factors and biofilm formation [13]. These properties significantly reduce the effectiveness of traditional treatment regimens.

*Belkova N.L. et al.* conducted a comparative genomic analysis of isolates obtained from blood, urine, and exudates, demonstrating the presence of mutations encoding resistance to novel beta-lactam antibiotics [3]. Another study revealed that K. pneumoniae isolates from trauma units more frequently exhibit polyresistance, especially in aspirates and purulent discharges [7].

To date, the diagnosis and treatment of infections caused by K. pneumoniae require not only awareness of general antibiotic resistance trends but also an understanding of the microbiological characteristics specific to each type of biological material. Integrating data from various sources allows for a more accurate analysis of antimicrobial susceptibility, which in turn supports the development of effective treatment strategies.

**The aim of the study** is to analyze the antibiotic susceptibility and resistance of Klebsiella pneumoniae isolated from different biological materials, in order to identify specific features of antimicrobial resistance depending on the source of the clinical isolate.

**Materials and methods**

The study utilized retrospective laboratory data on the antibiotic susceptibility of *Klebsiella pneumoniae* to various antimicrobial agents. The biological samples used for bacteriological analysis included sputum (n = 65), ENT materials (n = 45), urine (n = 45), cerebrospinal fluid (n = 9), and wound exudate (n = 5). The analysis included 15 antibiotics, among them: Ceftriaxone, Cefazolin, Cefuroxime, Cefepime, Piperacillin, Minocycline, Imipenem, Levofloxacin, Nitrofurantoin, Ceftriaxidime, Meropenem, Tobramycin, Amikacin, and Trimethoprim.

For quantitative analysis, relative susceptibility and resistance were calculated for each antibiotic based on the biological material tested.

The following formulas were used:

1) Susceptibility = (Number of susceptible isolates / Total number of isolates for the material) × 100

2) Resistance = (Number of resistant isolates / Total number of isolates for the material) × 100

Data were entered into Microsoft Excel for initial sorting and calculation of susceptibility and resistance percentages. Statistical analysis was performed using IBM SPSS Statistics, applying descriptive statistical methods.

***Results***

Table 1 presents the number of Klebsiella pneumoniae strains identified as either susceptible or resistant to antibiotics across five types of biological materials: sputum, ENT organs, urine, cerebrospinal fluid, and wound samples. The highest number of isolates was obtained from sputum (65) and ENT materials (45), while significantly fewer strains were isolated from cerebrospinal fluid (9) and wounds (5). The susceptibility analysis showed that antibiotics such as Piperacillin and Imipenem demonstrated high levels of susceptibility across all sample types, particularly in sputum and ENT materials. Conversely, Cefazolin and Nitrofurantoin showed higher levels of resistance, indicating limited effectiveness of these drugs in treating infections caused by K. pneumoniae.

Table 2 presents the percentage of Klebsiella pneumoniae susceptibility to various antibiotics depending on the type of biological material: sputum, ENT organs, urine, cerebral canal, and wound. The highest levels of susceptibility were observed for the antibiotics Minocycline and Imipenem, which showed consistently strong results exceeding 85% across all sample types, including sputum and urine. Piperacillin also demonstrated high susceptibility, particularly in urine (88%) and sputum (81.5%). Cefepime, Cefuroxime, and Levofloxacin were characterized by moderately high susceptibility levels (ranging from 60% to 80%) across all studied biological materials. In contrast, Nitrofurantoin and Trimethoprim showed lower susceptibility rates, not exceeding 55% in most sample types, indicating their limited effectiveness in treating infections caused by Klebsiella pneumoniae.

*Table 1.*

**Number of susceptible and resistant Klebsiella pneumoniae isolates by sample type.**

| Antibiotic | Sputum (65) | | ENT Organs (45) | | Urine (45) | | Cerebral Canal (9) | | Wound (5) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Sus | Res | Sus | Res | Sus | Res | Sus | Res | Sus | Res |
| Ceftriaxone | 42 | 23 | 27 | 18 | 28 | 17 | 6 | 3 | 3 | 2 |
| Cefazolin | 35 | 30 | 23 | 22 | 21 | 24 | 5 | 4 | 2 | 3 |
| Cefuroxime | 47 | 18 | 32 | 13 | 31 | 14 | 6 | 3 | 4 | 1 |
| Cefepime | 51 | 14 | 31 | 14 | 33 | 12 | 7 | 2 | 3 | 2 |
| Piperacillin | 53 | 12 | 41 | 4 | 40 | 5 | 7 | 2 | 4 | 1 |
| Minocycline | 60 | 5 | 39 | 6 | 41 | 4 | 8 | 1 | 4 | 1 |
| Imipenem | 61 | 4 | 40 | 5 | 42 | 3 | 8 | 1 | 4 | 1 |
| Levofloxacin | 50 | 15 | 31 | 14 | 38 | 7 | 7 | 2 | 3 | 2 |
| Nitrofurantoin | 32 | 33 | 22 | 23 | 22 | 23 | 4 | 5 | 2 | 3 |
| Ceftrazidime | 48 | 17 | 22 | 23 | 37 | 8 | 6 | 3 | 2 | 3 |
| Meropenem | 43 | 22 | 37 | 8 | 38 | 7 | 6 | 3 | 4 | 1 |
| Tobramycin | 37 | 28 | 24 | 21 | 24 | 21 | 4 | 5 | 3 | 2 |
| Amikacin | 57 | 8 | 39 | 6 | 35 | 10 | 7 | 2 | 4 | 1 |
| Trimethoprim | 34 | 31 | 24 | 21 | 23 | 22 | 5 | 4 | 3 | 2 |

*Table 2.*

**Percentage of Klebsiella pneumoniae Susceptibility to Antibiotics.**

| Antibiotic | Sputum (%) | ENT Organs (%) | Urine (%) | Cerebral Canal (%) | Wound (%) |
|---|---|---|---|---|---|
| Ceftriaxone | 64.6 | 60.0 | 62.2 | 66.7 | 60.0 |
| Cefazolin | 53.6 | 51.7 | 46.6 | 55.6 | 57.1 |
| Cefuroxime | 72.5 | 71.1 | 68.9 | 66.7 | 80.0 |
| Cefepime | 78.0 | 68.9 | 73.3 | 77.8 | 60.0 |
| Piperacillin | 81.5 | 63.2 | 88.0 | 77.8 | 80.0 |
| Minocycline | 92.3 | 86.7 | 91.1 | 88.9 | 80.0 |
| Imipenem | 93.8 | 88.9 | 93.3 | 88.9 | 80.0 |
| Levofloxacin | 76.9 | 68.9 | 84.4 | 77.8 | 60.0 |
| Nitrofurantoin | 49.3 | 48.0 | 48.0 | 44.4 | 40.0 |
| Ceftrazidime | 73.7 | 48.9 | 82.1 | 66.7 | 66.7 |
| Meropenem | 66.0 | 82.1 | 84.0 | 66.7 | 80.0 |
| Tobramycin | 56.6 | 53.3 | 53.3 | 44.4 | 60.0 |
| Amikacin | 87.7 | 86.7 | 77.8 | 77.8 | 80.0 |
| Trimethoprim | 52.3 | 53.3 | 50.0 | 55.6 | 60.0 |

Table 3 shows the percentage of resistance of Klebsiella pneumoniae to various antibiotics depending on the type of biological material: sputum, ENT organs, urine, cerebral canal, and wound. The highest resistance rates are observed for the antibiotics Cefepime, Ceftriaxone, and Piperacillin, especially in sputum and urine, where resistance levels reach 20–46%. Minocycline and Imipenem exhibit low resistance rates (from 6 to 20%) across all samples, confirming their high effectiveness. There is also a high resistance to Nitrofurantoin and Trimethoprim, ranging from 40–60%, indicating the limited clinical applicability of these drugs against Klebsiella pneumoniae.

*Table 3.*

**Percentage of Klebsiella pneumoniae resistance to antibiotics.**

| Antibiotic | Sputum (%) | ENT Organs (%) | Urine (%) | Cerebral Canal (%) | Wound (%) |
|---|---|---|---|---|---|
| Ceftriaxone | 35.4 | 40.0 | 37.8 | 33.3 | 40.0 |
| Cefazolin | 46.4 | 48.3 | 53.4 | 44.4 | 42.9 |
| Cefuroxime | 27.5 | 28.9 | 31.1 | 33.3 | 20.0 |
| Cefepime | 22.0 | 31.1 | 26.7 | 22.2 | 40.0 |
| Piperacillin | 18.5 | 36.8 | 12.0 | 22.2 | 20.0 |
| Minocycline | 7.7 | 13.3 | 8.9 | 11.1 | 20.0 |
| Imipenem | 6.2 | 11.1 | 6.7 | 11.1 | 20.0 |
| Levofloxacin | 23.1 | 31.1 | 15.6 | 22.2 | 40.0 |
| Nitrofurantoin | 50.7 | 52.0 | 52.0 | 55.6 | 60.0 |
| Ceftrazidime | 26.3 | 51.1 | 17.9 | 33.3 | 33.3 |
| Meropenem | 34.0 | 17.9 | 16.0 | 33.3 | 20.0 |
| Tobramycin | 43.4 | 46.7 | 46.7 | 55.6 | 40.0 |
| Amikacin | 12.3 | 13.3 | 22.2 | 22.2 | 20.0 |
| Trimethoprim | 47.7 | 46.7 | 50.0 | 44.4 | 40.0 |

Table 4 presents the average sensitivity and resistance rates of Klebsiella pneumoniae to various antibiotics, calculated based on data from different biological materials.

*Table 4.*

**Comparison of Average Sensitivity and Resistance Values by Antibiotic**

| Antibiotic | Average Sensitivity Percentage (%) | Average Resistance Percentage (%) |
|---|---|---|
| Ceftriaxone | 60.2 | 39.8 |
| Cefazolin | 54.2 | 45.8 |
| Cefuroxime | 64.6 | 35.4 |
| Cefepime | 71.1 | 28.9 |
| Piperacillin | 70.2 | 29.8 |
| Minocycline | 82.4 | 17.6 |
| Imipenem | 84.5 | 15.5 |
| Levofloxacin | 69.8 | 30.2 |
| Nitrofurantoin | 54.8 | 45.2 |
| Ceftrazidime | 67.3 | 32.7 |
| Meropenem | 70.4 | 29.6 |
| Tobramycin | 58.0 | 42.0 |
| Amikacin | 79.6 | 20.4 |
| Trimethoprim | 55.1 | 44.9 |

The highest sensitivity rates were observed for Imipenem (84.5%), Minocycline (82.4%), and Amikacin (79.6%), indicating the high effectiveness of these drugs against the studied strains. Antibiotics such as Cefepime, Piperacillin, and Meropenem also demonstrated relatively high sensitivity levels around 70%. At the same time, Nitrofurantoin, Cefazolin, Trimethoprim, and Tobramycin showed lower sensitivity rates (approximately 54–58%) and correspondingly high resistance rates (ranging from 42% to 45%), indicating limited clinical efficacy of these agents.

Table 5 presents the five antibiotics that demonstrated the highest levels of sensitivity of Klebsiella pneumoniae depending on the type of biological material: sputum, ENT organs, urine, cerebral canal, and wounds. Imipenem holds the leading position in sensitivity across all tested samples, with rates ranging from 80% (wound) to 93.8% (sputum), confirming its high effectiveness against K. pneumoniae. Minocycline and Amikacin also show consistently high results, ranking second and third respectively, with sensitivity ranging from 77.8% to 92.3%.

Piperacillin demonstrates high sensitivity levels, especially in urine and ENT samples, where it reaches over 88%. Cefepime ranks fifth for most materials, except for wound exudates, where Cefuroxime takes the fifth position with a sensitivity rate of 80%.

*Table 5.*

**Distribution of antibiotics with the highest sensitivity levels of Klebsiella pneumoniae by biological material**

| Biological Material | 1st Place | 2nd Place | 3rd Place | 4th Place | 5th Place |
|---|---|---|---|---|---|
| Sputum (n=65) | Imipenem (93.8%) | Minocycline (92.3%) | Amikacin (87.7%) | Piperacillin (81.5%) | Cefepime (78.5%) |
| ENT Organs (n=45) | Imipenem (88.9%) | Minocycline (86.7%) | Amikacin (86.7%) | Piperacillin (91.1%) | Cefepime (68.9%) |
| Urine (n=45) | Imipenem (93.3%) | Minocycline (91.1%) | Piperacillin (88.9%) | Amikacin (77.8%) | Cefepime (73.3%) |
| Cerebral Canal (n=9) | Imipenem (88.9%) | Minocycline (88.9%) | Amikacin (77.8%) | Piperacillin (77.8%) | Cefepime (77.8%) |
| Wound (n=5) | Imipenem (80.0%) | Minocycline (80.0%) | Amikacin (80.0%) | Piperacillin (80.0%) | Cefuroxime (80.0%) |

**Discussion**

Among the antibiotics studied, Imipenem, Minocycline, and Amikacin demonstrated the highest activity, with resistance rates generally not exceeding 20%. These drugs showed consistently high sensitivity levels (>80%) regardless of the biological material, making them potential first-line agents for the treatment of infections caused by K. pneumoniae. Moderate efficacy was observed for Piperacillin, Cefepime, Meropenem, and Levofloxacin, with sensitivity levels around 70% and more pronounced variability depending on the sample type. Meanwhile, Nitrofurantoin, Cefazolin, Trimethoprim, and Tobramycin exhibited low sensitivity rates (less than 60%) and high resistance levels, limiting their clinical use in treating infections caused by K. pneumoniae. The results of the sensitivity analysis of Klebsiella pneumoniae isolated from various biological materials reveal both general patterns and significant differences in antibiotic resistance mechanisms.

In the study by *Levchenko et al.,* based on a regional microbiological monitoring system, isolates from respiratory samples (sputum, bronchial aspirate) showed higher resistance to colistin and carbapenems compared to urine samples. The authors attribute this to systemic antibiotic therapy in patients with pneumonia [15].

*Gizatullina et al.* found that strains from wound exudates demonstrated aminoglycoside resistance in 80% of cases, while urinary isolates showed resistance in only 50%. This highlights the need for individualized therapy depending on the infection site [6].

Trizna and colleagues emphasize the high multidrug resistance of strains from postoperative wounds, pointing to the risk of superinfections in surgical departments [18].

The study by Kataeva et al. shows significant differences in resistance patterns in the lower respiratory tract of patients with community-acquired pneumonia, especially in COVID-19 cases. The prevalence of carbapenem-resistant K. pneumoniae strains reached 70% [11].

Finally, the work of *Yarets and Shevchenko* underscores the importance of local microbiological monitoring, demonstrating the dependence of sensitivity on hospitalization timing and sample collection conditions [21].

*Gordinskaya et al.* investigated the molecular-genetic mechanisms of resistance in Klebsiella pneumoniae isolates from hospitals in Nizhny Novgorod. They found that strains from the urogenital tract and sputum exhibited a high frequency of resistance to third-generation cephalosporins and carbapenems. This resistance was linked to the presence of plasmid genes bla_KPC and bla_OXA-48-like, highlighting the importance of molecular monitoring in clinical practice [7].

*Antonova and Zhiltsov* discussed the challenges of antibacterial therapy for hospital-acquired infections caused by carbapenemase-producing K. pneumoniae strains. The most resistant isolates were obtained from wounds and catheters. Combined therapy using colistin and tigecycline was recommended [1].

*Beloborodov et al.* emphasized the necessity of accurate sampling and identification of the infection site to select appropriate antibiotics. According to the "Sepsis Forum" guidelines, infections of the bloodstream or abdominal cavity caused by multidrug-resistant K. pneumoniae strains require parenteral administration of carbapenems and colistin [2].

*Mamchik et al.* studied K. pneumoniae strains isolated from wound exudates. These strains showed high resistance to fluoroquinolones, aminoglycosides, and even meropenem. Treatment escalation tactics were determined based on the infection site and clinical course [15].

*Yakovlev and Suvorova* focused on urinary tract infections. In urine samples from catheterized patients, a high prevalence of ESBL-producing K. pneumoniae strains was detected, underscoring the need for UTI prevention in catheterized patients [20].

*Kozlova and Barantsevich* analyzed K. pneumoniae strains isolated from wounds, blood, and respiratory tracts. The highest resistance was found in blood isolates (up to 70% resistance to cefepime and imipenem), reflecting the need for enhanced diagnostics and patient isolation [13].

A study by *Nirwati et al.* in Indonesia demonstrated a high level of antibiotic resistance and biofilm-forming ability in K. pneumoniae isolates primarily from respiratory samples (51.5%) and purulent discharges (16.2%). Approximately 54.5% of strains met the criteria for multidrug resistance, and 85.6% were capable of forming biofilms of varying intensity. Notably, biofilm-forming strains showed increased resistance to most antibiotics except meropenem, amikacin, and piperacillin-tazobactam. These findings highlight the importance of considering biofilm formation when isolating K. pneumoniae from sputum, aspirates, or purulent materials, as it is a key factor in therapy resistance and should influence antimicrobial regimen selection and treatment duration [24].

As *Navon-Venezia, Kondratyeva, and Carattoli* emphasize, Klebsiella pneumoniae is not only one of the most resistant Gram-negative pathogens but also a global "gateway" and vector for the transmission of antibiotic resistance genes. The authors highlight K. pneumoniae's role in the emergence of the "super-resistome" phenomenon, where strains simultaneously carry multiple β-lactamases (including KPC, OXA-48, and NDM-1), as well as aminoglycoside and fluoroquinolone resistance genes on mobile plasmids. Importantly, many of these genes are found in epidemiologically successful clones (ST258, ST11, ST147), which are capable of rapid intercontinental spread and are associated with hospital outbreaks. These data complement our analysis, indicating that strains isolated from blood and invasive sites are more likely to possess multiple resistance mechanisms than those from superficial samples, which is critical when choosing empirical therapy [23].

The study by *Ballén et al.* found that K. pneumoniae strains isolated from urine exhibited the highest antibiotic resistance at 64.91%, surpassing even blood (63.64%) and respiratory (51.35%) isolates. These uropathogenic strains also showed high ESBL (extended-spectrum β-lactamase) production and statistically significant resistance to fosfomycin (24.56%; p = 0.008). Moreover, nearly half (46.1%) of all biofilm-forming isolates were recovered from urine. This emphasizes that uropathogenic K. pneumoniae strains can combine antibiotic resistance, increased virulence, and biofilm formation, complicating treatment especially in patients with catheters or chronic UTIs. The authors stress the need for active monitoring not only of resistance but also of virulence factors such as the uge, rmpA, and iucA genes, which contribute to bacterial invasion and immune evasion [22].

These data confirm the key hypothesis: K. pneumoniae sensitivity strongly depends on the source of the biological material and the clinical context. Therefore, a standardized treatment approach is insufficient; a personalized antimicrobial strategy based on local data is necessary.

The highest resistance to β-lactams, carbapenems, and fluoroquinolones was observed in isolates from blood, sputum, tracheal aspirates, and wound exudates. Urine isolates also showed high resistance, particularly in cases of prolonged catheterization, often accompanied by biofilm formation and ESBL production, making them potential reservoirs for hospital transmission of resistance.

Recent studies also demonstrate that K. pneumoniae strains isolated from invasive sources more frequently carry multidrug resistance genes, including bla_KPC, bla_NDM, bla_OXA-48-like, as well as plasmids encoding resistance to amikacin and colistin. These findings underscore the necessity of molecular typing and local resistance monitoring.

**Conclusion**

Thus, the obtained data highlight the need for regular monitoring of antibiotic resistance and the rational selection of antibacterial therapy based on the sensitivity of specific strains and the type of infected biological material. This is especially relevant in the context of increasing antibiotic resistance and a limited arsenal of effective drugs.

The conducted analysis showed that Klebsiella pneumoniae remains one of the most significant and dangerous hospital pathogens due to its high frequency of antibiotic resistance, ability to form biofilms, and broad spectrum of virulence factors. The resistance of K. pneumoniae strains varies depending on the source of the biological material, which is influenced both by the physiological characteristics of the infection site and local antibiotic therapy.

Future research should focus on integrating molecular data with clinical observations to enable timely identification and containment of epidemiologically significant clones of K. pneumoniae.

***Study Limitations:*** *The single-center nature of the study may limit its generalizability, and the absence of long-term follow-up data restricts the assessment of post-discharge outcomes.*

***Author Contributions****: All authors contributed equally to the writing of this manuscript.*

***Conflict of Interest:*** *The authors declare no conflicts of interest. This material has not been submitted to other journals and is not under consideration elsewhere.*

***Funding:*** *No funding was received for this study.*

**Literature:**

1. *Антонова Е.Г., Жильцов И.В., Стахович И.И.* Антибактериальная терапия госпитальных инфекций, вызванных карбапенемазопродуцирующими штаммами K. pneumoniae // Вестник Витебского государственного медицинского университета. 2022. Т. 21. №. 3. С. 69-76.

2. *Белобородов В.Б., Голощапов О.В., Гусаров В.Г.,* и др. Методические рекомендации Российской некоммерческой общественной организации" Ассоциация анестезиологов-реаниматологов", Межрегиональной общественной организации" Альянс клинических химиотерапевтов и микробиологов", Межрегиональной ассоциации по клинической микробиологии и антимикробной химиотерапии (МАКМАХ), общественной организации" Российский Сепсис Форум"" Диагностика и антимикробная терапия инфекций, вызванных полирезистентными штаммами микроорганизмов" (обновление 2022 г.). Вестник анестезиологии и реаниматологии. 2022. Т.19. № 2. С. 84-114.

3. *Белькова Н.Л., Клименко Е.С.* и др. Биологические свойства и генетическая структура клинических изолятов комплекса видов Klebsiella pneumonia. Acta Biomedica Scientifica. 2024. Т.9. №1. С. 53-63.

4. *Божкова С.А., Гордина Е.М., Шнейдер О.В.* и др. Резистентность продуцирующих карбапенемазы штаммов Klebsiella pneumoniae, выделенных от пациентов с ортопедической инфекцией. Клиническая микробиология и антимикробная химиотерапия. 2020. Т. 22. №1. С. 47-52.

5. *Боронина Л.Г., Блинова С.М., Лавриненко Е.В.,* и др. Микобиота различных локусов у детей с онкогематологическими заболеваниями в стадии интенсивного лечения. Проблемы медицинской микологии. 2009. Т. 11. №.3. С. 10-15.

6. *Гизатуллина Л.Г., Бакиров А.Б., Масягутова Л.М.* и др. Чувствительность к антимикробным препаратам штаммов Klebsiella pneumoniae, выделенных у пациентов многопрофильного стационара. Гигиена и санитария. 2023. Т.102. №9. С. 909-913.

7. *Гординская Н.А., Борискина Е.В., Кряжев Д.В.* Фенотипические и молекулярно-генетические особенности антибиотикорезистентности клинических изолятов Klebsiella pneumoniae в стационарах Нижнего Новгорода. Клиническая микробиология и антимикробная химиотерапия. 2022. Т.24. №.3. С. 268-272.

8. *Гординская Н.А., Бруснигина Н.Ф., Алексеева А.Е.* и др. Молекулярная характеристика антибиотикорезистентных штаммов Klebsiella pneumoniae, выделенных в травматологических стационарах. Клиническая микробиология и антимикробная химиотерапия. 2017. Т.19. №.3. С. 243-246.

9. *Зулькарнаев А.Б., Ватазин А.В., Русанова Е. В.* и др. Пятилетний анализ микробного пейзажа центра трансплантологии и диализа (2011–2015). Урология. 2016. №.3. С. 14.

10. *Ивушкина Л.В., Миронов А.Ю.* Микробиологический мониторинг klebsiella pneumoniae и механизмы их резистентности к антимикробным препаратам у больных туберкулёзом г. Москвы. Клиническая лабораторная диагностика. 2024. Т. 69. №. 4. С.34-41

11. *Катаева Л.В., Вакарина А.А., Степанова Т.Ф.* и др. Микробиота нижних дыхательных путей при внебольничных пневмониях, в том числе ассоциированных с SARS-CoV-2. Журнал микробиологии, эпидемиологии и иммунобиологии. 2021. №. 5. С. 528-537.

12. *Козлова А.И., Тапальский Д.В.* Чувствительность к антибиотикам и бактериофагам клинических изолятов klebsiella pneumoniae с классическим и гипермукоидным фенотипами. Военная медицина. 2019. №. 1. С. 44-48.

13. *Козлова Н.С., Баранцевич Н.Е., Баранцевич Е.П.* Чувствительность к антибиотикам штаммов Klebsiella pneumoniae, выделенных в многопрофильном стационаре. Инфекция и иммунитет. 2018. Т 8. №1. С. 79-84.

14. *Левченко К.В., Мицура В.М.* Прогнозирование летального исхода у пациентов с пневмонией, вызванной карбапенемрезистентной Klebsiella pneumonia. Медико-биологические проблемы жизнедеятельности. 2025. №.1. С. 89-94.

15. *Мамчик Н.П., Батищева Г.А., Габбасова Н.В.* и др. Микробный пейзаж и уровень антибиотикорезистентности раневого отделяемого пациентов городского скоропомощного стационара. Медицинский альманах. 2016. №. 3 (43). С. 11-14.

16. *Миклис Н.И., Бурак И.И., и др.* Здоровье и окружающая среда. Здоровье. №.31. С. 190-197.

17. *Мухаметзянов А.М., Кайданек, Т.В., Латыпов А.А.* и др. Микробный пейзаж респираторного тракта детей с муковисцидозом: результаты мониторинга. Медицина. 2024. Т. 12. №. 4. С. 43-59.

18. *Тризна Н.М., Колядич Ж.В., Кузьмин Е.Н.,* и др. Эпидемиологическая характеристика и анализ чувствительности к антибиотикам ключевых возбудителей послеоперационных инфекционных осложнений у пациентов с опухолями полости рта и глотки. Современная стоматология. 2021. №.1(82). С. 63-67.

19. *Чернуха М.Ю., Кондратьева Е.И., Домблидес Э.А.* и др. Микробный пейзаж дыхательных путей у пациентов с первичной цилиарной дискинезией: пилотное исследование. Пульмонология. 2024. С. 1-8.

20. *Яковлев С.В., Суворова М.П.* Нозокомиальные инфекции мочевыводящих путей. Урология. 2016. Т.3. С. 45-64.

21. *Ярец Ю.И., Шевченко Н.И., Еремин В.Ф.* Методология микробиологического посева раневого отделяемого в рамках современных представлений о диагностике инфекционного процесса. Лабораторная служба. 2021. Т.10. №. 3. С. 33-42.

22. *Ballén V., Gabasa Y., Ratia C.,* et al. Antibiotic resistance and virulence profiles of Klebsiella pneumoniae strains isolated from different clinical sources. Frontiers in Cellular and Infection Microbiology. 2021. Vol. 11. p. 738223.

23. *Navon-Venezia S., Kondratyeva K., Carattoli A.* Klebsiella pneumoniae: a major worldwide source and shuttle for antibiotic resistance. FEMS microbiology reviews. 2017. Vol. 41. №. 3. p. 252-275.

24. *Nirwati H., Sinanjung K., Fahrunissa F.* et al. Biofilm formation and antibiotic resistance of Klebsiella pneumoniae isolated from clinical samples in a tertiary care hospital, Klaten, Indonesia. BMC proceedings. BioMed Central, 2019. Vol. 13. p. 1-8.

***References: [1-21]***

1. Antonova E.G., Zhil'tsov I.V., Stakhovich I.I. Antibakterial'naya terapiya gospital'nykh infektsij, vyzvannykh karbapenemazoproduktiruyushchimi shtammami K. pneumoniae [Antibacterial therapy of nosocomial infections caused by carbapenemase-producing K. pneumoniae strains]. *Vestnik Vitebskogo*

*gosudarstvennogo meditsinskogo universiteta* [Herald of Vitebsk State Medical University]. 2022. Vol. 21. №. 3. p. 69–76. [in Russian]

2. Beloborodov V.B., Goloshchapov O.V., Gusarov V.G., et al. Metodicheskie rekomendatsii "Diagnostika i antimikrobnaya terapiya infektsij, vyzvannykh polirezistentnymi shtammami mikroorganizmov" (obnovlenie 2022 g.) [Guidelines "Diagnosis and antimicrobial therapy of infections caused by multidrug-resistant microorganism strains" (updated 2022)]. *Vestnik anesteziologii i reanimatologii* [Anesthesiology and Intensive Care Bulletin]. 2022. Vol. 19. №. 2. p. 84–114. [in Russian]

3. Bel'kova N.L., Klimenko E.S., Nemchenko U.M. et al. Biologicheskie svojstva i geneticheskaya struktura klinicheskikh izolyatov kompleksa vidov Klebsiella pneumoniae [Biological properties and genetic structure of clinical isolates of the Klebsiella pneumoniae complex]. *Acta Biomedica Scientifica*. 2024. Vol.9. №.1. p.53–63. [in Russian]

4. Bozhkova S.A., Gordina E.M., Shnejder O.V., et al. Rezistentnost' karbapenemazoproduktiruyushchikh shtammov Klebsiella pneumoniae pri ortopedicheskikh infektsiyakh [Resistance of carbapenemase-producing Klebsiella pneumoniae strains in orthopedic infections]. *Klinicheskaya mikrobiologiya i antimikrobnaya khimioterapiya* [Clinical Microbiology and Antimicrobial Chemotherapy]. 2020. Vol.22. №.1. p.47–52. [in Russian]

5. Boronina L.G., Blinova S.M., Lavrinenko E.V. et al. Mikobiota razlichnykh lokusov u detej s onkogematologicheskimi zabolevaniyami [Mycobiota of various loci in children with oncohematological diseases]. *Problemy meditsinskoj mikologii* [Problems of Medical Mycology].2009. Vol. 11. №.3. p. 10–15. [in Russian]

6. Gizatullina L.G., Bakirov A.B., Masyagutova L. et al. Chuvstvitel'nost' k antimikrobnym preparatam shtammov Klebsiella pneumoniae v statsionare [Antimicrobial susceptibility of Klebsiella pneumoniae strains in a hospital setting]. *Gigiena i sanitariya* [Hygiene and Sanitation]. 2023. Vol. 102. №. 9. p. 909–913. [in Russian]

7. Gordinskaya N.A., Boriskina E.V., Kryazhev D.V. Fenotipicheskie i molekulyarno-geneticheskie osobennosti antibiotikorezistentnosti Klebsiella pneumoniae v Nizhnem Novgorode [Phenotypic and molecular characteristics of antibiotic resistance of Klebsiella pneumoniae in Nizhny Novgorod]. *Klinicheskaya mikrobiologiya i antimikrobnaya khimioterapiya* [Clinical Microbiology and Antimicrobial Chemotherapy]. 2022. Vol.24. №.3. p.268–272. [in Russian]

8. Gordinskaya N.A., Brusnigina N.F., Alekseeva A.E., et al. Molekulyarnaya kharakteristika rezistentnykh shtammov Klebsiella pneumoniae v travmatologii [Molecular characteristics of resistant Klebsiella pneumoniae strains in trauma units]. *Klinicheskaya mikrobiologiya i antimikrobnaya khimioterapiya* [Clinical Microbiology and Antimicrobial Chemotherapy]. 2017. Vol.19. №.3. p.243–246. [in Russian]

9. Zulkarnayev A.B., Vatazin A.V., Rusanova E.V., et al. Pyatiletnij analiz mikrobnogo pejzazha tsentra transplantologii i dializa (2011–2015) [Five-year analysis of the microbial landscape in a transplant and dialysis center]. *Urologiya* [Urology]. 2016. №. 3. p. 14. [in Russian]

10. Ivushkina L.V., Mironov A.Yu. Mikrobiologicheskij monitoring Klebsiella pneumoniae pri tuberkuleze v Moskve [Microbiological monitoring of Klebsiella pneumoniae in tuberculosis patients in Moscow]. *Klinicheskaya laboratornaya diagnostika* [Clinical Laboratory Diagnostics]. 2024. Vol. 69. №. 4. pp. 34-41 [in Russian]

11. Kataeva L.V., Vakarina A.A., Stepanova T.F., et al. Mikrobiota nizhnikh dykhatel'nykh putej pri vnebol'nichnykh pnevmoniyakh, vklyuchaya SARS-CoV-2 [Lower respiratory microbiota in community-acquired pneumonia including SARS-CoV-2]. *Zhurnal mikrobiologii, epidemiologii i immunobiologii* [Journal of Microbiology, Epidemiology and Immunobiology]. 2021. №5. p. 528–537. [in Russian]

12. Kozlova A.I., Tapal'skij D.V. Chuvstvitel'nost' Klebsiella pneumoniae s raznymi fenotipami k antibiotikam i bakteriofagam [Susceptibility of Klebsiella pneumoniae with different phenotypes to antibiotics and bacteriophages]. *Voennaya meditsina* [Military Medicine]. 2019. №1. p. 44–48. [in Russian]

13. Kozlova N.S., Barantsevich N.E., Barantsevich E.P. Chuvstvitel'nost' Klebsiella pneumoniae v mnogoprofil'nom statsionare [Antibiotic susceptibility of Klebsiella pneumoniae in a multidisciplinary hospital]. *Infektsiya i immunitet* [Infection and Immunity]. 2018. Vol.8. №1. p.79–84. [in Russian]

14. Levchenko K.V., Mitsura V.M. Prognozirovanie letal'nogo iskhoda pri pnevmonii, vyzvannoj karbapenemrezistentnoj Klebsiella pneumoniae [Predicting fatal outcome in pneumonia caused by carbapenem-resistant Klebsiella pneumoniae]. *Mediko-biologicheskie problemy zhiznedeyatel'nosti* [Medical and Biological Problems of Life Activity]. 2025. №1. p. 89–94. [in Russian]

15. Mamchik N.P., Batischeva G.A., Gabbasova N.V. et al. Mikrobnyj pejzazh i antibiotikorezistentnost' ran u patsientov v gospitale [Microbial landscape and antibiotic resistance of wounds in an emergency hospital]. *Meditsinskii al'manakh* [Medical Almanac]. 2016. №. 3 (43). p. 11–14. [in Russian]

16. Miklis N.I., Burak I.I., Izopol'skaya Zh.G. Zdorov'e i okruzhayushchaya sreda [Health and the Environment]. Zdorov'e [Health]. №. 31. p. 190–197. [in Russian]

17. Mukhametzyanov A.M., Kaidanek T.V., Latypov A.A., et al. Mikrobnyi pejzazh dykhatel'nykh putei pri mukovistsidoze u detei [Microbial landscape of the respiratory tract in children with cystic fibrosis]. *Meditsina* [Medicine]. 2024. Vol. 12. №. 4. p. 43–59. [in Russian]

18. Trizna N.M., Kolyadich Zh.V., Kuz'min E.N. et al. Epidemiologicheskaya kharakteristika i analiz chuvstvitel'nosti k antibiotikam klyuchevykh vozbuditelej posleoperatsionnykh infektsionnykh oslozhnenij u patsientov s opukholyami polosti rta i glotki [Epidemiological characteristics and antibiotic susceptibility analysis of key pathogens of postoperative infectious complications in patients with oral and pharyngeal tumors]. *Sovremennaya stomatologiya* [Modern Dentistry]. 2021. №. 1 (82). p. 63–67. [in Russian]

19. Chernukha M.Yu., Kondrat'eva E.I., Domblides E.A., et al. Mikrobnyj pejzazh dykhatel'nykh putei u patsientov s pervichnoi tsiliarnoy diskinziei: pilotnoe issledovanie [Microbial landscape of the respiratory tract in patients with primary ciliary dyskinesia: a pilot study]. Pul'monologiya [Pulmonology]. 2024. p.1–8. [in Russian]

20. Yakovlev S.V., Suvorova M.P. Nozokomial'nye infektsii mochevyvodyashchikh putej [Nosocomial urinary tract infections]. *Urologiya* [Urology] 2016. Vol. 3. p. 45–64. [in Russian]

21. Yarets Yu.I., Shevchenko N.I., Eremin V.F. Metodologiya mikrobiologicheskogo poseva ranevogo otdelyaemogo v ramkakh sovremennykh predstavlenij o diagnostike infektsionnogo protsessa [Methodology of microbiological wound discharge culture within the framework of modern concepts of infectious process diagnostics]. *Laboratornaya sluzhba* [Laboratory Service]. 2021. Vol. 10. №.3. p. 33–42. [in Russian].

**Information about the authors:**

**Mukasheva Gulbarshyn Darynkyzy** - Senior Teacher of the Department of Epidemiology and Biostatistics, NCJSC "Semey Medical University", Semey, Kazakhstan; E-mail: gulbarshyn_1_12@mail.ru; phone +7 775 220 07 45, https://orcid.org/0000- 0003-3490-5628;

**Maukayeva Saule Boranbayevna** - Candidate of Medical Sciences, Associate Professor of the Department of Infectious Diseases, Dermatovenerology and Immunology, NCJSC "Semey Medical University", Semey, Kazakhstan; phone: 8 705 529 66 75, e-mail: solly66@mail.ru, https://orcid.org/0000-0002-2679-6399;

**Kudaibergenova Nazym Konyrovna** - Candidate of Medical Sciences, Associate Professor of the Department of Infectious Diseases, Dermatovenerology and Immunology, NCJSC "Semey Medical University", Semey, Kazakhstan, phone: 8 705 188 0836, e-mail: nazym.kudaibergenova@smu.edu.kz, https://orcid.org/0000-0002-2679-6399;

**Shabdarbayeva Dariya Muratovna** – Doctor of Medical Sciences, Professor, Vice Rector for Science and Strategic Development", Semey Medical University", Semey, Kazakhstan, phone 8 707 365 82 71, e-mail: dariya_kz@bk.ru, https://orcid.org/0000-0001-9463-1935;

**Smailova Zhanargyl Kaiyrgaliyevna** - Candidate of Medical Sciences, Associate Professor, Vice Rector for Academic and Educational Work, NCJSC «Semey Medical University», phone 8 707 365 82 71, e-mail: zhanargul.smailova@smu.edu.kz; https://orcid.org/0000-0002-4513-4614;

**Tokayeva Alma Zeinollakizi -** Candidate of Medical Sciences, Associate Professor of the Department of Infectious Diseases, Dermatovenerology and Immunology, NCJSC "Semey Medical University", phone: 8 701 355 9338, e-mail: alma.tokayeva@smu.edu.kz, https://orcid.org/0000-0003-1238-9263, Semey, Kazakhstan;

**Smail Yerbol Muslimuly** - Candidate of Medical Sciences, Associate Professor of the Department of Infectious Diseases, Dermatovenerology and Immunology, NCJSC "Semey Medical University", phone: 8 705 528 8409, e-mail: erbol.smail@smu.edu.kz, https://orcid.org/0000-0003-3881-3747, Semey, Kazakhstan;

**Nuralinova Gulnar Inzhikanovna -** Candidate of Medical Sciences, Associate Professor of the Department of Infectious Diseases, Dermatovenerology and Immunology, NCJSC «Semey Medical University», phone: 8 705 409 41 09, e-mail: gulnarnuralinova5@gmail.com, https://orcid.org/0000-0002-0478-5154, Semey, Kazakhstan;

**Issabekova Zhanar Bakytzhanovna** - Assistant of the Department of Infectious Diseases, Dermatovenerology and Immunology, NCJSC "Semey Medical University", phone: 8 775 176 08 09, e-mail: zhanara_ib87@mail.ru, https://orcid.org/0000-0002-2744-0327, Semey, Kazakhstan;

**Karimova Saya Sayankyzy**- Assistant, department of infectious diseases, dermatovenerology and immunology, NCJSC «Semey Medical University», phone: 8 701 106 96 13, Kazakhstan. E-mail: saya.karimova.94@mail.ru, ORCID 0000-0002-1167-5375, Semey, Kazakhstan;

**Kozubayeva Dinara Begimhanovna -** Assistant, department of infectious diseases, dermatovenerology and immunology, NCJSC «Semey Medical University», phone: 8 775 342 16 44, Kazakhstan. E-mail: dinara_begimhanovna@mail.ru, ORCID 0000-0003-4937-708X, Semey, Kazakhstan.

**Goremykina Maiya Valentinovna -** Candidate of Medical Sciences, Associate Professor, Department of Internal Medicine and Rheumatology, NCJSC «Semey Medical University», 103 Abay Street, Semey, 071400, Kazakhstan; Email: maya.goremykina@smu.edu.kz; phone number: +7 (777) 390 8234; https://orcid.org/0000-0002-5433-7771

**Urazalina Nailya Muratkhanovna** - Candidate of Medical Sciences, Associate Professor of the Department of physiological disciplines named after honored scientist of the republic of Kazakhstan, professor T.A. Nazarova, NJSC "Semey Medical University", Semey, Kazakhstan; phone: 8 777 907 55 89, e-mail: hakim_15@mail.ru, https://orcid.org/0000-0003-0200-1763,

*** Corresponding author:**

**Karimova Saya Sayankyzy** - Assistant, department of infectious diseases, dermatovenerology and immunology, NCJSC «Semey Medical University», Semey, Kazakhstan; ORCID 0000-0002-1167-5375,

**Postal code:** Republic of Kazakhstan, 071400, Semey city, Abay Street 103.

**E-mail**: saya.karimova.94@mail.ru

**Phone:** 8 701 106 96 13

Received: 27 January 2025 / Accepted: 02 June 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2025.27.3.012***

***UDC 618.2-039.11:614.4***

This work is licensed under a Creative Commons Attribution 4.0 International License

# INFECTION CONTROL IN THE MATERNITY CARE SYSTEM: ASSESSMENT OF RESOURCE AVAILABILITY, HUMAN CAPACITY AND PROFESSIONAL DEVELOPMENT

**Gulnoza U. Aldabekova[1], https://orcid.org/0009-0009-1561-1094**
**Aiman A. Musina[1], https://orcid.org/0000-0001-8943-032X**
**Gulnara M. Kamalbekova[1], https://orcid.org/0000-0001-9883-6321**
**Zaituna G. Khamidullina[1], https://orcid.org/0000-0001-9100-694X**
**Zhuldyz S. Danbayeva[2],**
**Svetlana B. Abdrashidova[1],**
**Elmira M. Zhumabayeva[1],**
**Gulsim A. Kokisheva[1],**
**Gulyash A. Tanysheva[1], https://orcid.org/0000-0001-9531-5950**

**[1] NJSC «Astana Medical University», Astana, Republic of Kazakhstan;**
**[2] «City multifunctional hospital №3», Astana, Republic of Kazakhstan.**

**Abstract**

**Background and Objectives.** Infection safety in obstetric institutions is a critical component of the medical care quality and safety assurance system. **This study aims** to provide a comprehensive assessment of factors that may influence infection safety in obstetric settings, including the level of technical and pharmaceutical equipment, staff satisfaction with working conditions, interprofessional collaboration, and access to professional development opportunities.

**Materials and Methods.** A cross-sectional study was conducted from January 20 to February 20, 2025, involving 255 healthcare professionals working in obstetric institutions in Astana, Semey, and Kokshetau. Data was collected using Google Forms online platform. The sample included physicians and nursing personnel, along with professionals in medical rehabilitation, clinical diagnostics, administration, pharmacy, and related specialties.

**Results.** The study involved 255 health workers from obstetric facilities, including doctors 14.9% (N=38), nurses 73.3% (N=187), as well as medical rehabilitation specialists, clinical diagnostic workers, administrative and management staff, pharmacists and other specialists 11.8% (N=30).Among nursing staff, 78.7% (N=118) positively assessed the facility's equipment, while among physicians this indicator was only 11.3% (N=17)($p = 0.001$).A similar trend was observed in satisfaction with drug availability: 80.4% (N=123) of nurses versus 9.8% (N=15) of doctors ($p = 0.009$). Satisfaction with departmental staffing was reported by 74.2% (N=112) of nursing staff and only 13.2% (N=20) of doctors ($p = 0.07$). Laboratory diagnostics were considered accessible by 78.3% of nurses, compared to 10.2% of doctors ($p = 0.001$). Regarding specialist consultations (e.g., cardiologist, endocrinologist), 76.3% (N=129) of nurses were satisfied versus 14.2% (N=24) of doctors ($p < 0.0001$). While 11.6% (N=5) of doctors reported occasional misunderstandings with nursing staff, no statistically significant differences were observed in interprofessional communication ($p = 0.66$). Access to training and continuing education was satisfactory for 79.9% (N=123) of nursing staff but only 8.4% (N=13) of doctors ($p = 0.001$).

**Conclusion.** Significant differences were found between physicians and nursing staff in their perceptions of working conditions and infection safety factors. The most critically assessed areas included technical equipment, access to diagnostics, and opportunities for professional growth. The findings underscore the need for management decisions aimed at improving resources and expanding professional development programmes for health workers in obstetric facilities.

***Key words:*** satisfaction, risk, infection safety, maternity care organization.

***For citation:***

Aldabekova G.U., Musina A.A., Kamalbekova G.M., Khamidullina Z.G, Danbayeva Zh.S. Abdrashidova S.B., Zhumabayeva E.M., Kokisheva G.A., Tanysheva G.A. Infection control in the maternity care system: assessment of resource availability, human capacity and professional development // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 108-116. *doi 10.34689/SH.2025.27.3.012*

**Резюме**

# ИНФЕКЦИОННАЯ БЕЗОПАСНОСТЬ В СИСТЕМЕ РОДОВСПОМОЖЕНИЯ: ОЦЕНКА ОБЕСПЕЧЕННОСТИ РЕСУРСАМИ, КАДРОВОГО ПОТЕНЦИАЛА И ПРОФЕССИОНАЛЬНОГО РАЗВИТИЯ

**Гульноза У. Алдабекова[1],** https://orcid.org/0009-0009-1561-1094
**Айман А. Мусина[1],** https://orcid.org/0000-0002-0864-1238
**Гульнара М. Камалбекова[1],** https://orcid.org/0000-0001-9883-6321
**Зайтуна Г. Хамидуллина[1],** https://orcid.org/0000-0001-9100-694X
**Жулдыз С. Данбаева[2],**
**Светлана Б. Абдрашидова[1],**
**Эльмира М. Жумабаева[1],**
**Гульсум А. Кокишева[1],**
**Гульяш А. Танышева[1],** https://orcid.org/0000-0001-9531-5950

[1] НАО «Медицинский университет Астана», г. Астана, Республика Казахстан;
[2] ГКП на ПХВ «Многопрофильная городская больница №3», г. Астана, Республика Казахстан.

**Актуальность.** Инфекционная безопасность в организациях родовспоможения является важнейшей составляющей системы обеспечения качества и безопасности медицинской помощи. **Целью настоящего исследования** является комплексная оценка факторов, потенциально влияющих на уровень инфекционной безопасности в организациях родовспоможения, включая степень технической и медикаментозной оснащённости, удовлетворённость персонала условиями труда, уровень межпрофессионального взаимодействия и доступность возможностей профессионального развития.

**Материалы и методы.** Проведено поперечное исследование среди 255 медицинских работников организации включая врачей и медсестер организаций родовспоможения г. Астана, г. Семей, г. Кокшетау посредством программного сервиса Google Forms. Исследование проводилось в период с 20 января по 20 февраля 2025 года.

**Результаты.** В исследовании приняли участие 255 медицинских работников из организаций родовспоможения, включая врачей 14,9% (N=38), средний медицинский персонал 73,3% (N=187), а также специалистов по медицинской реабилитации, клинико-диагностических работников, административно-управленческий персонал, фармацевтов и прочих специалистов 11,8% (N=30). Средний медицинский персонал положительно оценили оснащённость учреждения 78,7% (N=118), в то время как среди врачей этот показатель составил лишь 11,3% (N=17) (p = 0,001). Аналогичная тенденция прослеживалась в оценке лекарственного обеспечения: удовлетворены наличием необходимых препаратов 80,4% (N=123) среднего персонала и только 9,8% (N=15) врачей (p = 0,009). Удовлетворённость укомплектованностью отделений профильными специалистами (акушер-гинекологами, акушерками, медицинскими сестрами) выразили 74,2% (N=112) среднего персонала и лишь 13,2% (N=20) врачей (p = 0,07). Доступ к лабораторной диагностике был оценён положительно 78,3% среднего медицинского персонала и только 10,2% врачей (p = 0,001). Удовлетворённость доступностью консультаций узких специалистов (кардиолог, эндокринолог и других) отметили 76,3% (N=129) среднего персонала и лишь 14,2% (N=24) врачей (p<0,0001). Наличие эпизодов недопонимания между врачами и средним медицинским персоналом указали 11,6% (N=5) врачей, однако статистически значимых различий между профессиональными группами не выявлено (p = 0,66). Доступ к обучающим мероприятиям и тренингам был удовлетворительным для 79,9% (N=123) среднего медицинского персонала и только 8,4% (N=13) врачей (p = 0,001).

**Выводы**. Установлены значимые различия в оценке условий труда и факторов инфекционной безопасности между врачами и средним медицинским персоналом. Наиболее критично респонденты оценивали оснащённость, доступ к диагностике и возможности профессионального роста. Полученные данные подчеркивают необходимость управленческих решений, направленных на улучшение ресурсного обеспечения и расширение программ повышения квалификации для медицинских работников родовспомогательных учреждений.

***Ключевые слова:*** *удовлетворенность, риск, инфекционная безопасность, организация родовспоможения.*

***Для цитирования:***

*Алдабекова Г.У., Мусина А.А., Камалбекова Г.М., Хамидуллина З.Г., Данбаева Ж.С., Абдрашидова С.Б., Жумабаева Э.М., Кокишева Г.А., Танышева Г.А.* Инфекционная безопасность в системе родовспоможения: оценка обеспеченности ресурсами, кадрового потенциала и профессионального развития // Наука и Здравоохранение. 2025. Т.27 (3), С. 108-116. doi: 10.34689/SH.2025.27.3.012

**Түйіндеме**

# БОСАНДЫРУ ҰЙЫМДАРЫНДАҒЫ ИНФЕКЦИЯЛЫҚ ҚАУІПСІЗДІК ЖҮЙЕСІ: РЕСУРСТЫҚ ҚАМТАМАСЫЗ ЕТІЛУІ, КАДРЛЫҚ ӘЛЕУЕТІ ЖӘНЕ КӘСІБИ ДАМУ ДЕҢГЕЙІН БАҒАЛАУ

**Гульноза У. Алдабекова[1],** https://orcid.org/0009-0009-1561-1094
**Айман А. Мусина[1],** https://orcid.org/0000-0002-0864-1238
**Гульнара М. Камалбекова[1],** https://orcid.org/0000-0001-9883-6321
**Зайтуна Г. Хамидуллина[1],** https://orcid.org/0000-0001-9100-694X
**Жулдыз С. Данбаева[2],**
**Светлана Б. Абдрашидова[1],**
**Эльмира М. Жумабаева[1],**
**Гульсум А. Кокишева[1],**
**Гульяш А. Танышева[1],** https://orcid.org/0000-0001-9531-5950

[1] **«Астана Медицина Университеті» ҚЕАҚ, Астана қ., Қазақстан Республикасы;**
[2]**«№3 Көпбейінді қалалық ауруханасы» ШЖҚ МКК, Астана қ., Қазақстан Республикасы.**

**Кіріспе.** Босандыру ұйымдарындағы инфекциялық қауіпсіздік – медициналық көмектің сапасы мен қауіпсіздігін қамтамасыз ету жүйесінің маңызды құрамдас бөлігі болып табылады. **Осы зерттеудің мақсаты** – босандыру ұйымдарындағы инфекциялық қауіпсіздік деңгейіне ықпал етуі мүмкін факторларды кешенді түрде бағалау. Оған техникалық және медикаментоздық жабдықталу деңгейі, персоналдың еңбек жағдайларына қанағаттануы, кәсіби топтар арасындағы өзара әрекеттесу деңгейі және кәсіби дамуға қолжетімділік сияқты аспектілер кіреді.

**Материалдар мен әдістері:** 2025 жылғы 20 қаңтар мен 20 ақпан аралығында Астана, Семей және Көкшетау қалаларындағы босандыру ұйымдарының дәрігерлері мен медбикелерін қоса алғанда, 255 медицина қызметкерінің қатысуымен көлденең зерттеу жүргізілді. Зерттеу Google Forms бағдарламалық сервисі арқылы жүзеге асырылды.

**Нәтижелер:** Зерттеуге босандыру ұйымдарының 255 медицина қызметкері қатысты, олардың ішінде дәрігерлер – 14,9% (N=38), орта медициналық персонал – 73,3% (N=187), сондай-ақ медициналық оңалту мамандары, клинико-диагностикалық қызметкерлер, әкімшілік-басқару персоналы, фармацевтер және басқа да мамандар – 11,8% (N=30) құрады.Орта медициналық персоналдың 78,7%-ы (N=118) мекеменің жабдықталуын оң бағаласа, дәрігерлер арасында бұл көрсеткіш тек 11,3% (N=17) болды (p = 0,001).Дәрілік қамтамасыз етуге баға беру де ұқсас үрдісті көрсетті: қажетті дәрілік заттардың жеткіліктілігіне орта медициналық персоналдың 80,4%-ы (N=123) қанағаттанғанын білдірсе, дәрігерлер арасында бұл көрсеткіш небәрі 9,8% (N=15) болды (p = 0,009).Профильді мамандармен (акушер-гинекологтар, акушерлер, мейірбикелер) бөлімшелердің жасақталуына 74,2% (N=112) орта медициналық персонал және 13,2% (N=20) дәрігер қанағаттанғанын көрсетті (p = 0,07).Зертханалық диагностикаға қолжетімділікке орта медициналық қызметкерлердің 78,3%-ы оң баға берсе, дәрігерлер арасында бұл көрсеткіш 10,2%-ды құрады (p = 0,001). Тар бейінді мамандардың (кардиолог, эндокринолог және т.б.) консультацияларына қолжетімділікке 76,3% (N=129) орта медициналық персонал және тек 14,2% (N=24) дәрігер қанағаттанғанын көрсетті (p<0,0001). Дәрігерлер мен орта медициналық қызметкерлер арасындағы өзара түсініспеушілік жағдайларының болуын дәрігерлердің 11,6%-ы (N=5) атап өтті, алайда кәсіби топтар арасында статистикалық тұрғыдан елеулі айырмашылық анықталған жоқ (p = 0,66). Оқу іс-шаралары мен тренингтерге қолжетімділік орта медициналық қызметкерлердің 79,9%-ы (N=123) үшін жеткілікті деп танылса, дәрігерлер арасында бұл көрсеткіш небәрі 8,4% (N=13) болды (p = 0,001).

**Қорытындылар:** Дәрігерлер мен орта медициналық персонал арасында еңбек жағдайлары мен инфекциялық қауіпсіздік факторларын бағалауда елеулі айырмашылықтар анықталды. Респонденттер ең көп сын айтқан аспектілер – мекемелердің жабдықталуы, диагностикалық қызметтерге қолжетімділік және кәсіби өсу мүмкіндіктері болды. Алынған деректер босандыру ұйымдарындағы медицина қызметкерлері үшін ресурстық қамтамасыз етуді жақсарту және біліктілікті арттыру бағдарламаларын кеңейтуге бағытталған басқарушылық шешімдердің қажеттілігін айқындайды.

***Түйін сөздер:*** *қанағаттанушылық, қауіп-қатер, инфекциялық қауіпсіздік, босандыру ұйымы.*

***Дәйексөз үшін:***

*Алдабекова Г.У., Мусина А.А., Камалбекова Г.М., Хамидуллина З.Г., Данбаева Ж.С., Абдрашидова С.Б., Жумабаева Э.М., Кокишева Г.А., Танышева Г.А.* Босандыру ұйымдарындағы инфекциялық қауіпсіздік жүйесі: ресурстық қамтамасыз етілуі, кадрлық әлеуеті және кәсіби даму деңгейін бағалау // Ғылым және Денсаулық. 2025. Т.27 (3), Б.108-116. doi: 10.34689/SH.2025.27.3.012

**Introduction**

Infection control in maternity care facilities is critical to healthcare quality and patient safety systems. The risk of healthcare-associated infections (HAIs) in obstetric and gynecological practice arises from both the heightened vulnerability of pregnant women, newborns, and parturient women, and the inherently invasive nature of numerous diagnostic and therapeutic procedures, including surgical deliveries, catheterization, and injectable therapies. According to estimates by the World Health Organization (WHO), up to 15% of women receiving care in maternity institutions experience some form of infectious complications, the majority of which could be prevented with adequate organizational resources and appropriate staff qualifications [1,2].

Among the most significant factors influencing the risk of HAIs in perinatal settings are the technical and pharmaceutical infrastructure levels, the availability and sufficiency of qualified personnel, adherence to sanitary and epidemiological protocols, and access to educational programs and infection control training.[3-5] Shortages in essential equipment (e.g., ultrasound machines, suction devices, sterile medical instruments), limited availability of antibiotics, and insufficient resources for emergency obstetric care considerably compromise the facility's capacity to respond promptly and effectively to infectious threats [6].

In addition, one of the most critical organizational factors influencing infection control remains the human resource capacity. A shortage of obstetrician-gynecologists, trained midwives, and nursing staff contributes to personnel overload, diminished adherence to infection control protocols, and an increased likelihood of medical errors [7]. Furthermore, low job satisfaction, limited opportunities for professional development, and insufficient interdisciplinary collaboration between physicians and mid-level healthcare personnel may also exacerbate risks associated with breaches in hygiene standards and patient safety regulations [8].

Despite the recognized importance of this issue, there is a lack of empirically grounded evidence in the national scientific literature regarding the relationship between infrastructure, human and educational resources, and infection control risks in maternity care institutions. This highlights the need for a comprehensive assessment of organizational and resource-related factors as perceived by healthcare personnel—factors that directly impact the implementation of infection control standards.

The objective of the present study is to conduct a comprehensive evaluation of factors potentially influencing the level of infection safety in maternity care facilities, including the availability and sufficiency of technical equipment and pharmaceutical supplies, staff satisfaction with working conditions, the degree of interprofessional collaboration, and access to professional development opportunities.

**Materials and Methods**

The study involved 255 healthcare professionals, including physicians and nurses, working in maternity care institutions in Astana, Semey, and Kokshetau. An observational, descriptive, cross-sectional study was conducted using an anonymous survey administered through Google Forms platform.

The research was carried out from January 20 to February 20, 2025. Participation in the survey was voluntary. Before data collection, informed consent was obtained from all participants. Respondents were assured that their involvement would not entail any negative consequences, that all responses would remain anonymous and be used exclusively for research purposes, and that confidentiality would be strictly maintained.

Incomplete responses were excluded from the analysis. The questionnaire was available in both Kazakh and Russian languages and was culturally and linguistically adapted by international standards. It was validated on a separate group of 25 healthcare professionals who did not take part in the main survey.

During validation, the instrument's reliability, validity, and sensitivity were assessed. Internal consistency was evaluated using Cronbach's alpha coefficient. The questionnaire demonstrated high internal reliability (Cronbach's $\alpha > 0.7$), indicating an acceptable level of consistency across the instrument's scales.

The questionnaire consisted of 23 items divided into two sections. The first section addressed demographic characteristics, including age, gender, work experience, level of education, and participation in relevant training programs. The second section focused on various aspects of medical care delivery.

Participants' professional positions were categorized into seven groups: physicians, nursing and mid-level medical staff, rehabilitation specialists, clinical and diagnostic personnel, administrative and managerial staff, pharmaceutical personnel, and specialists from other fields.

The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and was approved by the Ethics Committee of Astana Medical University (Protocol No. 10, dated November 26, 2024). Written informed consent was obtained from all participants prior to their inclusion in the study.

**Statistical Analysis**

Means and standard deviations (SD) were used to describe quantitative variables, while absolute (N) and relative (%) frequencies were used for qualitative variables. Pearson's chi-square ($\chi^2$) test or Fisher's exact test, where applicable, was employed for proportion comparisons. Significance levels were two-tailed, with statistical significance set at $p < 0.05$. Statistical analyses were performed using SPSS version 24.0.

**Results**

A total of 255 healthcare professionals from maternity care institutions participated in the study. Among them, 14.9% (N=38) were physicians, 73.3% (N=187) were nursing and mid-level medical staff, and 11.8% (N=30) represented other professional groups, including medical rehabilitation specialists, clinical and diagnostic personnel, administrative and managerial staff, pharmaceutical staff, and specialists from other fields. A cross-tabulation table presented data on participants' age, gender, workplace, and professional categories (Table 1).

Women accounted for 93.7% (N=239) of the total sample. The majority of nursing and mid-level medical staff belonged to the 45–60 age group (81.7%), suggesting an aging workforce and a potential need for future

replacement. In contrast, the physician group was predominantly represented by individuals aged 25–44 years, indicating a younger age structure among doctors compared to nursing staff.

The educational background of respondents varied: among nursing and mid-level personnel, secondary specialized education predominated (85.1%), whereas the majority of physicians held higher or postgraduate degrees (34.5%). These differences in educational attainment between professional categories were statistically significant ($p < 0.0001$), highlighting functional differentiation based on qualification levels.

*Table 1.*

**Association between socio-demographic characteristics and professional categories of respondents.**

| Variables | Professional Category | | | | | | | p |
|---|---|---|---|---|---|---|---|---|
| | Physicians abs. (%) | Nursing and mid-level medical staff abs. (%) | Rehabilitation specialists abs. (%) | Clinical and diagnostic personnel abs. (%) | Administrative and managerial staff abs. (%) | Pharmaceutical personnel abs. (%) | Specialists from other fields abs. (%) | |
| Age | | | | | | | | |
| 18-24 years | 3 (13%) | 14 (60,9%) | 3 (13%) | 1 (4,3%) | 0 | 1 (4,3%) | 1 (4,3%) | 0,11 |
| 25-34 years | 10 (19,2%) | 36 (69,2%) | 2 (3,8%) | 2 (3,8%) | 1 (1,9%) | 1(1,9%) | 0 | |
| 34-44 years | 15 (21,1%) | 48 (67,6%) | 1 (1,4%) | 1 (1,4%) | 5 (7%) | 0 | 1 (1,4%) | |
| 45-60 years | 10 (9,2%) | 89 (81,7%) | 2 (1,8%) | 2 (1,8%) | 3 (2,8%) | 2 (1,8%) | 1 (0,9%) | |
| Gender | | | | | | | | |
| Female | 31(13%) | 182 (76,2%) | 7 (2,9%) | 6 (2,5%) | 6 (2,5%) | 4 (1,7%) | 3 (1,3%) | <0,0001 |
| Male | 7 (43,8%) | 5 (31,3%) | 1 (6,3%) | 0 | 3 (18,8%) | 0 | 0 | |
| Education | | | | | | | | |
| Secondary specialized | 7 (4,2%) | 143 (85,1%) | 7 (4,2%) | 6 (3,6%) | 1 (0,6%) | 3 (1,8%) | 1 (0,6%) | <0,0001 |
| Higher education | 29 (34,5%) | 44 (52,4%) | 1 (1,2%) | 0 | 8 (9,5%) | 1 (1,2%) | 1 (1,2%) | |
| Master's degree | 1 (50%) | 0 | 0 | 0 | 0 | 0 | 1 (50%) | |
| Doctoral degree | 1 (100%) | 0 | 0 | 0 | 0 | 0 | 0 | |

The data analysis revealed statistically significant differences in job satisfaction across professional categories. These differences related to several key aspects, including availability of equipment and pharmaceuticals, staffing levels, access to diagnostic and consultative services, and opportunities for professional development (Table 2).

Assessment of satisfaction with the availability of basic medical equipment (such as ultrasound machines, cardiotocographs, etc.) revealed statistically significant differences between professional groups. Among nursing and mid-level staff, 78.7% (N=118) rated the equipment provision positively, whereas only 11.3% (N=17) of physicians shared this view ($p = 0.001$). A similar trend was observed in the evaluation of pharmaceutical supplies: 80.4% (N=123) of mid-level staff expressed satisfaction with the availability of necessary medications, compared to just 9.8% (N=15) of physicians ($p = 0.009$). These findings suggest that physicians adopt a more critical stance toward the adequacy of clinical resources.

Regarding satisfaction with staffing levels of key specialists (including obstetrician-gynecologists, midwives, and nurses), 74.2% (N=112) of nursing and mid-level personnel reported satisfaction, while only 13.2% (N=20) of physicians did so. Although this difference did not reach statistical significance ($p = 0.07$), a clear trend was noted indicating that physicians more frequently perceive staffing shortages as a major issue.

Access to laboratory diagnostics was rated positively by 78.3% of mid-level personnel, compared to only 10.2% of physicians ($p = 0.001$). Similar discrepancies were observed in assessments of instrumental diagnostics (such as ultrasound and radiographic imaging), with 76.9% of nursing and mid-level staff expressing satisfaction, versus just 12.6% of physicians ($p < 0.0001$). These results demonstrate a pronounced divergence in the perception of diagnostic service availability across professional categories.

Satisfaction with access to consultations from specialized medical professionals (e.g., cardiologists, endocrinologists) was reported by 76.3% (N=129) of nursing and mid-level staff, compared to only 14.2% (N=24) of physicians ($p < 0.0001$). Similarly, statistically significant differences were observed regarding the availability of medical devices and supplies: 76.4% (N=120) of mid-level personnel expressed satisfaction, whereas only 13.4% (N=21) of physicians did so ($p = 0.009$). These findings suggest that physicians more frequently report shortages in both human and technical resources required for the provision of comprehensive obstetric care.

Episodes of miscommunication between physicians and mid-level staff were noted by 11.6% (N=5) of physicians; however, no statistically significant differences between professional groups were found ($p = 0.66$). Difficulties encountered during patient consultations were more frequently reported by physicians (18.4%, N=7); nevertheless, the differences between professional categories did not reach statistical significance ($p = 0.8$).

*Table 2*

**Assessment of satisfaction with infrastructure, staffing, diagnostic services, and continuing education by professional category.**

| Variables | Professional Category | | | | | | | p |
|---|---|---|---|---|---|---|---|---|
| | Physicians abs. (%) | Nursing and mid-level medical staff abs. (%) | Rehabilitation specialists abs. (%) | Clinical and diagnostic personnel abs. (%) | Administrative and managerial staff abs. (%) | Pharmaceutical personnel abs. (%) | Specialists from other fields abs. (%) | |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 6 |
| **How would you assess the medical equipment available in your facility? (e.g., ultrasound machine, fetal CTG monitor, etc.)** | | | | | | | | |
| Satisfied | 17 (11,3%) | 118 (78,7%) | 1 (0,7%) | 6 (4%) | 3 (2%) | 3 (2%) | 2 (1,3%) | 0,001 |
| Somewhat satisfied | 16 (28,1%) | 35 (61,4%) | 1 (1,8%) | 0 | 5 (8,8%) | 0 | 0 | |
| Undecided | 4 (11,8%) | 23 (67,6%) | 5 (14,7%) | 0 | 0 | 1 (2,9%) | 1 (2,9%) | |
| Not satisfied | 1 (7,1%) | 11 (78,6%) | 1 (7,1%) | 0 | 1 (7,1%) | 0 | 0 | |
| **How satisfied are you with the availability of pharmaceutical supplies in your facility? (e.g., antibiotics, oxytocin, misoprostol tablets, PABAL ampoules, etc.)** | | | | | | | | |
| Satisfied | 15 (9,8%) | 123 (80,4%) | 2 (1,3%) | 3 (2%) | 5 (3,3%) | 3 (2%) | 2 (1,3%) | 0,009 |
| Somewhat satisfied | 12 (29,3%) | 27 (65,9%) | 0 | 1 (2,4%) | 1 (2,4%) | 0 | 0 | |
| Undecided | 5 (11,1%) | 30 (66,7%) | 4 (8,9%) | 1 (2,2%) | 3 (6,7%) | 1 (2,2%) | 1 (2,2%) | |
| Not satisfied | 6 (37,5%) | 7 (43,8%) | 2 (12,5%) | 1 (6,3%) | 0 | 0 | 0 | |
| **How satisfied are you with the staffing levels in your department? (e.g., obstetricians-gynecologists, midwives, nurses)** | | | | | | | | |
| Satisfied | 20 (13,2%) | 112 (74,2%) | 2 (1,3%) | 4 (2,6%) | 8 (5,3%) | 3 (2%) | 2 (1,3%) | 0,07 |
| Somewhat satisfied | 13 (22%) | 41 (69,5%) | 1 (1,7%) | 2 (3,4%) | 1 (1,7%) | 0 | 1 (1,7%) | |
| Undecided | 1 (3,1%) | 26 (81,3%) | 4 (12,5%) | 0 | 0 | 1(3,1%) | 0 | |
| Not satisfied | 4 (30,8%) | 8 (61,5%) | 1 (7,7%) | 0 | 0 | 0 | 0 | |
| **How satisfied are you with the implementation of laboratory diagnostic procedures?** | | | | | | | | |
| Satisfied | 17 (10,2%) | 130 (78,3%) | 2 (1,2%) | 6 (3,6%) | 6 (3,6%) | 3 (1,8%) | 2 (1,2%) | 0,001 |
| Somewhat satisfied | 13 (27,1%) | 33 (68,8%) | 0 | 0 | 1 (2,1%) | 0 | 1 (2,1%) | |
| Undecided | 4 (12,9%) | 20 (64,5%) | 5 (16,1%) | 0 | 1 (3,2%) | 1 (3,2%) | 0 | |
| Not satisfied | 4 (40%) | 4 (40%) | 1 (10%) | 0 | 1 (10%) | 0 | 0 | |
| **How satisfied are you with the implementation of instrumental diagnostic procedures? (e.g., radiographic, ultrasound)** | | | | | | | | |
| Satisfied | 23 (12,6%) | 140 (76,9%) | 2 (1,1%) | 5 (2,7%) | 7 (3,8%) | 3 (1,6%) | 2 (1,1%) | <0,0001 |
| Somewhat satisfied | 10 (22,2%) | 31 (68,9%) | 0 | 1 (2,2%) | 2 (4,4%) | 0 | 1 (2,2%) | |
| Undecided | 0 | 13 (68,4%) | 5 (26,3%) | 0 | 0 | 1 (5,3%) | 0 | |
| Not satisfied | 5 (55,6%) | 3 (33,3%) | 1 (11,1%) | 0 | 0 | 0 | 0 | |
| **How satisfied are you with the availability of consultations by specialized medical professionals?** | | | | | | | | |
| Satisfied | 24 (14,2%) | 129 (76,3%) | 2 (1,2%) | 4 (2,4%) | 5 (3%) | 3 (1,8%) | 2 (1,2%) | <0,0001 |
| Somewhat satisfied | 8 (19%) | 27 (64,3%) | 0 | 2 (4,8%) | 4 (9,5%) | 0 | 1 (2,4%) | |
| Undecided | 2 (5,4%) | 30 (81,1%) | 4 (10,8%) | 0 | 0 | 1 (2,7%) | 0 | |
| Not satisfied | 4 (57,1%) | 1 (14,3%) | 2 (28,6%) | 0 | 0 | 0 | 0 | |
| **How satisfied are you with the availability of medical consumables and devices in the perinatal center? (e.g., endotracheal tubes, laryngoscopes, suction catheters, wipes, etc.)** | | | | | | | | |
| Satisfied | 21 (13,4%) | 120 (76,4%) | 2 (1,3%) | 4 (2,5%) | 4 (2,5%) | 4 (2,5%) | 2 (1,3%) | 0,009 |
| Somewhat satisfied | 14 (26,4%) | 32 (60,4%) | 0 | 2 (3,8%) | 4 (7,5%) | 0 | 1 (1,9%) | |
| Undecided | 2 (5,6%) | 28 (77,8%) | 5 (13,9%) | 0 | 1 (2,8%) | 0 | 0 | |
| Not satisfied | 1 (11,1%) | 7 (77,8%) | 1 (11,1%) | 0 | 0 | 0 | 0 | |
| **Have there been cases of miscommunication between physicians and mid-level staff in your department?** | | | | | | | | |
| Yes | 5 (11,6%) | 36 (83,7%) | 1 (2,3%) | 0 | 1 (2,3%) | 0 | 0 | 0,66 |
| No | 33 (15,6%) | 151 (71,2%) | 7 (3,3%) | 6 (2,8%) | 8 (3,8%) | 4 (1,9%) | 3 (1,4%) | |

*Continuation of Table 2.*

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|---|---|---|---|---|---|---|---|---|
| **Do you experience difficulties when consulting with patients?** | | | | | | | | |
| Yes | 7 (18,4%) | 28 (73,7%) | 1 (2,6%) | 0 | 2 (5,3%) | 0 | 0 | 0,8 |
| No | 31 (14,3%) | 159 (73,3%) | 7 (3,2%) | 6 (2,8%) | 7 (3,2%) | 4 (1,8%) | 3 (1,4%) | |
| **How satisfied are you with opportunities to participate in professional training or seminars?** | | | | | | | | |
| Satisfied | 13 (8,4%) | 123 (79,9%) | 3 (1,9%) | 6 (3,9%) | 3 (1,9%) | 4 (2,6%) | 2 (1,3%) | 0,001 |
| Somewhat satisfied | 10 (18,2%) | 38 (69,1%) | 1 (1,8%) | 0 | 5 (9,1%) | 0 | 1 (1,8%) | |
| Undecided | 6 (26,1%) | 15 (65,2%) | 1 (4,3%) | 0 | 1 (4,3%) | 0 | 0 | |
| Not satisfied | 9 (39,1%) | 11 (47,8%) | 3 (13%) | 0 | 0 | 0 | 0 | |

Satisfaction with access to educational activities and training was reported by 79.9% (N=123) mid-level personnel, while only 8.4% (N=13) of physicians expressed satisfaction in this regard (p = 0.001). Furthermore, 39.1% (N=9) of physicians explicitly stated dissatisfaction with current opportunities for professional development. These results underscore the need for a systematic approach to clinical staff training, particularly for physicians, as they represent a key resource in ensuring the quality and safety of obstetric care

**Discussion**

mproving the quality of care in maternity institutions is not possible without a systematic analysis of the factors influencing infection safety. At present, the issues of resource availability, diagnostic capacity, staffing, and opportunities for professional development have become especially critical—particularly in the post-pandemic period, when healthcare systems have faced significant overload and limited operational capacity.

The findings of this study confirmed the presence of substantial differences in the perception of working conditions between physicians and mid-level medical personnel. Physicians reported significantly lower levels of satisfaction with technical equipment, pharmaceutical provision, access to diagnostic services, and opportunities for professional development. These differences were statistically significant and highlight a structural imbalance in the distribution of resources within healthcare facilities. Physicians - who are primarily responsible for clinical decision-making—were the most critical in their assessment of material and human resources. Similar patterns have been observed in European studies, which underscore the importance of aligning internal resource access with clinical responsibility [9].

According to the findings of our study, only 11.3% of physicians expressed satisfaction with the availability of essential equipment (e.g., ultrasound machines, cardiotocographs), compared to 78.7% of mid-level medical staff (p = 0.001). A similar disparity was observed in the assessment of pharmaceutical supply: only 9.8% of physicians were satisfied, in contrast to 80.4% of nursing personnel (p = 0.009). A comparable trend has been reported in European studies. For instance, *Sandall J. et al.* demonstrated that obstetric and gynecological institutions in Germany and Austria face challenges in the equitable distribution of resources among different staff categories, which in turn affects their level of professional satisfaction [9].

Diagnostic support was rated most critically by physicians. Only 10.2% of physicians were satisfied with access to laboratory diagnostics, compared to 78.3% of mid-level staff (p = 0.001). Likewise, satisfaction with access to instrumental diagnostics (e.g., ultrasound and radiographic examinations) was reported by just 12.6% of physicians versus 76.9% of nursing personnel (p < 0.0001). These findings are consistent with the results of a systematic review by *Lawn J.E et al.,* which emphasized that limited access to timely diagnostic services is a risk factor for infectious and obstetric complications in middle-income countries [10].

The issue of staffing adequacy was also perceived more acutely by physicians, only 13.2% of whom expressed satisfaction, compared to 74.2% of mid-level medical personnel. This imbalance reflects a broader human resource challenge commonly observed in the healthcare systems of post-Soviet countries. As noted by *Campbell et al.,* the shortage of obstetricians-gynecologists and neonatologists contributes to increased workloads, reduced clinical vigilance, and a higher likelihood of medical errors [11]. These findings highlight the urgent need to revise current human resource policies and to develop mechanisms for retaining and motivating qualified professionals [12].

One of the most significant findings of this study was the pronounced disparity in access to professional development opportunities. Only 8.4% of physicians reported satisfaction with available training programs, whereas 79.9% of mid-level staff assessed them positively (p = 0.001). This discrepancy may indicate structural barriers within the system of continuing medical education, such as limited program availability, insufficient funding, or a mismatch between educational offerings and the practical needs of physicians. According to the CDC (2022), continuing medical education is a critical component of efforts to reduce the incidence of healthcare-associated infections and to improve the quality of clinical practice [13].

Despite the differences in perceptions of resource availability, the study did not reveal significant disparities in how interprofessional collaboration and communication with patients were perceived. This may indicate the presence of an established culture of teamwork. However, the sustainability of such collaboration is directly dependent on the availability of resources and educational support [14].

Thus, the findings of this study support the need for reforming management approaches in maternity care institutions. Implementing a risk-oriented management model, conducting regular internal audits of staff satisfaction, expanding targeted educational programs - particularly for physicians — and ensuring equitable access

to resources are essential measures for strengthening the resilience of maternity facilities against both infectious and organizational threats.

At the same time, the interpretation of these results should take into account several limitations. First, the study relied on self-reported data, which may reflect subjective perceptions of working conditions influenced by individual experiences and expectations. Second, the cross-sectional study design limits the ability to establish causal relationships between the variables.

**Conclusion**

The findings of this study revealed significant differences in the perception of working conditions and infection safety between physicians and mid-level medical personnel in maternity care institutions. The most critically assessed areas included the availability of technical equipment, diagnostic resources, and opportunities for professional development. To enhance the resilience of obstetric and gynecological services, management strategies should focus on ensuring equitable access to resources, expanding continuing education programs, and implementing a risk-oriented approach to workforce organization.

***Conflict of interest.*** *No conflicts of interest have been declared.*

***Authors' Contributions.*** *All authors participated equally in the writing of this article. This material has not been previously submitted for publication in other publications and is not under consideration by other publishers.*

***Funding.*** *No funding was provided. There was no third-party funding or medical representation in the conduct of this work.*

***Literature:***

1. *Безымянный А.С., Мингазова Э.Н.* .Профессиональное выгорание медицинских работников и факторы, его определяющие // Проблемы социальной гигиены, здравоохранения и истории медицины. 2024. №2. URL: https://cyberleninka.ru/article/n/professionalnoe-vygoranie-meditsinskih-rabotnikov-i-faktory-ego-opredelyayuschie (дата обращения: 16.06.2025).

2. *Герасименко А.В., Чумаков М.Э.* Опыт внедрения системы инфекционной безопасности в Перинатальном центре // Ремедиум Приволжье. 2014. №6 (126). URL: https://cyberleninka.ru/article/n/opyt-vnedreniya-sistemy-infektsionnoy-bezopasnosti-v-perinatalnom-tsentre (дата обращения: 17.06.2025).

3. *Хромова Н.Л., Баринова Е.В., Орлов А.Б., Ликстанов М.И.* Результаты внедрения элементов инфекционного контроля в акушерском стационаре // МиД. 2001. №5–6 (6–7). URL: https://cyberleninka.ru/article/n/rezultaty-vnedreniya-elementov-infektsionnogo-kontrolya-v-akusherskom-statsionare

4. World Health Organization. Global Guidelines for the Prevention of Surgical Site Infection. Geneva: WHO; 2016.

*5. Allegranzi B., Pittet D.* Role of hand hygiene in healthcare-associated infection prevention. J Hosp Infect. 2009 Dec;73(4):305-15. doi: 10.1016/j.jhin.2009.04.019. Epub 2009 Aug 31. PMID: 19720430.

6. CDC. Infection Control in Healthcare Settings. CDC. https://www.cdc.gov/infection-control/hcp/index.html

7. *Blinov D.V., Hasan P.L., Mnatsakanyan A.N., Korabelnikov D.I., Safarov A.T., Pavlova N.V., Zakharova N.S., Ponomarev D.A., Petrenko D.A.* Early menopause and premature ovarian insufficiency: problems and perspectives. Obstetrics, Gynecology and Reproduction. 2020;14(3):328-345. (In Russ.) https://doi.org/10.17749/2313-7347/ob.gyn.rep.2020.173

8. *Bhutta Z.A., Cabral S., Chan C.W., Keenan W.J.* Reducing maternal, newborn, and infant mortality globally: an integrated action agenda. Int J Gynaecol Obstet. 2012 Oct;119 Suppl 1:S13-7. doi: 10.1016/j.ijgo.2012.04.001. Epub 2012 Aug 9. PMID: 22883919.

9. *Sandall, Jane & Homer, Caroline & Sadler, Euan & Rudisill, C. & Bourgeault, Ivy & Bewley, Susan & Nelson, Pauline & Cowie, L. & CoopeC &. & Curry, Natasha.* (2011). Staffing in maternity units. Getting the right people in the right place at the right time.

*10. Lawn J.E., Blencowe H., Oza S., You D., Lee A.C., Waiswa P., Lalli M., Bhutta Z., Barros A.J., Christian P., Mathers C., Cousens S.N.,* Lancet Every Newborn Study Group. Every Newborn: progress, priorities, and potential beyond survival. Lancet. 2014 Jul 12;384(9938):189-205. doi: 10.1016/S0140-6736(14)60496-7. Epub 2014 May 19. Erratum in: Lancet. 2014 Jul 12;384(9938):132. PMID: 24853593.

*11. Campbell J.,* et al. Maximizing the impact of community-based practitioners in the quest for universal health coverage, 2015.

*12. Stones W., Nair A.* Metrics for maternity unit staffing in low resource settings: Scoping review and proposed core indicator. Front Glob Womens Health. 2023 Mar 15;4:1028273. doi: 10.3389/fgwh.2023.1028273. PMID: 37009093; PMCID: PMC10050730.

13. Centers for Disease Control and Prevention. The One & Only Campaign injection safety training materials. https://www.cdc.gov/healthcare-associated-infections/index.html.

14. WHO. COVID-19 STRATEGY UPDATE. 14 April 2020. Geneva: World Health Organization; 2020 (https://www.who.int/docs/default-source/coronaviruse/covid-strategy-update-14april2020.pdf, accessed 8 June 2020)

***References: [1-3]***

1. Bezymyannyi A.S., Mingazova E.N. Professional'noe vygoranie meditsinskikh rabotnikov i faktory, ego opredelyayuschiye [Professional burnout of healthcare workers and its determining factors]. *Problemy sotsial'noi gigieny, zdravookhraneniya i istorii meditsiny* [Problems of social hygiene, health care and history of medicine]. 2024. №2. URL: [https://cyberleninka.ru/article/n/professionalnoe-vygoranie-meditsinskih-rabotnikov-i-faktory-ego-opredelyayuschie](https://cyberleninka.ru/article/n/professionalnoe-vygoranie-meditsinskih-rabotnikov-i-faktory-ego-opredelyayuschie) (accessed: 16.12.2024). [in Russian]

2. Gerasimenko A.V., Chumakov M.E. Opyt vnedreniya sistemy infektsionnoi bezopasnosti v Perinatal'nom tsentre [Experience of implementing an infection safety system in a perinatal center]. *Remedium Privolzh'e.* 2014. №6 (126). URL: [https://cyberleninka.ru/article/n/opyt-vnedreniya-sistemy-infektsionnoy-bezopasnosti-v-perinatalnom-tsentre](https://cyberleninka.ru/article/n/opyt-vnedreniya-sistemy-infektsionnoy-bezopasnosti-v-perinatalnom-tsentre) (accessed: 17.11.2024). [in Russian]

3. Hromova N.L., Barinova E.V., Orlov A.B., Likstanov M.I. Rezul'taty vnedreniya elementov infektsionnogo kontrolya v akusherskom statsionare [Results of implementing infection control elements in a maternity hospital]. *MiD*. 2001. №5–6 (6–7). URL: [https://cyberleninka.ru/article/n/rezultaty-vnedreniya-elementov-infektsionnogo-kontrolya-v-akusherskomstatsionare](https://cyberleninka.ru/article/n/rezultaty-vnedreniya-elementov-infektsionnogo-kontrolya-v-akusherskom-statsionare). (accessed: 17.11.2024). [in Russian]

**Information about the authors:**
**Gulnoza U. Aldabekova** - second-year doctoral candidate (PhD track 8D10103 “Public Health”), Department of Public Health and Epidemiology, Astana Medical University (Non-Commercial JSC), Astana 010000, Republic of Kazakhstan; ORCID: https://orcid.org/0009-0009-1561-1094
**Aiman A. Musina,** MD, DSc - Professor and Head, Department of Public Health and Epidemiology, Astana Medical University (Non-Commercial JSC), Astana 010000, Republic of Kazakhstan; ORCID: https://orcid.org/0000-0001-8943-032X
**Gulnara M. Kamalbekova,** PhD - Professor, Department of Public Health and Epidemiology, Astana Medical University (Non-Commercial JSC), Astana 010000, Republic of Kazakhstan; ORCID: https://orcid.org/0000-0001-9883-6321
**Zaituna G. Khamidullina,** PhD, MD - Associate Professor, Head of the Department of Obstetrics and Gynecology No. 1, Astana Medical University (Non-Commercial JSC), Astana, Republic of Kazakhstan; ORCID: https://orcid.org/0000-0001-9100-694X
**Zhuldyz S. Danbayeva PhD,** MD - Associate Professor, «City multifunctional hospital №3», Astana010000, Republic of Kazakhstan.
**Svetlana B. Abdrashidova** - Assistant, Department of Obstetrics and Gynecology No. 1, Astana Medical University (Non-Commercial JSC), Astana 010000, Republic of Kazakhstan.
**Elmira M. Zhumabayeva** - Assistant, Department of Obstetrics and Gynecology No. 1, Astana Medical University (Non-Commercial JSC), Astana 010000, Republic of Kazakhstan
**Gulsim A. Kokisheva** - Assistant, Department of Obstetrics and Gynecology No. 1, Astana Medical University (Non-Commercial JSC), Astana 010000, Republic of Kazakhstan.
**Gulyash A. Tanysheva -** Candidate of Medical Sciences, Head of the Department of Obstetrics and Gynecology, NCJSC «Semey Medical University», phone 8(777)153-53-57, email gulyash1965@mail.ru, https://orcid.org/0000-0001-9531-5950, 103 Abay Street, Semey, Kazakhstan.

**Corresponding author:**
**Gulnoza U. Aldabekova** — second-year doctoral candidate (PhD program 8D10103 “Public Health”), Department of Public Health and Epidemiology, Astana Medical University (Non-Commercial JSC), Astana, Republic of Kazakhstan
**Postal code:** 4 Azerbayeva Street, Apt. 184, Astana 010000, Republic of Kazakhstan
**E-mail:** aldabekova.g@amu.kz
**Phone:** +7 708 047 71 70

Received: 02 February 2025 / Accepted: 16 June 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2025.27.3.013***

***UDC 616.248-053.6(574.41)***

This work is licensed under a Creative Commons Attribution 4.0 International License

# CLINICAL AND IMMUNOLOGICAL CHARACTERISTICS OF BRONCHIAL ASTHMA IN CHILDREN AND ADOLESCENTS IN THE ABAY REGION

**Andrei Furlan[1], https://orcid.org/0009-0004-7603-8731**
**Gulbarshyn D. Mukasheva*[2], https://orcid.org/0000-0003-3490-5628**
**Saule B. Maukayeva[2], https://orcid.org/0000-0002-2679-6399**
**Nazym K. Kudaibergenova[2], https://orcid.org/0000-0002-6165-7677**
**Dariya M. Shabdarbayeva[2], https://orcid.org/0000–0001–9463–1935**
**Zhanargyl K. Smailova[2], https://orcid.org/0000-0002-4513-4614**
**Botagoz S. Turakhanova[2], http://orcid.org/0009-0003-0480-7063**
**Dinara B. Kozubayeva[2], https://orcid.org/0000-0003-4937-708X**
**Maiya V. Goremykina[2], https://orcid.org/0000-0002-5433-7771**
**Zhanar B. Issabekova[2], https://orcid.org/0000-0002-2744-0327**
**Saya S. Karimova[2], http://orcid.org/0000-0002-1167-5375**
**Nailya M. Urazalina[2], https://orcid.org/0000-0003-0200-1763**

**[1] University of Medicine and Pharmacy "Victor Babeș" Timișoara, Romania;**
**[2] NCJSC «Semey Medical University», Semey, Republic of Kazakhstan.**

**Abstract**

**Background:** Bronchial asthma is one of the most widespread chronic respiratory conditions in children and adolescents. Its development and progression are strongly influenced by environmental exposures and immunological responses.

**This study aimed** to assess the clinical features and immunological profiles of asthma in pediatric patients in the Abay region of Kazakhstan, focusing on symptom patterns, biomarker levels, and allergic history.

**Materials and methods:** A retrospective analysis was carried out based on the medical records of 71 children aged 1 to 17 years with a confirmed diagnosis of asthma. The evaluation included clinical symptom assessment and spirometry. Statistical analyses were conducted using descriptive methods, T-tests, and chi-square tests.

**Results:** The most frequently reported symptoms were cough (76.1%) and dyspnea (59.2%). Nearly one-third of participants lived in damp housing conditions, which showed a statistically significant association with respiratory complaints ($p < 0.05$). Moderate asthma was observed in 80.3% of cases, and 19.7% were classified as mild. Among those tested, elevated levels of ECP and IgE were more common in moderate cases and among those exposed to allergens.

**Conclusion:** Children and adolescents with asthma in the Abay region are often exposed to environmental triggers such as humidity and seasonal allergens. These factors appear to influence both the severity of clinical symptoms and the levels of immunological markers. The findings highlight the importance of early identification of environmental risks and support the use of ECP and IgE levels in guiding personalized asthma management strategies.

***Key words:*** *Bronchial asthma; Adolescents; Environmental exposure; Biomarkers; Clinical characteristics.*

***For citation:***

Furlan A.,Mukasheva G.D., Maukayeva S.B., Kudaibergenova N.K., Shabdarbayeva D.M., Smailova Zh.K., Turakhanova B.S., Kozubayeva D.B., Goremykina M.V., Issabekova Zh.B., Karimova S.S., Urazalina N.M. Clinical and immunological characteristics of bronchial asthma in children and adolescents in the Abay region // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 117-124. *doi 10.34689/SH.2025.27.3.013*

**Резюме**

# КЛИНИКО-ИММУНОЛОГИЧЕСКАЯ ХАРАКТЕРИСТИКА БРОНХИАЛЬНОЙ АСТМЫ У ДЕТЕЙ И ПОДРОСТКОВ В АБАЙСКОЙ ОБЛАСТИ

**Андрей Фурлан[1], https://orcid.org/0009-0004-7603-8731**
**Гүлбаршын Д. Мукашева*[2], https://orcid.org/0000-0003-3490-5628**
**Сауле Б. Маукаева[2], https://orcid.org/0000-0002-2679-6399**
**Назым К. Кудайбергенова[2], https://orcid.org/0000-0002-6165-7677**

**Дария М. Шабдарбаева[2],** https://orcid.org/0000–0001–9463–1935
**Жанаргуль К. Смаилова[2],** http://orcid.org/0000-0002-4513-4614
**Ботагоз С. Тураханова[2],** http://orcid.org/0009-0003-0480-7063
**Динара Б. Козубаева[2],** https://orcid.org/0000-0003-4937-708X
**Майя В. Горемыкина[2],** https://orcid.org/0000-0002-5433-7771
**Жанар Б. Исабекова[2],** https://orcid.org/0000-0002-2744-0327
**Сая С. Каримова[2],** http://orcid.org/0000-0002-1167-5375
**Найля М. Уразалина[1],** https://orcid.org/0000-0003-0200-1763

**[1] Университет медицины и фармации имени Виктора Бабеша, Тимишоара, Румыния;**
**[2] НАО «Медицинский университет Семей», г. Семей, Республика Казахстан.**

**Введение:** Бронхиальная астма — одно из наиболее распространённых хронических заболеваний дыхательных путей у детей и подростков. На её развитие и течение значительное влияние оказывают факторы окружающей среды и иммунологические особенности.

**Цель:** Целью настоящего исследования является анализ клинических проявлений и иммунологических показателей астмы у детей в Абайской области Казахстана, с акцентом на симптоматику, уровень биомаркеров и аллергологический анамнез.

**Материалы и методы:** Проведено ретроспективное исследование медицинских карт 71 ребёнка в возрасте от 1 до 17 лет с подтверждённым диагнозом бронхиальной астмы. Оценка включала анализ клинических симптомов и данные спирометрии. Статистическая обработка выполнена с применением описательных методов, t-теста и $\chi^2$-теста.

**Результаты:** Наиболее частыми симптомами были кашель (76,1%) и одышка (59,2%). Примерно треть участников проживала во влажных условиях, что показало статистически значимую связь с респираторными жалобами ($p < 0,05$). У 80,3% пациентов была диагностирована астма средней степени тяжести, у 19,7% — лёгкая форма. Повышенные уровни ECP и IgE чаще отмечались у пациентов с более тяжёлым течением заболевания и при наличии контакта с аллергенами.

**Заключение:** Дети и подростки в Абайской области часто подвергаются воздействию факторов риска, таких как влажность и сезонные аллергены, что может усугублять течение астмы. Результаты подчёркивают важность раннего выявления таких факторов и использование показателей ECP и IgE при персонализированном подходе к лечению астмы.

***Ключевые слова:*** *Бронхиальная астма; Подростки; Факторы окружающей среды; Биомаркеры; Клинические признаки.*

***Для цитирования:***

*Фурлан А., Мукашева Г.Д., Маукаева С.Б., Кудайбергенова Н.К., Шабдарбаева Д.М., Смаилова Ж.К., Тураханова Б.С., Козубаева Д.Б., Горемыкина М.В., Исабекова Ж.Б., Каримова С.С., Уразалина Н.М.* Клинико-иммунологическая характеристика бронхиальной астмы у детей и подростков в Абайской области // Наука и Здравоохранение. 2025. Т.27 (3), С. 117-124. doi: 10.34689/SH.2025.27.3.013

**Түйіндеме**

# АБАЙ ОБЛЫСЫНДАҒЫ БАЛАЛАР МЕН ЖАСӨСПІРІМДЕРДЕГІ БРОНХИАЛДЫ АСТМАНЫҢ КЛИНИКАЛЫҚ ЖӘНЕ ИММУНОЛОГИЯЛЫҚ ЕРЕКШЕЛІКТЕРІ

**Андрей Фурлан[1],** https://orcid.org/0009-0004-7603-8731
**Гүлбаршын Д. Мукашева*[2],** https://orcid.org/0000-0003-3490-5628
**Сауле Б. Маукаева[2],** https://orcid.org/0000-0002-2679-6399
**Назым К. Кудайбергенова[2],** https://orcid.org/0000-0002-6165-7677
**Дария М. Шабдарбаева[2],** https://orcid.org/0000–0001–9463–1935
**Жанаргуль К. Смаилова[2],** http://orcid.org/0000-0002-4513-4614
**Ботагоз С. Тураханова[2],** http://orcid.org/0009-0003-0480-7063
**Динара Б. Козубаева[2],** https://orcid.org/0000-0003-4937-708X
**Майя В. Горемыкина[2],** https://orcid.org/0000-0002-5433-7771
**Жанар Б. Исабекова[2],** https://orcid.org/0000-0002-2744-0327
**Сая С. Каримова[2],** http://orcid.org/0000-0002-1167-5375
**Найля М. Уразалина[1],** https://orcid.org/0000-0003-0200-1763

[1] **«Виктор Бабеш» медицина және фармацевтика университеті, Тимишоара қ., Румыния;**
[2] **«Семей медицина университеті» КеАҚ, Семей қ., Қазақстан Республикасы.**

**Кіріспе:** Бронхиалды астма – балалар мен жасөспірімдер арасында жиі кездесетін созылмалы тыныс алу ауруы. Оның пайда болуы мен өршуіне қоршаған орта факторлары мен иммунологиялық өзгерістер елеулі әсер етеді.

**Мақсаты:** Бұл зерттеу Абай облысындағы балалардағы астманың клиникалық белгілері мен иммунологиялық көрсеткіштерін, сондай-ақ аллергиялық анамнезді талдауды мақсат етті.

**Зерттеу материалдары мен әдістері:** Зерттеу 1–17 жас аралығындағы 71 баланың медициналық карталары негізінде ретроспективті түрде жүргізілді. Қатысушыларда бронхиалды астманың расталған диагнозы болды. Клиникалық бағалау симптомдарды талдау мен спирометрияны қамтыды. Статистикалық талдау сипаттамалық әдістермен, t-тест және $\chi^2$-тест арқылы жүргізілді.

**Нәтижелер:** Ең жиі кездесетін симптомдар жөтел (76,1%) және ентікпе (59,2%) болды. Қатысушылардың шамамен үштен бірі ылғалды үй жағдайында тұрып, бұл тыныс алу шағымдарымен статистикалық тұрғыда байланыс көрсетті ($p < 0.05$). Орташа ауырлықтағы астма 80,3% жағдайда, жеңіл түрі 19,7% жағдайда анықталды. Биомаркерлерді бағалау нәтижесінде ECP мен IgE деңгейлері орташа ауырлықтағы астмада және аллерген әсеріне ұшыраған балаларда жоғары болды.

**Қорытынды:** Абай облысындағы балалар мен жасөспірімдер жиі ылғалдылық пен маусымдық аллергендердің әсеріне ұшырайды. Бұл факторлар клиникалық симптомдардың ауырлығына және иммунологиялық көрсеткіштерге ықпал етуі мүмкін. Зерттеу қоршаған орта әсерлерін ерте анықтау мен ECP және IgE деңгейлерін астманы басқару стратегияларын жекешелендіруде қолданудың маңыздылығын көрсетеді.

***Кілт сөздер:*** *Бронхиалды астма, Жасөспірімдер; Қоршаған орта, Биомаркерлер, Клиникалық белгілер.*

***Дәйексөз үшін:***

*Фурлан А., Мукашева Г.Д., Маукаева С.Б., Кудайбергенова Н.К., Шабдарбаева Д.М., Смаилова Ж.К., Тураханова Б.С., Козубаева Д.Б., Горемыкина М.В., Исабекова Ж.Б., Каримова С.С., Уразалина Н.М.* Абай облысындағы балалар мен жасөспірімдердегі бронхиалды астманың клиникалық және иммунологиялық ерекшеліктері // Ғылым және Денсаулық. 2025. Т.27 (3), Б. 117–124. doi: 10.34689/SH.2025.27.3.013

**Introduction**

Asthma is a chronic inflammatory disease of the airways, characterized by intermittent episodes of wheezing, shortness of breath, and coughing, typically occurring in the early morning or at night [17]. The pathophysiology of asthma is complex and not fully understood, primarily due to the intricate interactions between genetic predispositions and environmental factors. The degree of airway obstruction and hyper-reactivity is largely determined by these interactions [9]. Asthma is increasingly recognized as a major global public health issue, currently affecting an estimated 330 million people worldwide [12]. Although various management strategies are being implemented, epidemiological data show a worrying rise in asthma cases in low- and middle-income countries (LMICs) [8]. In contrast, incidence rates in high-income nations have largely stabilized [12]. These contrasting trends highlight the need for more in-depth epidemiological studies to better understand the underlying causes—particularly environmental factors like air pollution, which has been strongly linked to both increased prevalence and severity of asthma symptoms [5].

Among the biological mechanisms associated with asthma, inflammatory mediators such as Eosinophilic Cationic Protein (ECP) and Immunoglobulin E (IgE) play a central role in triggering and intensifying symptoms. Studies have shown that higher levels of ECP mRNA and IgE are associated with more severe asthma, underscoring the importance of inflammation in the disease's progression [8].

As of now, there have been no large-scale, population-based studies specifically examining asthma in the Abay Region. Given its distinct environmental and socio-demographic conditions, there is a clear need for targeted research in this area. A comprehensive retrospective analysis could help identify whether asthma patterns in this region differ from those observed in other parts of Kazakhstan. Key aspects such as living conditions, personal and family allergy histories, and individual asthma profiles may contribute to region-specific trends and deserve closer investigation. Environmental pollutants have been shown to contribute to the severity and exacerbation of asthma symptoms, highlighting the necessity of an in-depth analysis of these factors [3].

Official statistics report asthma prevalence in Kazakhstan at 19.5 per 1000 (2%) among adults, with wheezing symptoms affecting 254 per 1000 (25.4%) individuals [18]. This discrepancy suggests a gap between reported diagnoses and symptomatic presentation, underscoring the need for improved diagnostic methods. Independent studies estimate that asthma affects 23.5% of individuals under the age of 17, indicating significant underdiagnosis in the country [4].

**This study aims** to offer a well-rounded understanding of the clinical and immunological features of bronchial asthma in children and adolescents living in the Abay Region of Kazakhstan. Special attention is given to their living conditions, history of allergic diseases, and the frequency of asthma-related symptoms.

**Materials and Methods**

A retrospective observational study was carried out to explore the clinical and immunological characteristics of asthma among children and teenagers residing in the Abay Region of the Republic of Kazakhstan.

*Inclusion Criteria:* Participants aged 0 to 17 years who were living in the Abay Region at the time of the study.

*Exclusion Criteria:* Individuals older than 17 years or those not residing in the Abay Region during the study period.

The analysis was based on the medical records of 71 pediatric patients, collected from the Family Polyclinic in the city of Semey, located at 97 Dostoevsky Street. Since the research was retrospective in nature and all patient data were anonymized, informed consent was not required. Тема исследования утверждена на заседании Этической комиссии (№ и дата Протокола заседания)

*Statistical Analysis.* Descriptive statistics were used to summarize the data. To determine statistically significant differences, chi-square tests and independent t-tests were applied. All analyses were conducted using SPSS software, version 26.0, with a significance threshold set at $p < 0.05$.

**Results**

The study examined a range of factors including socio-demographic data, clinical symptoms, living environments, allergy history, and specific asthma-related features among the participants. A detailed summary is provided in Table 1.

*Table 1.*

**Socio-demographic, clinical, environmental, and allergy characteristics of study participants.**

| Variables | | | n | % |
|---|---|---|---|---|
| **Socio-demographic Characteristics** | Gender | male | 43 | 60.6% |
| | | female | 28 | 39.4% |
| | Age group | 1-5 | 21 | 29.6% |
| | | 5-10 | 39 | 54.9% |
| | | 11-17 | 11 | 15.5% |
| **Clinical Characteristics** | Cough | yes | 54 | 76.1% |
| | | no | 17 | 23.9% |
| | Dyspnea | yes | 42 | 59.2% |
| | | no | 29 | 40.8% |
| **Environmental and Housing Conditions** | Type of housing | apartment | 35 | 49.3% |
| | | house | 36 | 50.7% |
| | Nasal congestion | yes | 31 | 43.7% |
| | | no | 40 | 56.3% |
| | Dampness | yes | 26 | 36.6% |
| | | no | 45 | 63.4% |
| **Allergy History** | Family allergy history | yes | 51 | 71.8% |
| | | no | 20 | 28.2% |
| | Insect allergy | yes | 28 | 39.4% |
| | | no | 43 | 60.6% |
| | Animals in the house | yes | 28 | 39.4% |
| | | no | 43 | 60.6% |
| | Allergy to medications | yes | 18 | 25.4% |
| | | no | 53 | 74.6% |
| | Seasonal allergies | yes | 15 | 21.1% |
| | | no | 56 | 78.9% |
| | Food allergies | yes | 23 | 32.4% |
| | | no | 48 | 67.6% |
| | Household allergies | yes | 18 | 25.4% |
| | | no | 53 | 74.6% |
| | Skin allergies | yes | 18 | 25.4% |
| | | no | 53 | 74.6% |
| **Spirometry Results** | Breathing | normal | 57 | 80.3% |
| | | abnormal | 14 | 19.7% |
| | Spirometry | no spirometry | 43 | 60.6% |
| | | normal | 12 | 16.9% |
| | | restrictive | 15 | 21.1% |
| | | obstructive | 1 | 1.4% |
| **Asthma Characteristics** | Newly diagnosed asthma | yes | 40 | 56.3% |
| | | no | 31 | 43.7% |
| | Persistent asthma | yes | 62 | 87.3% |
| | | no | 9 | 12.7% |
| | Severity of the asthma | mild | 14 | 19.7% |
| | | Moderate-severe | 57 | 80.3% |

Out of the 71 children and adolescents included in the analysis, 43 (60.6%) were boys and 28 (39.4%) were girls. The average age was 7.24 years, with participants ranging from 1 to 17 years old, offering a broad snapshot of the pediatric population. For analytical purposes, participants were divided into three age groups: 1–5 years (29.6%, n=21), 5–10 years

(54.9%, n=39), and 11–17 years (15.5%, n=11). The most represented group was the 5–10 year range, suggesting that the majority of cases occurred among younger children.

The majority of children in the study experienced typical asthma-related symptoms. Coughing was the most frequently reported complaint (76.1%, n = 54), followed by shortness of breath (59.2%, n = 42) and nasal congestion (43.7%, n = 31). These symptoms were central to evaluating the clinical status of each child and reflect common manifestations of asthma in pediatric patients.

Participants were almost evenly split between different types of housing: 36 children (50.7%) lived in standalone houses, while 35 (49.3%) lived in apartments. Dampness was present in the homes of 26 children (36.6%), which is notable given its established role in worsening respiratory conditions, including asthma.

Allergy-related factors played a significant role in the study. A family history of allergies was found in 71.4% of cases (n=51), suggesting a hereditary link to asthma. Additionally, 39.4% (n=28) reported insect allergies, and the same percentage had pets at home, both of which are potential asthma triggers. Other reported allergic conditions included drug allergies (25.4%, n=18), seasonal allergic responses (21.1%, n=15), food allergies (32.4%, n=23), sensitivity to household allergens (25.4%, n=18), and epidermal allergens (25.4%, n=18).

At the time of clinical evaluation, 80.3% (n=57) of children showed normal breathing, while 15.5% (n=11) presented with wheezing. For more than half of the participants (56.3%, n=40), the diagnosis of asthma was made for the first time during the study period. Most cases (87.3%, n=62) were classified as persistent asthma. Regarding severity, 19.7% (n=14) were mild cases, whereas 80.3% (n=57) were categorized as moderate to severe.

Spirometry was not performed in 43 cases (60.6%), which poses certain limitations in evaluating pulmonary function. Among the 28 patients who underwent testing, 16.9% (n=12) had normal results, 21.1% (n=15) demonstrated restrictive patterns, and 1.4% (n=1) showed signs of obstructive dysfunction.

Table 2 presents the analysis of clinical characteristics, ECP, and IgE levels. In participants with mild asthma, the mean ECP was 38.1 (SD=18.3) and the mean IgE was 134 (SD=81). In those with moderate asthma, the mean ECP increased to 51.0 (SD=37.2), and the mean IgE rose to 518 (SD=551). Statistically, IgE levels showed a strong correlation with asthma severity, with a p-value of 0.001.

*Table 2.*

**ECP and IgE levels, linked to individual asthma characteristics of the participants.**

| Variables | | ECP | | p-value | IgE | | p-value |
|---|---|---|---|---|---|---|---|
| | | M | SD | | M | SD | |
| Severity of the asthma | mild | 38.1 | 18.3 | 0.35 | 134 | 81 | **0.01** |
| | moderate-severe | 51.0 | 37.2 | | 518 | 551 | |
| Dampness | yes | 39.6 | 29.1 | **0.04** | 444 | 579 | 0.490 |
| | no | 53.6 | 36.7 | | 441 | 486 | |
| Seasonal allergies | yes | 56.9 | 34.5 | 0.149 | 862 | 761 | **0.009** |
| | no | 46.2 | 34.5 | | 330 | 364 | |
| Food allergies | yes | 55.3 | 41.3 | 0.127 | 612 | 666 | 0.28 |
| | no | 45.2 | 30.8 | | 361 | 413 | |
| Household allergies | yes | 44.8 | 26.7 | 0.304 | 782 | 793 | **0.001** |
| | no | 49.7 | 37.0 | | 327 | 319 | |

Environmental factors were found to influence biomarker levels. Participants living in damp conditions had a mean ECP of 39.6 (SD=29.1) and a mean IgE of 444 (SD=579). The p-values for ECP and IgE were 0.004 and 0.0490, respectively, indicating a statistically significant correlation. In contrast, those living in dry conditions had lower levels of both ECP (mean=53.6, SD=36.7) and IgE (mean=441, SD=486). Seasonal allergies were also significantly associated with elevated ECP and IgE levels (mean ECP=56.9, SD=34.5; mean IgE=862, SD=761), with p-values of 0.0149 for ECP and 0.0009 for IgE.

Food and household allergies were likewise correlated with higher biomarker levels. Participants with food allergies had an average ECP level of 55.3 (SD= 1.3) and IgE level of 612 (SD=666), with p-values of 0.0127 for ECP and 0.028 for IgE. In contrast, those with household allergies had an average ECP of 44.8 (SD=26.7) and IgE of 782 (SD=793), with p-values of 0.0304 for ECP and 0.0001 for IgE.

Table 3 shows the relationship between nasal congestion, seasonal allergies, and asthma severity in pediatric patients. It compares two groups: those with mild asthma and those with moderate-to-severe asthma.

*Table 3.*

**Relationship between Nasal Congestion, Seasonal Allergies, and Asthma Severity in Pediatric Patients.**

| Variables | | Severity of the asthma | | | | p-value |
|---|---|---|---|---|---|---|
| | | mild | | moderate-severe | | |
| | | n | % | n | % | |
| Nasal congestion | yes | 1 | 7.1% | 30 | 52.6% | **0.02** |
| | no | 13 | 92.9% | 27 | 47.4% | |
| Seasonal allergies | yes | 0 | 0% | 15 | 26.3% | **0.031** |
| | no | 14 | 100% | 42 | 73.7% | |

For nasal congestion, the table reveals that only 7.1% (1 out of 14) of children with mild asthma reported nasal congestion, while 52.6% (30 out of 57) of those with moderate-to-severe asthma experienced it. The p-value of 0.02 indicates that this association is statistically significant, suggesting that nasal congestion is more common in children with more severe forms of asthma. Regarding seasonal allergies, none of the children with mild asthma reported seasonal allergies, while 26.3% (15 out of 57) of those with moderate-to-severe asthma had a history of seasonal allergies. The p-value of 0.031 indicates a statistically significant relationship between seasonal allergies and asthma severity.

**Discussion**

The findings of this study generally align with earlier research demonstrating the role of eosinophilic cationic protein (ECP) and immunoglobulin E (IgE) in the pathogenesis and severity of bronchial asthma. However, certain discrepancies were noted, which may be attributed to the unique environmental and demographic context of the Abay Region. For instance, the variation in ECP and IgE levels among children living in damp conditions or exposed to specific allergens may reflect the influence of local environmental factors. This underlines the importance of conducting region-specific studies, as international data alone may not fully account for local variables that affect how asthma presents and progresses.

Bronchial asthma continues to pose a significant public health challenge in the Abay Region. Its prevalence appears to be driven by a combination of environmental exposures such as poor housing conditions and systemic factors, including possible gaps in early diagnosis and access to care. Addressing these challenges continues to pose difficulties for effective disease management in the regional healthcare setting. A study on respiratory diseases in countries of the Commonwealth of Independent States (CIS) revealed a prevalence of 19.5 asthma cases per 1000 individuals, with wheezing symptoms affecting approximately 25% of the adult population [16,18]. A broader trend of increasing asthma prevalence has been observed across Central Asia, suggesting that environmental and lifestyle factors significantly impact the epidemiology of asthma in the region. Specifically, industrial emissions and particulate matter (PM) in the Abay region are likely contributing to the rising number of respiratory diseases. Extensive studies on air pollution in major cities of Kazakhstan indicate that air quality often fails to meet safety standards, which correlates with increased respiratory issues among the population [6, 20]. During the cold season, elevated levels of PM exacerbate asthma attacks and other respiratory illnesses. Although direct studies on the correlation between air pollution levels and asthma symptoms in Kazakhstan are limited, data from neighboring regions suggests similar patterns [20]. High rates of smoking and obesity in the population are also contributing to the increasing number of asthma cases [16, 14]. Research on the ADRB2 gene in Kazakhstan has found certain genetic variations that might make people more prone to asthma, suggesting that genetics play a role in asthma susceptibility and development [1, 2]. The economic impact of underreporting asthma is significant, as it often leads to a loss of productivity. The differences between official statistics and independent studies highlight the need for more accurate data collection and reporting [20, 16]. Urban areas, where industrial activity is more concentrated, would benefit from better diagnostic methods and improved asthma management strategies [14, 19].

Timely diagnosis has been shown to significantly impact the long-term management of asthma. Early diagnosis can reduce the frequency and severity of asthma exacerbations. Studies indicate that children diagnosed early are less likely to experience severe symptoms compared to those diagnosed later [13]. The early implementation of diagnostic methods such as spirometry and bronchial challenge tests is crucial for recognizing asthma at its onset. Spirometry is commonly used to evaluate lung function, while bronchial challenge tests help determine airway hyperresponsiveness both are essential tools in the assessment of asthma. Research into asthma exacerbations has contributed significantly to improving approaches to diagnosis and treatment. Importantly, children diagnosed with asthma before the age of six are more likely to experience more frequent and severe symptoms of the disease. [15].

A number of previous studies have consistently demonstrated a link between elevated levels of immunoglobulin E (IgE) and eosinophilic cationic protein (ECP) and greater asthma severity [10, 11]. The results of this study support those findings, particularly with regard to IgE, which showed a statistically significant association with asthma severity ($p = 0.001$). In contrast, no significant correlation was observed between ECP levels and disease severity ($p > 0.05$), suggesting that the role of ECP in asthma may be influenced by additional factors or may vary depending on specific environmental or individual conditions. These results highlight the importance of conducting further research in the Abay Region to better understand the involvement of ECP in asthma-related inflammation.

Additionally, environmental factors, especially damp living conditions, appeared to have an impact on biomarker levels. Participants living in moisture-damaged or humid dwellings exhibited higher concentrations of both IgE and ECP, reinforcing the established understanding that environmental exposures can significantly contribute to asthma exacerbation regardless of geographic context [10]. An interesting finding in this study was that nasal congestion was more commonly seen in children with milder asthma, while a history of seasonal allergies was linked to more severe cases. This is different from what previous studies have shown, suggesting that asthma in the Abay region might have some unique characteristics that need further exploration. The clinical significance of these results is clear. With more than half of the participants (56.3%) being newly diagnosed, it highlights the importance of early detection and timely intervention. For children with a family history of allergies, keeping track of symptoms like nasal congestion and seasonal allergies could help identify asthma at an earlier stage [7].

**Conclusion**

This study sheds light on the role of environmental and allergic factors in the development of bronchial asthma among children and adolescents in the Abay region. Damp housing and seasonal allergens were frequently linked to more severe symptoms. Children with higher ECP and IgE levels tended to have more pronounced forms of asthma, reinforcing their potential use as clinical indicators.

The fact that over half of the children were newly diagnosed suggests that asthma remains underdiagnosed in pediatric care. These results highlight the importance of early identification—especially in children with allergic family histories or persistent respiratory symptoms.

Improving living conditions, particularly by addressing indoor dampness, and implementing allergen control strategies may help reduce asthma severity. Routine testing for ECP and IgE could also support more accurate risk assessment and individualized treatment planning.

***Study Limitations:*** *The single-center nature of the study may limit its generalizability, and the absence of long-term follow-up data restricts the assessment of post-discharge outcomes.*

***Author Contributions****: All authors contributed equally to the writing of this manuscript.*

***Conflict of Interest:*** *The authors declare no conflicts of interest. This material has not been submitted to other journals and is not under consideration elsewhere.*

***Funding:*** *No funding was received for this study.*

***References:***

1. *Akparova A., Abishev M., Abdrakhmanova B.* et al. Identification of the unique and common genes for asthma and chronic obstructive pulmonary disease: a case-control study in Kazakhstan. International Journal of Biology and Chemistry. 2018. Vol. 11. №. 2. p. 21-27.

2. *Akparova A., Aripova A., Abishev M.* et al. An investigation of the association between ADRB2 gene polymorphisms and asthma in Kazakh population. The clinical respiratory journal. 2020. Vol. 14. №. 6. p. 514-520.

3. *Alqahtani J.M.* Asthma and other allergic diseases among Saudi schoolchildren in Najran: the need for a comprehensive intervention program. Annals of Saudi Medicine. 2016. VOL. 36. №. 6. p. 379-385.

4. *Altynova N.K., Khamdiyeva, O.K., Zhaniyazov, Z.A.* et al. A genome-wide association study for different types allergic diseases. International Journal of Biology and Chemistry. 2022. Vol. 15. №. 2. p. 25-39.

5. *Anenberg S.C., Henze D.K., Tinney V. et al.* Estimates of the global burden of ambient PM 2.5, ozone, and NO 2 on asthma incidence and emergency room visits. Environmental health perspectives. 2018. Vol. 126. №. 10. p. 107004.

6. *Assanov D., Zapasnyi V., Kerimray A.* Air quality and industrial emissions in the cities of Kazakhstan. Atmosphere. 2021. Vol. 12. №. 3. p. 314.

7. *Begum A., Sattar H., Sattar A.N.* et al. Serum Eosinophilic cationic protein (ECP) as an effective biological marker to monitor therapy in bronchial asthma patients. Bangladesh Journal of Medical Microbiology. 2011. Vol. 5. №. 1. p. 3-7.

8. *Bharadwaj P., Verma R., Deshkar A.M.* et al. Asthma and Obesity-the Recent Advancements. MVP Journal of Medical Sciences. 2015. p. 124-127.

9. *Dharmage S.C., Perret J.L., Custovic A.* Epidemiology of asthma in children and adults. Frontiers in pediatrics. 2019. Vol. 7. p. 246.

10. *Kovačević S., Bogić M., Perić-Popadić A.* et al. The serum eosinophil cationic protein concentration in patients with bronchial asthma and its correlation with severity and exacerbation of the disease. Jugoslovenska medicinska biohemija. 2003. Vol. 22. №. 3. p. 249-253.

11. *Lin S., Yan D., Chao H.* Influence of atopy and concomitant sinusitis on serum eosinophil cationic protein levels in asthmatic children. Pediatric Asthma Allergy & Immunology. 2000. Vol. 14. №. 3. p. 197-203.

12. *Lion-Cachet H.C., Musonda J.M.M., Omole O.B.* Severe asthma in South Africa: A literature review and management approach for primary care. South African Family Practice. 2021. Vol. 63. №. 1. p. 5179.

13. *Lynch B. A., Van Norman C. A., Jacobson R.M.,* et al. Impact of delay in asthma diagnosis on health care service use. Allergy and asthma proceedings: the official journal of regional and state allergy societies. 2010. Vol.31. №.4. p. e48.

14. *Mamyrbekova S., Iskakova G., Faizullina K.* et al. The diagnostic accuracy of spirometry versus peak expiratory flow test for follow-up of adult asthma patients at primary care level. Allergy & Asthma Proceedings. 2022. VOL. 43. №. 5. p. e58-e64.

15. *Nasreen S., Wilk P., Mullowney T.* et al. Asthma exacerbation trajectories and their predictors in children with incident asthma. Annals of Allergy, Asthma & Immunology. 2019. Vol. 123. №. 3. p. 293-300. e2.

16. *Nugmanova D., Sokolova L., Feshchenko Y.* et al. The prevalence, burden and risk factors associated with bronchial asthma in commonwealth of independent states countries (Ukraine, Kazakhstan and Azerbaijan): results of the CORE study. BMC pulmonary medicine. 2018. Vol. 18. p. 1-11.

17. *Sa-Sousa A., Morais-Almeida M., Azevedo L.F.* et al. Prevalence of asthma in Portugal-the Portuguese national asthma survey. Clinical and translational allergy. 2012. Vol. 2. p. 1-12.

18. *Tabyshova A., Emilov B., Postma M.J.* et al. Prevalence and economic burden of respiratory diseases in central Asia and Russia: a systematic review. International Journal of Environmental Research and Public Health. 2020. Vol. 17. №. 20. p. 7483.

19. *Turdaliyeva B., Kulzhanov M., Akhmetov V.* et al. Unraveling the Relationship Between Cultural Food Habits and Chronic Obstructive Pulmonary Disease in Men: A Case-Control Study in Kazakhstan. 2023. p. 1-15.

20. *Vinnikov D., Tulekov Z., Raushanova A.* Occupational exposure to particulate matter from air pollution in the outdoor workplaces in Almaty during the cold season. PLoS One. 2020. Vol. 15. №. 1. p. e0227447

**Information about the authors:**
**Furlan Andrei,** Student of University of Medicine and Pharmacy "Victor Babeș" Timișoara, Romania, https://orcid.org/0009-0004-7603-8731
**Mukasheva Gulbarshyn Darynkyzy** - Senior Teacher of the Department of Epidemiology and Biostatistics, NCJSC "Semey Medical University", Semey, Kazakhstan; E-mail: gulbarshyn_1_12@mail.ru; phone +7 775 220 07 45, https://orcid.org/0000-0003-3490-5628;
**Maukayeva Saule Boranbayevna** - Candidate of Medical Sciences, Associate Professor of the Department of Infectious Diseases, Dermatovenerology and Immunology, NCJSC «Semey Medical University» phone: 8 705 529 66 75, e-mail: solly66@mail.ru, https://orcid.org/0000-0002-2679-6399, Semey, Kazakhstan;
**Kudaibergenova Nazym Konyrovna** - Candidate of Medical Sciences, Associate Professor of the Department of Infectious Diseases, Dermatovenerology and Immunology, NCJSC «Semey Medical University», phone: 8 705 188 08 36, e-mail: nazym.kudaibergenova@smu.edu.kz, https://orcid.org/0000-0002-6165-7677, Semey, Kazakhstan;
**Shabdarbayeva Dariya Muratovna** – Doctor of Medical Sciences, Professor, Vice Rector for Science and Strategic Development", NCJSC «Semey Medical University», phone 8 707 365 82 71, e-mail: dariya_kz@bk.ru, https://orcid.org/0000-0001-9463-1935, Semey, Kazakhstan;
**Smailova Zhanargyl Kaiyrgaliyevna** - Candidate of Medical Sciences, Associate Professor, Vice Rector for Academic and Educational Work, NCJSC «Semey Medical University», phone 8 707 365 82 71, e-mail: zhanargul.smailova@smu.edu.kz; https://orcid.org/0000-0002-4513-4614
**Turakhanova Botagoz Seilovna -** Assistant, department of infectious diseases, dermatovenerology and immunology, NCJSC «Semey Medical University», phone: 8 778 177 12 25, Kazakhstan. E-mail: botagoz.turakhanova@smu.edu.kz, ORCID 0009-0003-0480-7063, Semey, Kazakhstan;
**Kozubayeva Dinara Begimhanovna -** Assistant, department of infectious diseases, dermatovenerology and immunology, NCJSC «Semey Medical University», phone: 8 775 342 16 44, Kazakhstan. E-mail: dinara_begimhanovna@mail.ru, ORCID 0000-0003-4937-708X, Semey, Kazakhstan;
**Goremykina Maya Valentinovna** - Candidate of Medical Sciences, Associate Professor, Department of Internal Medicine and Rheumatology, NCJSC «Semey Medical University», 103 Abay street, Semey, 071400, Kazakhstan; Email: maya.goremykina@smu.edu.kz; phone number: +7 (777) 390 8234; https://orcid.org/0000-0002-5433-7771;
**Issabekova Zhanar Bakytzhanovna** - Assistant of the Department of Infectious Diseases, Dermatovenerology and Immunology, NCJSC "Semey Medical University", phone: 8 775 176 08 09, e-mail: zhanara_ib87@mail.ru, https://orcid.org/0000-0002-2744-0327, Semey, Kazakhstan;
**Karimova Saya Sayankyzy** - Assistant, department of infectious diseases, dermatovenerology and immunology, NCJSC «Semey Medical University», phone: 8 701 106 96 13, Kazakhstan. E-mail: saya.karimova.94@mail.ru, ORCID 0000-0002-1167-5375, Semey, Kazakhstan;
**Urazalina Nailya Muratkhanovna** - Candidate of Medical Sciences, Associate Professor of the Department of physiological disciplines named after honored scientist of the republic of Kazakhstan, professor T.A. Nazarova, NJSC "Semey Medical University", Semey, Kazakhstan; phone: 8 777 907 55 89, e-mail: hakim_15@mail.ru, https://orcid.org/0000-0003-0200-1763,

***Correspondence author:**
**Mukasheva Gulbarshyn Darynkyzy** - Senior Teacher of the Department of Epidemiology and Biostatistics, NCJSC "Semey Medical University", Semey, Kazakhstan,
**Postal code:** Republic of Kazakhstan, 071400, Semey city, Abay Street 103.
**E-mail:** gulbarshyn_1_12@mail.ru
**Phone:** +7 775 220 07 45

Received: 09 August 2024 / Accepted: 15 April 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2024.27.3.014***

***UDC 616.344-002-031.84***

This work is licensed under a Creative Commons Attribution 4.0 International License

# EXPERIENCE USING CAPSULE ENDOSCOPY

**Laura K. Yerdalieva [1-2], https://orcid.org/0009-0005-1489-2227**
**Aisulu E. Gainutdin[1-2], https://orcid.org/0000-0002-5629-3848**
**Alexander V. Nersesov[1-2], https://orcid.org/0000-0002-8601-3966**
**Aigul M. Raisova[1-2], https://orcid.org/0000-0001-8799-3401**
**Dinara S. Suleimenova[1-2], https://orcid.org/0000-0002-6239-0580**
**Nazugum A. Ashimova[1-2], https://orcid.org/0000-0003-1011-1452**
**Saltanat S. Madenova[1-2], https://orcid.org/0009-0005-3513-3318**
**Maygul A. Shamshidinova[1-2], https://orcid.org/0000-0001-7765-6401**
**Gulzukhram U. Abdullaeva[1-2],**
**Akmaral Arzhyl G. Zhakipova[3], https://orcid.org/0000-0002-2012-5754**
**Zarina S. Seitkabilova[1],**
**Gaukhar A. Baiduisenova[1], https://orcid.org/0009-0009-2091-9501**
**Bek S. Yerengaiyp[1-2], https://orcid.org/0009-0004-8831-828X**
**Feruza N. Nurbekova[1]**

**[1] Kazakh National Medical University named after S.D. Asfendiyarov, Department of Gastroenterology, Almaty, Republic of Kazakhstan;**
**[2] Interna Clinic - Institute of Gastroenterology, Hepatology and Metabolism, Almaty, Republic of Kazakhstan;**
**[3] Semey Medical University, Department of pathological anatomy and forensic medicine, Semey, Republic of Kazakhstan.**

**Abstract**

**Relevance:** Based on the analysis of the results of videocapsular endoscopy of 84 patients with signs of gastrointestinal pathology and the results of a pathoanatomic examination of biopsy material taken during colonoscopy of the same 84 patients (52 of them have biopsy results), the reliability, features, principles and possibilities of using capsule endoscopy as a research method for diseases of the gastrointestinal tract are determined in the article.

**Aim:** to determine the effectiveness of capsule endoscopy in the diagnosis of gastrointestinal disease.

**Materials and methods:** From 2022 to 2023 84 capsule endoscopy studies (hereinafter referred to as CE) were conducted at the Interna clinic in Almaty. Patient identification data, diagnoses, reasons for examination, and underlying disease were collected. The results of the examination were collected and analyzed, and the results of the pathoanatomical examination of the biopsy material of the same patients were studied, which were conducted by the laboratory of Pathomorphology in the conditions of the A.N. Syzganov National Scientific Center of Surgery JSC.

**Results:** The research material presents the diagnostic capabilities of capsule endoscopy for the detection of diseases of the gastrointestinal tract.

**Conclusions:** Videocapsular endoscopy is a modern, non-invasive and highly informative research method that helps solve many issues of diagnosis and choice of therapeutic tactics in diseases of the small intestine. In Kazakhstan, capsule endoscopic method has been carrying out since 2014 and due to evolving burden of bowel disease worldwide, including Kazakhstan, where the quality of research on capsule endoscopy meets international standards, we undoubtedly consider that further research is needed for its wider introduction into clinical practice.

***Key words:*** *capsule endoscopy, biopsy, gastrointestinal tract.*

***For citation:***

Yerdalieva L.K., Gainutdin A.E., Nersesov A.V., Raisova A.M., Suleimenova D.S., Ashimova N.A., Madenova S.S., Shamshidinova M.A., Abdullaeva G.U., Zhakipova A.A., Seitkabilova Z.S., Baiduisenova G.A., Yerengaiyp B.S., Nurbekova F.N. Experience using capsule endoscopy // Nauka i Zdravookhranenie [Science & Healthcare]. 2025. Vol.27 (3), pp. 125-134. doi 10.34689/SH.2025.27.3.014

**Резюме**

# ОПЫТ ИСПОЛЬЗОВАНИЯ КАПСУЛЬНОЙ ЭНДОСКОПИИ

**Лаура К. Ердалиева[1-2], https://orcid.org/0009-0005-1489-2227**
**Айсулу Е. Гайнутдин[1-2], https://orcid.org/0000-0002-5629-3848**
**Александр В. Нерсесов[1-2], https://orcid.org/0000-0002-8601-3966**
**Айгуль М. Раисова[1-2], https://orcid.org/0000-0001-8799-3401**
**Динара С. Сулейменова[1-2], https://orcid.org/0000-0002-6239-0580**
**Назугум А. Ашимова[1-2], https://orcid.org/0000-0003-1011-1452**
**Салтанат С. Маденова[1-2], https://orcid.org/0009-0005-3513-3318**
**Майгуль А. Шамшидинова[1-2], https://orcid.org/0000-0001-7765-6401**
**Гульзухрам У. Абдуллаева[1-2],**
**Акмарал А. Жакипова[3], https://orcid.org/0000-0002-2012-5754**
**Зарина С. Сейткабилова[1],**
**Гаухар А. Байдуйсенова[1], https://orcid.org/0009-0009-2091-9501**
**Бек С. Еренгайып[1-2], https://orcid.org/0009-0004-8831-828X**
**Феруза Н. Нурбекова[1],**

**[1] НАО «Казахский Национальный медицинский университет им. С.Д. Асфендиярова», Кафедра гастроэнтерологии, г. Алматы, Республика Казахстан;**
**[2] Interna Clinic - Институт гастроэнтерологии, гепатологии и метаболизма, г. Алматы, Республика Казахстан;**
**[3] НАО «Медицинский университет Семей», Кафедра патологической анатомии и судебной медицины, г. Семей, Республика Казахстан.**

**Актуальность:** Видеокапсульная эндоскопия является современным, неинвазивным и высокоинформативным методом исследования, который помогает решить многие вопросы диагностики и выбора лечебной тактики при заболеваниях тонкого кишечника. В данной статье показаны диагностические возможности применения капсульной эндоскопии для выявления заболеваний желудочно-кишечного тракта у 84 пациентов и описан клинический случай диагностики и постановки точного диагноза.

**Цель работы:** определение эффективности капсульной эндоскопии в диагностике заболевании ЖКТ.

**Материалы и методы:** С 2022г. по 2023г. В Interna clinic в Алматы было проведено 84 исследовании капсульной эндоскопии (далее КЭ). Собирались идентификационные данные пациентов, диагнозы, причины обследования, основное заболевание. Результаты КЭ были собраны и проанализированы, а также были изучены результаты патологоанатомического исследования биологического материала этих же пациентов, которые были проведены в лаборатории патоморфологии в условиях АО «Национальный научный центр хирургии им. А.Н. Сызганова».

**Результаты:** В исследовательском материале представлены диагностические возможности капсульной эндоскопии для выявления заболевании желудочно-кишечного тракта.

**Выводы:** Качество исследования капсульной эндоскопии соответствует мировым стандартам, но, несомненно, необходимы дальнейшие исследования для более широкого внедрения ее в клиническую практику. В Казахстане капсульный эндоскопический метод применяется с 2014 года, и в связи с растущим распространением заболеваний кишечника во всем мире, включая Казахстан, где качество исследований в области капсульной эндоскопии соответствует международным стандартам, мы, несомненно, считаем, что необходимы дальнейшие исследования для его более широкого внедрения в клиническую практику

***Ключевые слова**: капсульная эндоскопия, биопсия, желудочно-кишечный тракт.*

***Для цитирования:***

*Ердалиева Л.К., Гайнутдин А.Е., Нерсесов А.В., Раисова А.М., Сулейменова Д.С., Ашимова Н.А., Маденова С.С., Шамшидинова М.А., Абдуллаева Г.У., Жакипова А.А., Сейткабилова З.С., Байдуйсенова Г.А., Еренгайып Б.С., Нурбекова Ф.Н.* Опыт использования капсульной эндоскопии // Наука и Здравоохранение. 2025. Т.27 (3). С. 125-134. doi 10.34689/SH.2025.27.3.014

**Түйіндеме**

# КАПСУЛАЛЫҚ ЭНДОСКОПИЯНЫ ҚОЛДАНУ ТӘЖІРИБЕСІ

**Лаура К. Ердалиева[1-2], https://orcid.org/0009-0005-1489-2227**
**Айсулу Е. Гайнутдин[1-2], https://orcid.org/0000-0002-5629-3848**
**Александр В. Нерсесов[1-2], https://orcid.org/0000-0002-8601-3966**
**Айгуль М. Раисова[1-2], https://orcid.org/0000-0001-8799-3401**
**Динара С. Сулейменова[1-2], https://orcid.org/0000-0002-6239-0580**
**Назугум А. Ашимова[1-2], https://orcid.org/0000-0003-1011-1452**
**Салтанат С. Маденова[1-2], https://orcid.org/0009-0005-3513-3318**
**Майгуль А. Шамшидинова[1-2], https://orcid.org/0000-0003-1011-1452**
**Гульзухрам У. Абдуллаева[1-2],**
**Акмарал А. Жакипова[3], https://orcid.org/0000-0002-2012-5754**
**Зарина С. Сейткабилова[1],**
**Гаухар А. Байдуйсенова[1], https://orcid.org/0009-0009-2091-9501**
**Бек С. Еренгайып[1-2], https://orcid.org/0009-0004-8831-828X**
**Феруза Н. Нурбекова[1],**

**1 «С.Ж. Асфендияров атындағы Қазақ ұлттық медицина университеті» КЕАҚ, Гастроэнтерология кафедрасы, Алматы қ., Қазақстан Республикасы;**
**2 Interna Clinic - Гастроэнтерология, Гепатология және Метаболизм институты, Алматы қ., Қазақстан Республикасы;**
**3 «Семей медицина университеті» КЕАҚ, Патологиялық анамтомия және соттық медицина кафедрасы, Семей қ., Қазақстан Республикасы.**

**Өзектілігі:** Мақалада асқазан-ішек жолдарының патологиясының белгілері бар 84 пациенттің бейнекапсулалық эндоскопия нәтижелерін және осы 84 пациенттің колоноскопиясы кезінде алынған биопсиялық материалды патологиялық-анатомиялық зерттеу нәтижелерін талдау негізінде (оның 52-сінде биопсия нәтижелері бар) асқазан-ішек жолдарының ауруларында зерттеу әдісі ретінде капсулалық эндоскопияны қолданудың сенімділігі, ерекшеліктері, принциптері мен мүмкіндіктері анықталды.

**Мақсаты:** асқазан-ішек ауруларын диагностикалауда капсулалық эндоскопияның тиімділігін анықтау**.**

**Материалдар мен әдістер:** 2022 жылдан 2023 жылға дейін Алматыдағы Interna clinic-те капсулалық эндоскопияға (бұдан әрі-КЭ) 84 зерттеу жүргізілді. Пациенттердің сәйкестендіру деректері, диагноздары, тексеру себептері, негізгі ауру жиналды. Еэ нәтижелері жиналды және талданды, сондай-ақ ұлттық ғылыми хирургия орталығы АҚ жағдайында патоморфология зертханалары жүргізген осы пациенттердің биопсиялық материалын патологиялық-анатомиялық зерттеу нәтижелері зерттелді. А. Н. Сызғанова.

**Нәтижелер:** Зерттеу материалы асқазан-ішек жолдарының ауруларын анықтау үшін капсулалық эндоскопияның диагностикалық мүмкіндіктерін ұсынады.

**Қорытындылар:** Видеокапсулалық эндоскопия-бұл қазіргі заманғы, инвазивті емес және өте ақпараттандырылған зерттеу әдісі, ол көптеген диагностикалық мәселелерді шешуге және аш ішек ауруларында емдеу тактикасын таңдауға көмектеседі. Капсулалық эндоскопияны зерттеудің сапасы әлемдік стандарттарға сәйкес келеді, бірақ оны клиникалық тәжірибеге кеңінен енгізу үшін қосымша зерттеулер қажет.

**Түйінді сөздер:** капсулды эндоскопия, биопсия, асқазан- ішек жүйесі.

***Дәйексөз үшін:***

*Ердалиева Л.К., Гайнутдин А.Е., Нерсесов А.В., Раисова А.М., Сулейменова Д.С., Ашимова Н.А., Маденова С.С., Шамшидинова М.А., Абдуллаева Г.У., Жакипова А.А., Сейткабилова З.С., Байдуйсенова Г.А., Еренгайып Б.С., Нурбекова Ф.Н.* Капсулалық эндоскопияны қолдану тәжірибесі // ғылым және Денсаулық сақтау. 2025. Т.27 (3). Б. 125-134. doi 10.34689/SH.2025.27.3.014

**Relevance**

Capsule endoscopy is currently widely used as a method of diagnosing diseases of the small intestine. It is considered a minimally invasive method of diagnosing inflammatory and tumor diseases of the gastrointestinal tract.

This study can be used as a screening method for detecting gastrointestinal cancer, as well as in patients who either refused colonoscopy or it is contraindicated for one reason or another. It is mainly used to identify the cause of gastrointestinal blood loss or bleeding, for example, ulcers, tumors or vascular malformations of the small intestine, to determine the degree of damage to the small intestine. (Figure 1,2).

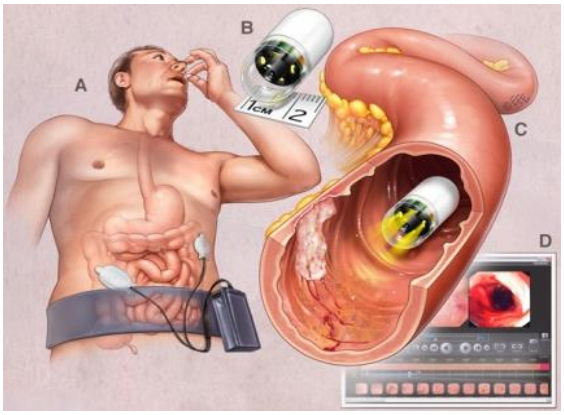



**Figure 1. Process of the capsule endoscopic examination**

**Figure 2. "MicroCam" endoscopic capsule which is used for the examination process.**

**Materials and methods:**

From 2022 to 2023 84 capsule endoscopy studies were conducted at the «Interna clinic» in Almaty. Experienced gastroenterologists and endoscopists selected patients who were in need to diagnose diseases of the small intestine, according to methodological recommendations.

This project was implemented as follows: All capsule endoscopies were performed on an outpatient basis at the Interna clinic. After carrying out explanatory work on the examination and tests, all patients signed an informed consent and proceeded an examination. The patient followed a non-slag diet, excluded from the diet for 3 days (drugs that can stain the mucous membrane and contents of the intestine, products containing small seeds: grains, nuts, grapes, poppy seeds; milk, beetroot, borscht, greens); On the day of preparation, they drank only transparent liquids (transparent broth, green tea, still water) during the day in unlimited quantities. Next step patients depleted their intestines with preparations based on Polyethylene glycol (PEG) and electrolytes. On the day of installation of the capsule endoscopy receiver, the patient swallowed the capsule on his own, and 24 hours later handed over the capsule endoscopy receiver to the doctor. After receiving the images from the patient, they were encrypted. Separation from the dome of the caecum to the ileum, assessment of the visible area and detection of damage were performed using an artificial intelligence algorithm, and the analyzed images were evaluated and confirmed by an endoscopist and gastroenterologist. Also, out of 84 patients, 52 patients underwent colonoscopy with biopsy and were compared with the results of capsule endoscopy.

Patient identification data, diagnosis, reasons for examination, underlying disease and the result of capsule endoscopy examination and biopsy results were collected. The results of capsule endoscopy, such as the passage time through the stomach, duodenum, small intestine and colon, as well as the delay or complications of capsule endoscopy in the small intestine, were collected and studied. The results of the pathomorphological examination of the biopsy material of the same patients, which were performed in the laboratory of pathomorphology in conditions of the A.N. Syzganov National Scientific Center of Surgery, were considered.

**Results:**

Among 84 patients, the average age of all patients was 41.3 years, min: 9 years, max: 77 years.

The number of female patients is 51, the average age was 44.4 years min: 18 years, max: 77 years, the number of male patients is 33, the average age was 36.6 years, min: 9 years, max:62 years. According to the results of capsule endoscopy: Crohn's disease – 41(48,8%), ulcerative colitis – 8 (9,5% ), celiac disease - 9 (10,7%), others - 26 (31%).

*Table 1.*

**Results of the actual study divided by gender, symptoms and diagnosed diseases.**

| | |
|---|---|
| **The gender** | |
| Man | 51(60,7) |
| Women | 33(39,3) |
| **Symptoms** | |
| Abdominal pain | 36(42,8%) |
| Chronic diarrhea | 33(39,3%) |
| Weight Loss | 4(4,7%) |
| Gastrointestinal bleeding | 3(3,6%) |
| Constipation | 2(2,4) |
| Anemia | 6(7,2) |
| **Nosology** | |
| Crohn's disease | 41(48,8%) |
| Ulcerative colitis | 8(9,5%) |
| Celiac disease | 9(10,7%) |
| Enteritis | 15(17,8%) |
| Focal colitis | 7(8,3%) |
| Erosive colitis | 2(2,3%) |
| Polyp | 2(2,3%) |

According to the results of the pathoanatomic examination of the biopsy material (Chart 1), there are 52 patients in total. The number of male patients is 20, of which ulcerative colitis – 1 (5%), Crohn's disease – 6 (30%), celiac disease-3 (15%), others- 10 (50%).

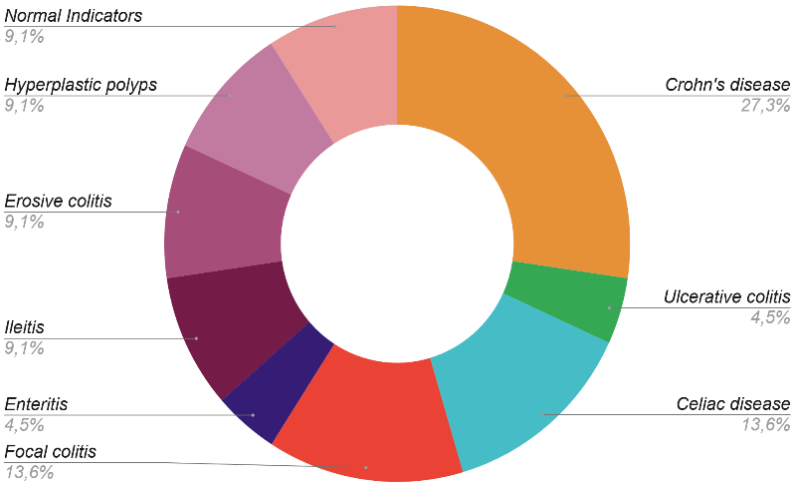



**Figure 1. Process of the capsule endoscopic examination.**

The total number of patients with biopsy results is 52.
Men – 20. Of these:

- UC – 1;
- CD – 6;
- Celiac disease – 10;
- Others – 10:

1. Focal colitis – 3 (13.6%)
2. Enteritis – 1 (4.5%)
3. Ileitis – 2 (9.1%)
4. Erosive colitis – 2 (9.1%)
5. Hyperplastic polyps – 2 (9.1%)
6. Normal Indicators – 2 (9.1%)

**Figure 2. "MicroCam" endoscopic capsule which is used for the examination process.**

**Chart 1. The results of the histological examination in male group of patients.**

**The total number of female patients with biopsy results is 32. Of these:**

- **UC – 6;**
- **CD – 13;**
- **Celiac disease – 3;**
- **Others – 10:**

1. **Focal colitis – 4 (11.4%)**
2. **Enteritis – 1 (2.9%)**
3. **Ileitis – 4 (11.8%)**
4. **Lymphocytic ileitis – 1 (2.9%)**
5. **Lymphangiectasia of the small intestine – 1 (2.9%)**
6. **Normal Indicators – 2 (5.9%)**

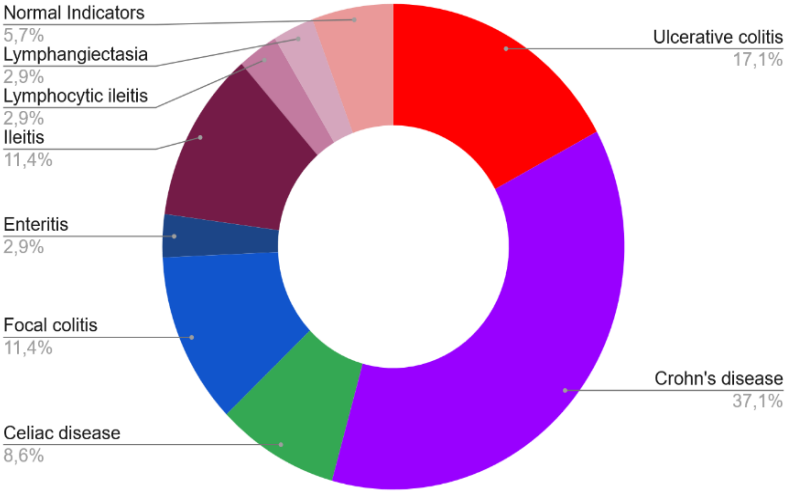



**Chart 2. The results of the histological examination in female group of patients.**

The number of female patients is 32 (Chart 2). Of these, ulcerative colitis – 6 (18,8), Crohn's disease – 13 (40,6%), celiac disease – 3 (9,4%), others- 10 (31,3%).

Thus, when comparing the results of the capsule endoscopy and the results of the biopsy in 49 cases, the conclusions were similar, which corresponds to 94.2%. In 1 case, an incomplete capsule endoscopy study, where morphologically celiac disease was confirmed - 2%, in 1 case, the patient was observed with ulcerative colitis disease, with capsule endoscopy, normal small intestine parameters, morphology corresponded to Crohn's disease - 2%, in 1 case, the patient was observed with Crohn's disease disease, with capsule endoscopy, normal small intestine parameters, morphology corresponded to ulcerative colitis - 2%.

**Clinical Case**

Patient V., 37 years old, complained of nausea, lack of appetite, dry mouth, bloating, weakness. The disease debuted in 2020 with intoxication syndrome, fever, abdominal pain. She was hospitalized at her place of residence. Then she received inpatient treatment at the Taldykorgan regional hospital, therapy was performed with steroids, with further improvement in her condition, then a diagnosis of Celiac disease was made during the examination. The patient is on a gluten-free diet. This deterioration has been observed since September 2021, in the form of dyspeptic phenomena, fever. According to the colonoscopy, there is no pathology. According to the EGDS, celiac disease. Crohn's disease of the small intestine, diffuse atrophic gastritis. Celiac disease, atypical form, resistant type, morphological stage March 3b. Results of MR enterography: duodenitis, jejunitis, upper mesenteric artery syndrome is not excluded. Against the background of activity, systemic steroids were started in summer of 2022. 27.08.2022 was started induction with Ustekinumab, 21.11.2022 – the second dose. It is known from the anamnesis that the patient has no bad habits, heredity for IBD does not exacerbate, from concomitant diseases: mild asthma, secondary generalized osteoporosis. Vitamin D deficiency. The patient's height is 168 cm, weight is 50 kg. BMI = 17.7 kg/cm2. She underwent an examination in November 2022.

**According to the EGDS data from 2022:** Celiac disease. Erosive bulboadenitis. Crohn's disease of the small intestine. Antral subatrophic gastritis.

**According to colonoscopy data from 2022:** Crohn's disease of the small intestine. Internal hemorrhoids.

**According to histology data from 2022:** The morphological picture corresponds to M.N. Marsh III b celiac disease: pronounced atrophy of the villi of the small intestine.

**According to capsule endoscopy data from 2022**: scallopiness, mosaicism of the mucous membrane and micronodularity in the proximal part of the small intestine. Diffuse villous edema was observed throughout the small intestine, except for the terminal ileum. Focal ulceration was noted in the middle part of the small intestine.

**Diagnosis:** Crohn's disease of the small intestine, minimal activity. Biological therapy with Ustekinumab since 08.27.2022. Celiac disease, resistant type, severe. Morphological stage of Marsh 3 b. (Figure 3-6).

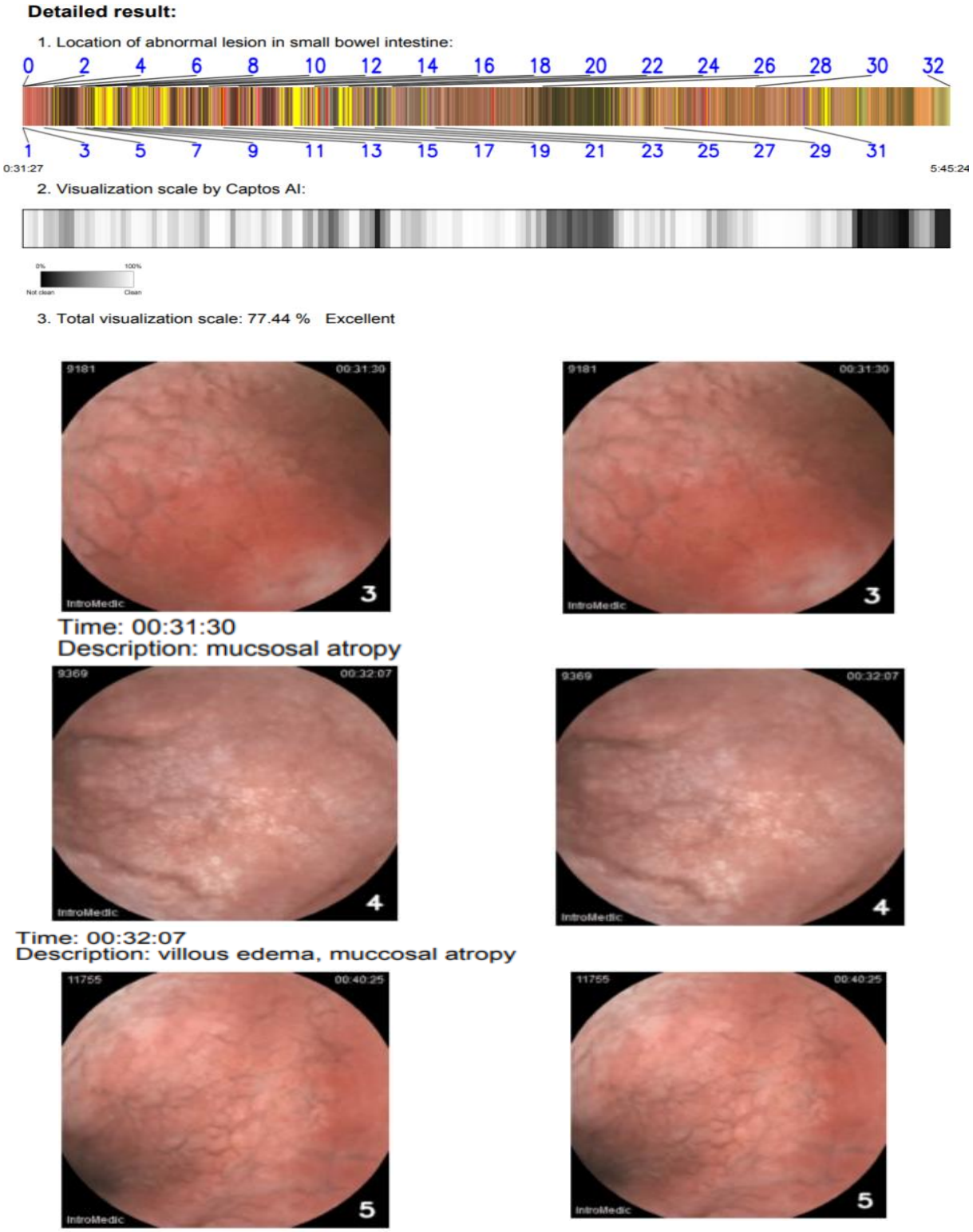
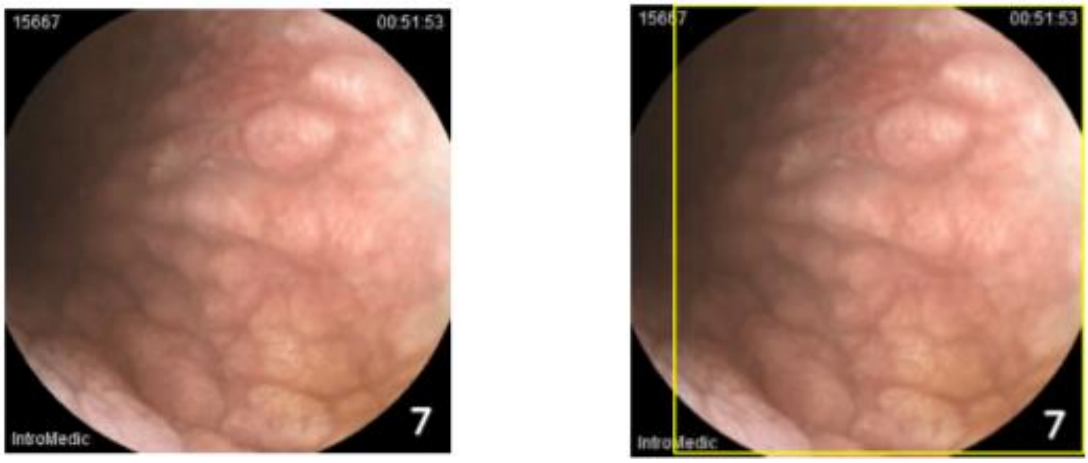
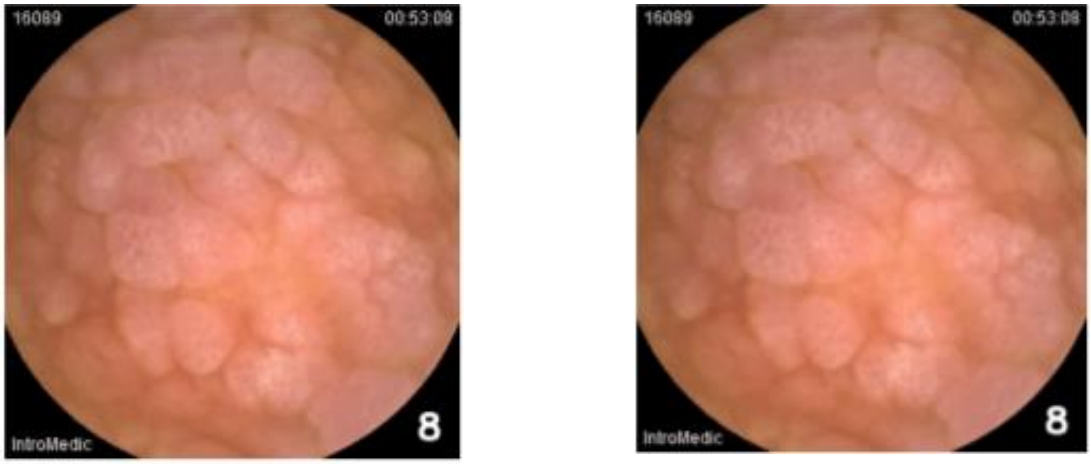



**Figure 3. Signs of Celiac disease as mucosal atrophy in small intestine.**




Time: 00:51:53
Description: scalloping, mosaic pattern, and micronodularity




Time: 00:53:08
Description: scalloping, mosaic pattern, and micronodularity

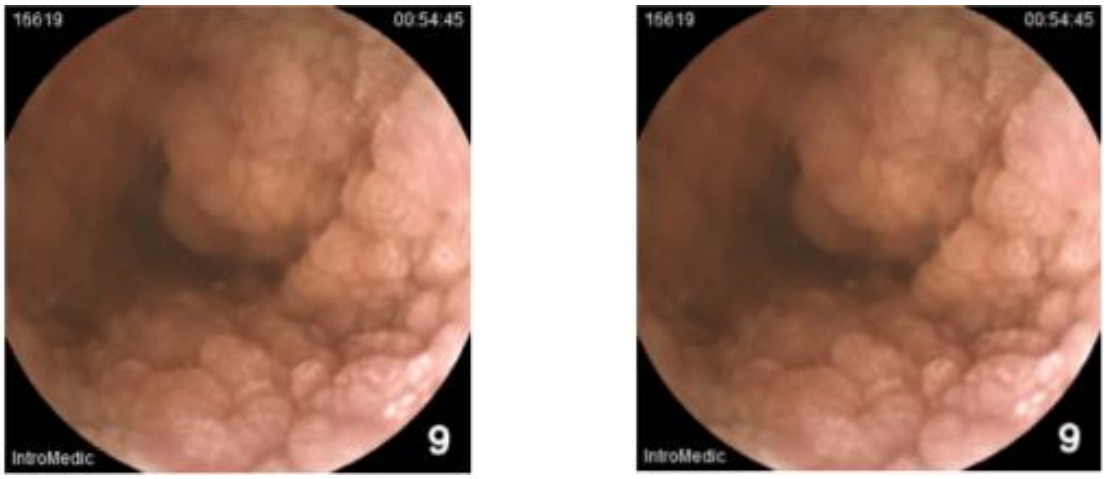



**Figure 4.** Alterations of the mucous membrane in the proximal part of the small intestine.

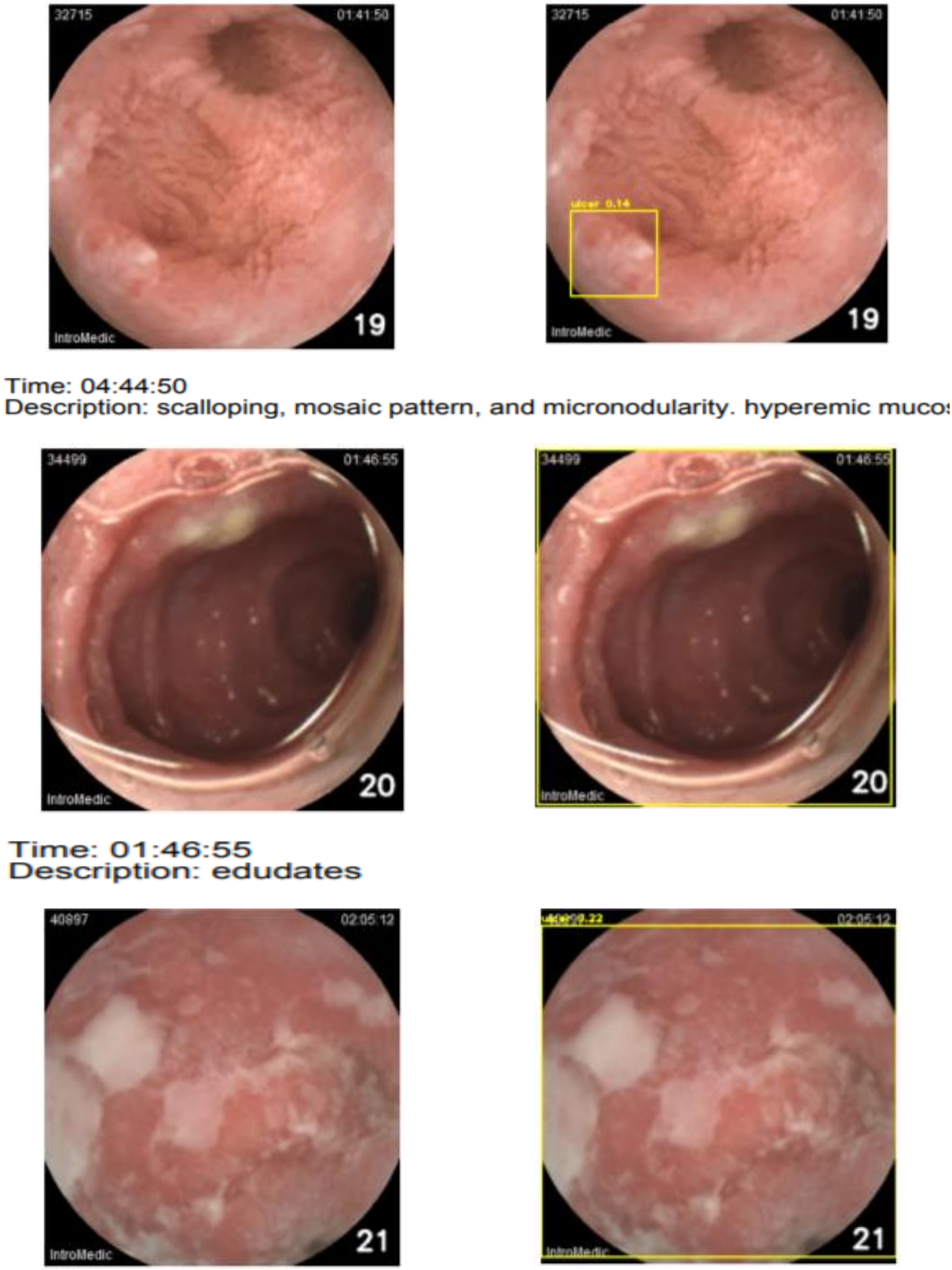



**Figure 5. Signs of inflammatory process in small intestine.**

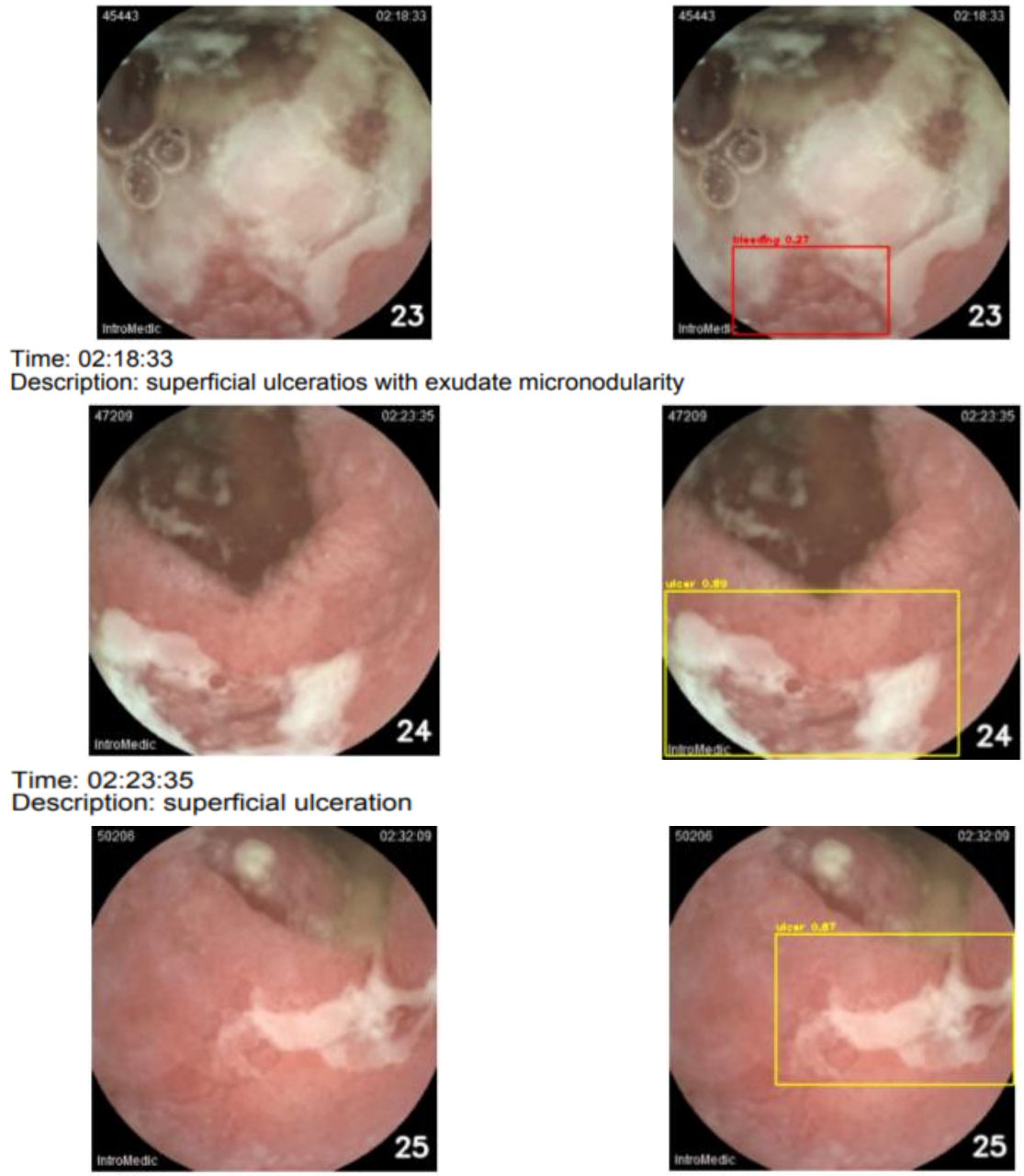



**Figure 6. Ulcerative process in small intestine.**

**Conclusions:**

Videocapsular endoscopy is a modern, non-invasive and highly informative research method that helps solve many issues of diagnosis and choice of therapeutic tactics in diseases of the small intestine. In Kazakhstan, capsule endoscopic method has been carrying out since 2014 and due to evolving burden of bowel disease worldwide, including Kazakhstan, where the quality of research on capsule endoscopy meets international standards, we undoubtedly consider that further research is needed for its wider introduction into clinical practice.

***Conflict of interest.*** *We declare no conflict of interest.*

***Authors' contributions.*** *All authors made an equal contribution to the development of the concept, execution, processing of results and writing the article. We declare that this material has not previously been published and is not under consideration by other publishers.*

***Financing.*** *None.*

***Literature:***

1. *Kaibullayeva J., Ualiyeva A., Oshibayeva A., Dushpanova A., Marshall J.K.* Prevalence and patient awareness of inflammatory bowel disease in Kazakhstan: a cross-sectional study. Intest Res 2020. 18(4):430-437. . DOI: 10.5217/ir.2019.00099.

2. *Enns R.A., Hookey L., Armstrong D., et al.* Clinical Practice Guidelines for the Use of Video Capsule Endoscopy. Gastroenterology, 2017. 152(3):497-514. DOI: 10.1053/j.gastro.2016.12.032.

3. *Ju J., Oh H.S., Lee Y.J. et al.* Clean mucosal area detection of gastroenterologists versus artificia intelligence in small bowel capsule endoscopy. Medicine 2023.102(6):e32883. (In eng). DOI: 10.1097/MD.0000000000032883.

4. *Leandri C., Bordacahar B., Ribiere S., et al.* Usefulness of small-bowel capsule endoscopy in

gastrointestinal bleeding. Presse Med 2017.46(10):903-910. (In fre). DOI: 10.1016/j.lpm.2017.07.006.

5. *Cheung D.Y., Kim J.S., Shim K.N., Choi M.G.* The Usefulness of Capsule Endoscopy for Small Bowel Tumors. Clin Endosc 2016. 49(1):21-5. (In eng). DOI: 10.5946/ce.2016.49.1.21.

6. *Robertson A.R., Yung D.E., Douglas S., Plevris J.N., Koulaouzidis A.* Repeat capsule endoscopy in suspected gastrointestinal bleeding. Scandinavian journal of gastroenterology 2019. 54(5):656-661. (In eng). DOI: 10.1080/00365521.2019.1606932.

7. *Pennazio M., Rondonotti E., Despott E.J., et al.* Small-bowel capsule endoscopy and device-assisted enteroscopy for diagnosis and treatment of small-bowel disorders: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2022. Endoscopy 2023.55(1):58-95. (In eng). DOI: 10.1055/a-1973-3796.

8. *Tominaga K., Sato H., Yokomichi H., et al.* Variation in small bowel transit time on capsule endoscopy. Ann Transl Med 2020. 8(6):348. DOI: 10.21037/atm.2020.02.40.

9. *Vani Sojitra, Pranathi Royal Naradasu, Krina Manojbhai Patel, et al.* Evolving burden of inflammatory bowel disease in women from 1990-2019: Global, regional, national variations, age dynamics, and implications for global health, Inflammatory Bowel Diseases, Volume 30, Issue Supplement_1, February 2024, Pages S30–S31, https://doi.org/10.1093/ibd/izae020.068

**Information about the authors:**

**Yerdalieva Laura Kerimbaevna** - Kazakh National Medical University named after S.D. Asfendiyarov, Department of Gastroenterology, Almaty, Kazakhstan; Interna Clinic - Institute of Gastroenterology, Hepatology and Metabolism, Almaty, Kazakhstan, +77015007263, yerlaura@mail.ru

**Gainutdin Aisulu Ermekovna** - Kazakh National Medical University named after S.D. Asfendiyarov, Department of Gastroenterology, Almaty, Kazakhstan; Interna Clinic - Institute of Gastroenterology, Hepatology and Metabolism, Almaty, Kazakhstan, +77473387471 aisulu_gainutdin@mail.ru, https://orcid.org/0000-0002-5629-3848.

**Nersesov Alexander Vitalevich** - Kazakh National Medical University named after S.D. Asfendiyarov, Department of Gastroenterology, Almaty, Kazakhstan; Interna Clinic - Institute of Gastroenterology, Hepatology and Metabolism, Almaty, Kazakhstan, +77788190642, alexander.nersesov@gmail.com, https://orcid.org/0000-0002-8601-3966.

**Raisova Aigul Muratovna** - Kazakh National Medical University named after S.D. Asfendiyarov, Department of Gastroenterology, Almaty, Kazakhstan; Interna Clinic - Institute of Gastroenterology, Hepatology and Metabolism, Almaty, Kazakhstan, +77772175410, Ram79@mail.ru, https://orcid.org/0000-0001-8799-3401.

**Dinara S. Suleimenova -** Kazakh National Medical University named after S.D. Asfendiyarov, Department of Gastroenterology, Almaty, Kazakhstan; Interna Clinic - Institute of Gastroenterology, Hepatology and Metabolism, Almaty, Kazakhstan, +77017358527, s.dinara.s@mail.ru, https://orcid.org/0000-0002-6239-0580

**Ashimova Nazugum Adilzhanovna** - Kazakh National Medical University named after S.D. Asfendiyarov, Department of Gastroenterology, Almaty, Kazakhstan; Interna Clinic - Institute of Gastroenterology, Hepatology and Metabolism, Almaty, Kazakhstan, +77475662295, anazugum@inbox.ru, https://orcid.org/0000-0003-1011-1452.

**Madenova Saltanat Sabitovna** - Kazakh National Medical University named after S.D. Asfendiyarov, Department of Gastroenterology, Almaty, Kazakhstan; Interna Clinic - Institute of Gastroenterology, Hepatology and Metabolism, Almaty, Kazakhstan, +77017130084, madenova.s@kaznmu.kz, https://orcid.org/0009-0005-3513-3318.

**Maygul A. Shamshidinova** - Kazakh National Medical University named after S.D. Asfendiyarov, Department of Gastroenterology, Almaty, Kazakhstan; Interna Clinic - Institute of Gastroenterology, Hepatology and Metabolism, Almaty, Kazakhstan, +77014484855, maigul.1981@mail.ru, https://orcid.org/0000-0001-7765-6401

**Gulzukhram U. Abdullaeva -** Kazakh National Medical University named after S.D. Asfendiyarov, Department of Gastroenterology, Almaty, Kazakhstan; Interna Clinic - Institute of Gastroenterology, Hepatology and Metabolism, Almaty, Kazakhstan, +77013112892. gulzuxram@gmail.com

**Zhakipova Akmaral Arzhyl- Gaipovna -** Semey Medical University, Department of pathological anatomy and forensic medicine, Semey, Republic of Kazakhstan; zhakipova_akmaral@mail.ru, https://orcid.org/0000-0002-2012-5754

**Zarina S. Seitkabilova -** Kazakh National Medical University named after S.D. Asfendiyarov, Department of Gastroenterology, Almaty, Kazakhstan; Interna Clinic - Institute of Gastroenterology, Hepatology and Metabolism, Almaty, Kazakhstan, +77784733933, zari90.90@mail.ru

**Baiduisenova Gauhar Almatovna** - Kazakh National Medical University named after S.D. Asfendiyarov, Department of Gastroenterology, Almaty, Kazakhstan, 87476016495, gbaidu@bk.ru, https://orcid.org/0009-0009-2091-9501

**Bek Yerengaiyp Samatuly -** Kazakh National Medical University named after S.D. Asfendiyarov, Department of Gastroenterology, Almaty, Kazakhstan. 87085410018 bek.erengaiyp97@mail.ru, https://orcid.org/ 0009-0004-8831-828X

**Feruza N. Nurbekova** - Kazakh National Medical University named after S.D. Asfendiyarov, Department of Gastroenterology, Almaty, Kazakhstan; Interna Clinic - Institute of Gastroenterology, Hepatology and Metabolism, Almaty, Kazakhstan, +77477507056, nurbekovaf@list.ru

***Correspondence author:**

**Gainutdin Aisulu Ermekovna** - Kazakh National Medical University named after S.D. Asfendiyarov, Department of Gastroenterology, Almaty, Kazakhstan; Interna Clinic - Institute of Gastroenterology, Hepatology and Metabolism, Almaty, Kazakhstan, https://orcid.org/0000-0002-5629-3848

**Post address**: Kazakhstan, Almaty.

**E-mail:** aisulu_gainutdin@mail.ru

**Phone:** +7 747 338 74 71

Received: 29 January 2025 / Accepted: 30 April 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2025.27.3.015***

***UDC* 616-036.21**

This work is licensed under a Creative Commons Attribution 4.0 International License

# SURGICAL TREATMENT OF LEGG-CALVE-PERTHES DISEASE IN CHILDREN

**Nazym A. Tuktiyeva[1], https://orcid.org/0000-0002-4024-6705**

**Bolatbek A. Dossanov[2], https://orcid.org/0000-0001-9816-7404**

**Yersin T. Zhunussov[3], https://orcid.org/0000-0002-1182-5257**

**Gapsamet M. Abdulvakhabov[1] https://orcid.org/0009-0004-1097-8202**

**[1] NCJSC «Semey Medical University», Department of Traumatology and Pediatric Surgery, Semey, Republic of Kazakhstan;**
**[2] NCJSC «Astana Medical University», Department of Pediatric Surgery, Astana, Republic of Kazakhstan;**
**[3] International Science Center of Traumatology and Orthopedics. Almaty. Republic of Kazakhstan.**

**Abstract**

**Introduction.** Legg-Calve-Perthes disease is an idiopathic aseptic avascular osteonecrosis of the epiphysis of the femoral bone head. The age of diagnosis of the disease is usually between 4 and 12 years-old age, with an average of 6 years-old age. The course and prognosis of Perthes disease is difficult to predict. The prognosis of the disease depends on the age of the child, on the site of damage to the epiphysis of the femoral head, on the level of the destroyed height of the lateral column of the pineal gland.

**Materials and methods.** The study design is a prospective controlled clinical trial. From 2018 to 2022, 10 children with Legg-Calve-Perthes disease were operated. Under general anesthesia, the patient underwent hardware unloading of the hip joint under X-ray control. The age of the patients ranged from 7 to 11 years-old, 9 cases were boys, 1 case was a girl and all cases were one-sided. The duration of treatment in the device ranged from 28 to 39 days. Radiologically, the severity of the disease and the indications for surgery were set according to the classifications of Salter-Thomson and Catterall.

**Results** The follow-up period ranged from 6 months to 4 years, with an average of 2 years. A total of 10 patients (9 boys and 1 girl) were enrolled in this study. The median age at symptom onset was 8.3 years-old (range 7–11 years-old) and the median age of having surgery was 9.1 years-old (range 7–11 years-old). Five cases are right-sided hip lesions, the remaining five are left-sided hip lesions. In the present study, there was not a single case of bilateral hip lesion. At the time of surgery, two patients had 2nd stage of the disease, eight patients had 3rd stage of the disease (20% in the second stage of the disease, 80% in the third stage). Distraction was performed over an average of 14 days (range 10-17 days). The median duration of AEF wearing was 30.6 days (range 28–39 days).

**Conclusions**. Hardware unloading of the hip joint is currently a promising treatment for Legg-Calve-Perthes disease, which has a future. This method of treatment has advantages such as simplicity of technique, minimal complication rate, short period of hospitalization, correction of shortening, since it increases the length of the limb, shorten the recovery time of the femoral head. Providing radiographic sphericity of the femoral head improves the range of motion of the hip joint.

***Key words:*** *Legg-Calve-Perthes disease, hardware unloading, epiphyseal index, Modified Harris Hip score, Stulberg classification.*

***For citation:***

*Tuktiyeva N.A., Dossanov B.A., Zhunussov Ye.T. Abdulvakhabov G.M.* Surgical treatment of Legg-Calve-Perthes disease in children // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 135-142. *doi 10.34689/SH.2025.27.3.015*

**Резюме**

# ХИРУРГИЧЕСКОЕ ЛЕЧЕНИЕ БОЛЕЗНИ ЛЕГГ-КАЛЬВЕ-ПЕРТЕСА У ДЕТЕЙ

**Назым А. Туктиева[1], https://orcid.org/0000-0002-4024-6705**

**Болатбек А. Досанов[2], https://orcid.org/0000-0001-9816-7404**

**Ерсын Т. Жунусов[3], https://orcid.org/0000-0002-1182-5257**

**Гапсамет М. Абдулвахабов[1] https://orcid.org/0009-0004-1097-8202**

**1 НАО «Медицинский университет Семей», Кафедра травматологии и детской хирургии, г. Семей, Республика Казахстан;**
**[2] НАО «Медицинский университет Астана», Кафедра детской хирургии, г. Астана, Республика Казахстан;**
**[3] Международный научный Центр Траватологии и Ортопедии, г. Алматы, Республика Казахстан.**

**Введение.** Болезнь Легг-Кальве-Пертеса это идиопатический асептический аваскулярный остеонекроз эпифиза головки бедренной кости. Возраст постановки диагноза заболевания обычно составляет от 4 до 12 лет, в среднем в

6 лет. Течение и прогноз болезни Пертеса тяжело предсказать. Прогноз заболевания зависит от возраста ребенка, от участка поражения эпифиза головки бедра, от уровня разрушенной высоты латерального столба эпифиза.

**Материалы и методы.** Дизайном исследования является проспективное контролируемое клиническое исследование. С 2018 года по 2022 год в было прооперировано 10 детей с заболеванием Легг-Кальве-Пертеса. В условиях общей анестезии пациенту выполнялся аппаратная разгрузка тазобедренного сустава под рентгенологическим контролем. Возраст пациентов варьировался от 7 до 11 лет, 9 случаев мальчики, 1 случай девочка, и все случаи были односторонними. Продолжительность лечения в аппарате варьировалось от 28 до 39 дней. Рентгенологически тяжесть заболевания и показания к операции выставляли по классификациям Солтера-Томсона и Каттералла.

**Результаты.** Период наблюдения составлял от 6 месяцев до 4 лет, в среднем 2 года. В общей сложности в это исследование были включены 10 пациентов (9 мальчиков и 1 девочка). Средний возраст на момент появления симптомов составлял 8,3 года (диапазон 7–11 лет), а средний возраст на момент операции составлял 9,1 лет (диапазон 7–11 лет). Пять случаев правостороннее поражение тазобедренного сустава, остальные пять - левостороннее поражение тазобедренного сустава. В настоящем исследовании не было ни одного случая с двусторонним поражением тазобедренного сустава. На момент операции у двоих пациентов было 2 степень заболевания, у восьмерых 3 стадия заболевания (20% на второй стадии заболевания, 80% на третей стадии). Дистракция проводилась в среднем в течение 14 дней (диапазон 10-17 дней). Средняя продолжительность ношения АВФ составила 30,6 дней (диапазон 28–39 дней).

**Выводы**. Аппаратная разгрузка тазобедренного сустава в настоящее время является перспективным методом лечения болезни Легга- Кальве- Пертеса, у которого есть будущее. Этот метод лечения имеет преимущества, как простота техники, минимальная частота осложнений, короткий период госпитализации, коррекция укорочения, поскольку оно увеличивает длину конечности, сократит сроки восстановления головки бедра. Обеспечивая рентгенографическую сферичность головки бедренной кости улучшает диапазон движения тазобедренного сустава.

***Ключевые слова:*** *болезнь Легга-Кальве-Пертеса, аппаратная разгрузка, эпифизарный индекс, Modified Harris Hip score, классификация по Stulberg.*

***Для цитирования:***

*Туктиева Н.А., Досанов Б.А., Жунусов Е.Т., Абдулвахабов Г.М. Хирургическое лечение болезни Легг-Кальве-Пертеса у детей* // Наука и Здравоохранение. 2025. Т.27 (3), С. 135-142. doi: 10.34689/SH.2025.27.3.015

**Түйіндеме**

# БАЛАЛАРДАҒЫ ЛЕГГ-КАЛЬВЕ-ПЕРТЕС АУРУЫНЫҢ ХИРУРГИЯЛЫҚ ЕМІ

**Назым А. Туктиева[1], https://orcid.org/0000-0002-4024-6705**

**Болатбек А. Досанов[2], https://orcid.org/0000-0001-9816-7404**

**Ерсын Т. Жунусов[3], https://orcid.org/0000-0002-1182-5257**

**Гапсамет М. Абдулвахабов[1] https://orcid.org/0009-0004-1097-8202**

**[1] "Семей медицина университеті» КЕАҚ, Травматология және балалар хирургиясы кафедрасы, Семей қ., Казақстан Республикасы;**

**[2] «Астана медицина Университеті» КЕАҚ, Балалар хирургиясы кафедрасы, Астана қ,, Казақстан Республикасы;**

**[3] Халықаралық травматология және ортопедия ғылыми орталығы. Алматы қ., Қазақстан Республикасы.**

**Кіріспе.** Легг-Кальве-Пертес ауруы — бұл жамбас сүйегінің басының эпифизінің идиопатиялық асептикалық аваскулярлық остеонекрозы. Диагноз негізінен 4-тен 12 дейінгі жаста, көбінесе 6 жаста қойылады. Аурудың ағымы мен болжамы баланың жасына, жамбас сүйегі басының эпифизінің зақымданған аймағына және эпифиздің бүйір бағанының биіктігінің бұзылу деңгейіне байланысты.

**Материалдар мен әдістер.** Зерттеу дизайны проспективті бақыланатын клиникалық зерттеу болып табылады. 2018-2022 жылдар аралығында Легг-Кальве-Пертес ауруымен 10 балаға ота жасалды. Жалпы анестезия жағдайында пациентке жамбас буынын рентген бақылауымен аппараттық жеңілдету жүргізілді. Пациенттердің жасы 7-ден 11 жасқа дейін, 9 ұл және 1 қыз болды, барлық жағдайлар біржақты болды. Аппаратта емдеу ұзақтығы 28-ден 39 күнге дейін өзгерді. Аурудың ауырлығын және операция көрсеткіштерін рентген арқылы Salter-Thompson және Catterall классификациялары бойынша анықтады.

**Нәтижелер.** Бақылау кезеңі 6 айдан 4 жылға дейін, орта есеппен 2 жылды құрады. Зерттеуге 10 пациент (9 ұл және 1 қыз) енгізілді. Симптомдардың пайда болған сәтіндегі орташа жас 8,3 жасты (7–11 жас), ал ота жасалған сәттегі орташа жас 9,1 жасты (7–11 жас) құрады. Бес жағдайда оң жақ жамбас буыны, қалған бесеуінде сол жақ жамбас буыны зақымдалды. Зерттеуде екі жақты зақымдалу жағдайлары тіркелген жоқ. Ота кезінде екі пациентте аурудың 2 сатысы, сегіз пациентте 3 сатысы анықталды (20% — 2-саты, 80% — 3-саты). Орташа дистракция кезеңі 14 күн (10-17 күн), ал аппаратты кию ұзақтығы орта есеппен 30,6 күн (28–39 күн) болды.

**Қорытынды.** Жамбас буынын аппараттық жеңілдету қазіргі уақытта Легг-Кальве-Пертес ауруын емдеудің болашағы зор әдісі болып табылады. Бұл әдістің техникасының қарапайымдылығы, асқынулардың минималды жиілігі, қысқа ауруханада болу кезеңі, аяқтың ұзындығын арттыра отырып, қысқаруды түзету сияқты артықшылықтары бар. Жамбас

басының қалпына келу уақытын қысқартады және рентгенологиялық түрде эпифиз басының сфералық формасын сақтауды қамтамасыз етеді, бұл жамбас буынының қозғалыс диапазонын жақсартады.

***Түйінді сөздер:*** *Легг-Кальве-Пертес ауруы, аппараттық жеңілдету, эпифизарлық индекс, Modified Harris.*

***Дәйексөз үшін:***

*Туктиева Н.А., Досанов Б.А., Жунусов Е.Т., Абдулвахабов Г.М.* Легг-Кальве-Пертес ауруының хирургиялық емі // Ғылым және Денсаулық. 2025. Т.27 (3), Б. 135-142. doi: 10.34689/SH.2025.27.3.015

**Introduction**

Legg-Calve-Perthes disease is an idiopathic aseptic avascular osteonecrosis of the epiphysis of the femoral head [1]. The age of diagnosis of the disease is usually between 4 and 12 years-old age, with an average of 6 years-old age. The course and prognosis of Perthes disease is difficult to predict. The prognosis of the disease depends on the age of the child, on the site of the lesion of the epiphysis of the femoral head, on the level of the destroyed height of the lateral column of the pineal gland [2]. The prognosis of the disease assesses the sphericity of the femoral head and the congruence of the hip joint, the height of the lateral column of the epiphysis, that is, the height of the femoral head and the range of motion of the hip joint [3]. In our study, most patients were treated in the later stages of the disease and children older than 7-8 years, when there is already an insufficient range of motion of the hip. In the worst development of the disease, this condition can lead to degenerative osteoarthritis in childhood.

The explanations for this fact lie in the fact that the acetabulum is not able to adapt to the congruence of the deformed femoral head due to a decrease in the elasticity of the acetabulum [4], there is less time for growth and remodeling of the femoral head [5].

The method of treating Perthes disease in the age categories above 7 years causes a lot of controversy. The main principles of treatment have traditionally been to lighten the load and unload the femoral head [6]. Various surgical treatment options have been proposed, but they have some inherent drawbacks. Osteotomy of the femur with varus rearrangement can even increase the mismatch of the hip, as well as shorten the limb [7]. Valgus osteotomy of the femur can lead to unloading of the deformed head, but it can increase the lateral subluxation of the femoral head [8]. None of these procedures affect the underlying avascular process of the femoral head. The acetabulum lateral shelf procedure [9], Salter's osteotomy [10], Chiari's osteotomy [11], and triple osteotomy [12] aim to change the orientation or increase the size of the acetabulum and provide greater support for the femoral head. However, these approaches do not reduce the pressure on the femoral head or change the shape of the femoral head. No conventional treatment has shown any statistically significant efficacy in improving the outcome of Perthes disease.

Distraction of the hip joint with the help of an external fixation apparatus of the Ilizarov type is a relatively new method of treating Perthes disease. The concept of this method of treatment is that by creating space in the joint and removing the load on the articular surface, synovial circulation improves. It contributes to the fibrous restoration of articular cartilage defects and additionally preserves the intact part of the femoral head [13]. We present our results from this prospective study to evaluate the effect of hip relief on a selected group of patients over 7 years of age with Perthes disease.

For a long time, it was not clear why some patients have minimal clinical and radiological manifestations with a quick recovery, while others have a pronounced picture of pathology with a long course of the disease and a poor outcome. Various classifications were proposed, which to some extent made it possible to predict the final result of the course of the disease. According to these classifications, the outcome of the disease depends on the volume (degree) of damage to the head. That is, the more the head is affected, the worse the outcome of the disease will be. In our study, the indications for surgery were set according to the classifications of Salter-Thomson [14] and Catterall [15]. The Catterall classification was proposed in 1971 in order to clarify the indications for various types of treatment and to provide an early prediction of the course of the disease

The classification is based on X-ray examination data in the fragmentation stage

Type I: less than 25% involvement.

Type II: 50% involvement, the lateral part is static.

Type III: 75% involvement, collapse of the lateral part of the head.

Type IV: full involvement.

The Salter-Thompson classification was proposed in 1984 for the prediction and selection of treatment. It is based on determining the length of the subchondral fracture site. The authors believe that the development of the disease depends solely on the degree of damage to the femoral head in the early stages and distinguish only two groups: group A: less than 50% involvement of the width of the femoral head, group B: more than 50% involvement.

**The aim of the study was to** evaluate the results of surgical treatment of Legg-Calve-Perthes disease in children.

**Materials and methods.**

The study design is a prospective controlled clinical trial. There is an informed consent of the patient's parents for the interventions and further description in the publications of the results of treatment. Informed consent was signed by all parents of the children involved prior to the start of the study. They were informed that participation was voluntary and could opt out at any time. None of them received anything in return for their participation. The management of the clinic is aware of the interventions carried out and does not object to the issue of covering the results in the open press. The study is approved by the Ethics Committee from Protocol No. 2 of 25.10.2018 and the research is carried out within the framework of a doctoral dissertation. The study was conducted in accordance with the principles of the Declaration of Helsinki.

From 2018 to 2022, 10 children with Legg-Calve-Perthes disease were operated on in our institution.

The inclusion criteria were as follows:

1. Age over 7 years-old.
2. Perthes disease at stages 2, 3 of the disease.
3. Strong traffic restriction.
4. Pain.

The age of the patients ranged from 7 to 11 years-old, 9 cases were boys, 1 case was a girl and all cases were one-sided.

Quantitative variables did not obey the law of normal distribution. The Wilcoxon criterion was applied.

**Operational equipment**

Under conditions of general anesthesia, the patient underwent unloading of the hip joint under X-ray control. The surgical intervention included the installation of a rod apparatus for external fixation using the technology developed by us (patent No. 5386, 2021 was obtained), the correct dosed distraction system, using telescopic rods. Figure 1.

The half-rings of the Ilizarov apparatus were used as supporting elements. [16] The surgery was performed under general anesthesia. In the nadacetabular region of the pelvis and in the upper third of the thigh, 2 rods were held in different planes, the device is installed and fixed on the supporting elements of the external fixation apparatus (Figure 3).

**Figure 1. Distraction system of the external fixation apparatus according to the Ilizarov type.**

**Figure 2. Intraoperative photograph during the installation of the distraction system of the external fixation apparatus on the hip joint.**

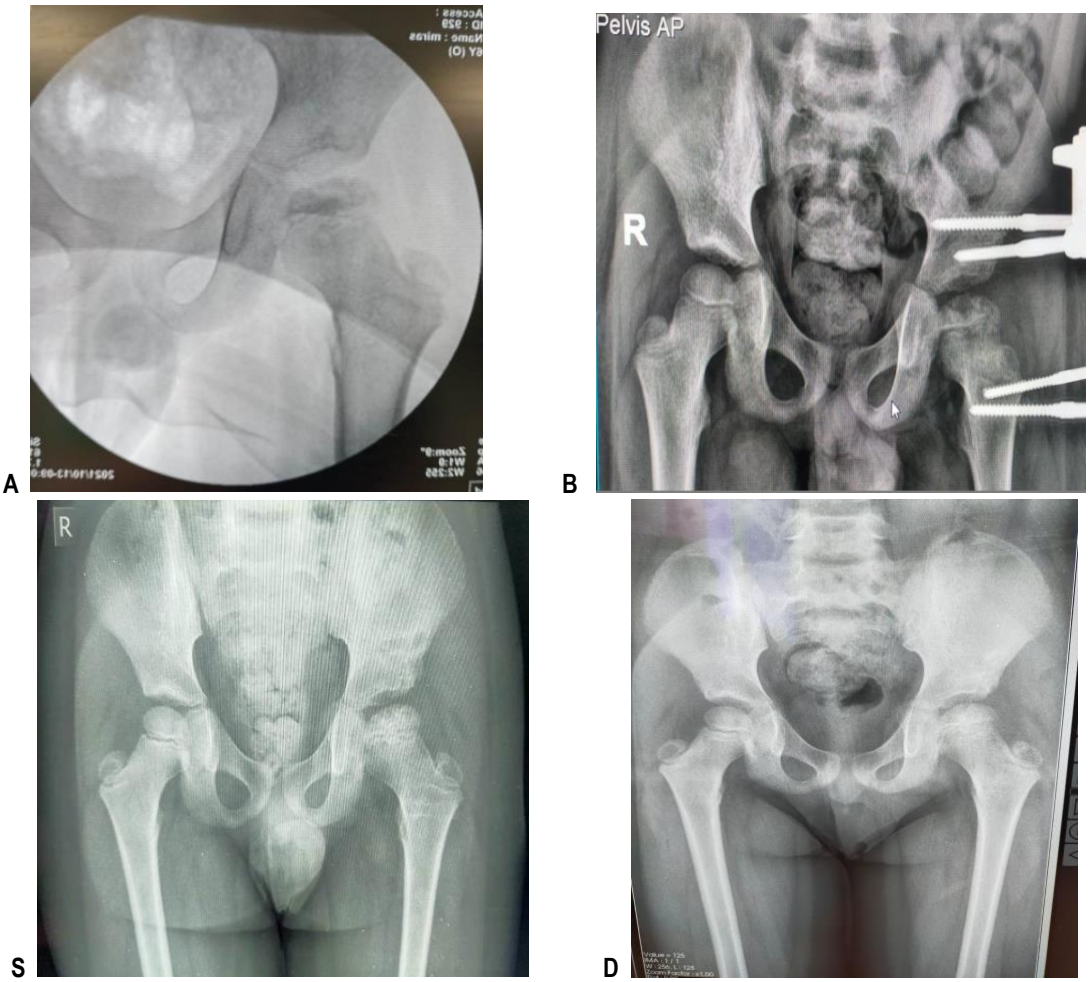



**Figure 3. A 7-year-old patient with Perthes disease. (a) The deformation, a decrease in the height of the head, with the presence of a pathological compression fracture of the epiphysis, is determined. Perthes disease in the stage of compression fracture and fragmentation (II-III stages). (b) on the 22nd day after the installation of the distraction system of the external fixation apparatus. (c) Radiograph after removal of the machine. After 3 months from the date of surgery. Perthes disease is under recovery. (e) after 10 months with an improvement in the epiphyseal index.**

The femoral head is given an internal rotation of up to 20°. In the postoperative period, distraction begins during the operation by 1 mm, then by day 3, since the postoperative period is accompanied by pain syndrome for an average of three days, at a rate of 1 mm per day until the correction of the Shenton line is completed. After reaching the planned value, all elements of the rod are blocked until the device is removed. During the treatment, control radiography of the pelvis and hip joints was performed after 7, 14, 28 days (Figure 2).

The patient began to walk with a gradually increasing load from the first day after surgery with the help of crutches. The pain syndrome was not pronounced, complications were observed in the form of superficial inflammation of the soft tissues in the area of the rods.

**Results**

Radiologically, the severity of the disease and the indications for surgery were set according to the classifications of Salter-Thompson and Catterall. Ten patients were classified in Salter-Thompsjn group B; seven patients in group 4 and three patients in group 3 according to the Catterall classification, this means severe damage to the pineal gland, where the lateral segment of the epiphysis of the femoral head is involved in the lesion, this is a prognostic factor for an unfavorable outcome of the disease.

For preoperative evaluation, anteroposterior and lateral radiographs of the pelvis in the Launstein pose were obtained.

The follow-up period ranged from 6 months to 4 years, with an average of 2 years. A total of 10 patients (9 boys and 1 girl) were enrolled in this study. The median age at symptom onset was 8.3 years-old (range 7–11 years-old) and the median age of having surgery was 9.1 years-old (range 7–11 years-old). Five cases are right-sided hip lesions, the remaining five are left-sided hip lesions. In the present study, there was not a single case of bilateral hip lesion. At the time of surgery, two patients had 2nd stage of the disease, eight patients had 3rd stage of the disease (20% in the second stage of the disease, 80% in the third stage). Distraction was performed over an average of 14 days (range 10-17 days). The median duration of AEF wearing was 30.6 days (range 28–39 days). None of these patients underwent any additional surgery. General characteristics of these patients are given in Table 1.

*Table 1.*

**Characteristics of operated patients.**

| # | Sex | Age at debut | Age during surgical treatment | Duration of AEF wearing (days) | Duration of distraction (days) | Salter-Thomsor Classification | Catteral Classification | Stulberg Classifica tion | omplications | Affected joint |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Male | 9 | 10 | 36 | 10 | B | 4 | I | | Left |
| 2 | Male | 7 | 8 | 34 | 14 | B | 4 | III | Inflammation of the soft tissues | Right |
| 3 | Male | 7 | 11 | 30 | 16 | B | 4 | II | | Right |
| 4 | Female | 8 | 8 | 30 | 14 | B | 4 | II | | Left |
| 5 | Male | 9 | 10 | 28 | 14 | B | 4 | II | | Right |
| 6 | Male | 8 | 8 | 39 | 15 | B | 3 | IV | Contracture | Left |
| 7 | Male | 7 | 11 | 37 | 13 | B | 3 | II | | Left |
| 8 | Male | 8 | 10 | 33 | 16 | B | 3 | II | | Right |
| 9 | Male | 9 | 8 | 31 | 17 | B | 4 | II | | Left |
| 10 | Male | 8 | 7 | 38 | 11 | B | 4 | II | | Right |

The results of treatment were assessed by the volume of motion in the hip joint 3 months after surgery and comparing them with preoperative parameters, Table No. 2. The degree of recovery of the epiphysis of the femoral head was assessed by comparing the preoperative and postoperative epiphyseal index.

*Table 2.*

**The range of motion of the hip joint before and after surgery.**

| # | Inflection | | Allocating | | External rotation | | Internal rotation | |
|---|---|---|---|---|---|---|---|---|
| | Before surgery | After surgery | Before surgery | After surgery | Before surgery | After surgery | Before surgery | After surgery |
| 1 | 55° | 90° | 12° | 35° | 21° | 33° | 8° | 24° |
| 2 | 60° | 95° | 14° | 39° | 20° | 34° | 10° | 25° |
| 3 | 80° | 110° | 13° | 37° | 22° | 35° | 7° | 21° |
| 4 | 50° | 89° | 15° | 38° | 19° | 32° | 10° | 30° |
| 5 | 55° | 95° | 10° | 30° | 21° | 34° | 9° | 25° |
| 6 | 55° | 90° | 15° | 37° | 20° | 35° | 10° | 26° |
| 7 | 70° | 95° | 17° | 39° | 22° | 35° | 7° | 22° |
| 8 | 65° | 95° | 15° | 35° | 21° | 33° | 12° | 30° |
| 9 | 50° | 120° | 12° | 40° | 15° | 40° | 7° | 30° |
| 10 | 40° | 60° | 12° | 20° | 14° | 25° | 8° | 15° |

In a clinical examination performed 3 months after hip relief, the flexion range increased by an average of 40°, from 55° before surgery to 95° after surgery. Statistically significant differences were observed, p=0.005. The range of internal rotation increased by an average of 16° from 9° before surgery to 25° after surgery (p=0.005) and the range of external rotation increased by an average of 13° from 21° before surgery to 34° (p=0.005), and the angle of lead increased by an average of 23° from 14° before surgery to 37° postoperatively (p=0.005).

*Table 3.*

**Radiological results.**

| # | Epiphyseal index (outcome) | Epiphyseal index (final) | Stulberg Classification |
|---|---|---|---|
| 1 | 0,65 | 0,95 | I |
| 2 | 0,5 | 0,7 | III |
| 3 | 0,54 | 0,85 | II |
| 4 | 0,56 | 0,81 | II |
| 5 | 0,6 | 0,83 | II |
| 6 | 0,41 | 0,54 | IV |
| 7 | 0,55 | 0,85 | II |
| 8 | 0,58 | 0,86 | II |
| 9 | 0,67 | 0,8 | II |
| 10 | 0,68 | 0,86 | II |

The epiphyseal index showed a significant increase of an average of 0,24 from 0,18 to 0,31 postoperative surgery. There were statistically significant differences in the epiphyseal index before and after surgery, p = 0.005. According to the Stulberg classification [16], there was one class I hip, seven class II hips, one class III hip and one class IV hip, there were no class V results, diagram 1.

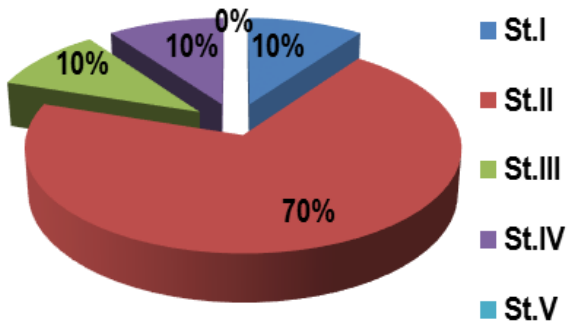



**Diagram 1. Results according to the Stulberg classification.**

The functional state of the hip joint was assessed using the Modified Harris Hip score questionnaire [17] three months, six months and nine months after surgery. At final follow-up, the average hip score for mHHS improved from 68 points before surgery to 85 points after surgery, p < 0.005.

In two patients, there was an infection around the rods, we believe that the cause is the mechanical removal of the hemorrhagic crust during the next dressings, which formed after surgery.

All patients were satisfied with the results, with the exception of one, the patient developed a deformity of the femoral head of the type of coxa plana.

A 7-year-old patient with Legg-Calve-Perthes disease of the left hip joint underwent hardware unloading using an external fixation device, the device was used for 33 days. The range of motion increased by 30° in flexion, 10° in internal rotation, and 5° in abduction compared to preoperative measurements. On X-ray evaluation, the epiphyseal index increased from 16 before surgery to 26 after surgery. The Modified Harris Hip score improved from 69 points before surgery to 85 points after surgery. Thus, the hip was assigned to class II according to Stulberg, which indicates a satisfactory treatment result (Figure 2).

**Discussion**

Various treatments have been introduced to treat Legg-Calve-Perthes disease. However, the final criteria for the treatment of the disease have not been established, since the exact causes, pathogenesis and pathology of the disease are not fully understood. The prognosis and course of the disease are diverse and unpredictable, it can lead to degenerative arthritis in early childhood. The prognosis is worse in patients older than 6-8 years, primarily due to the fact that the remaining time for bone growth and repair is relatively short, and the depression of the femoral head progresses further due to physical reasons, such as decreased elasticity at the acetabulum [17-18].

During ischemia, the femoral head is subjected to pressure overload, even when the patient is at rest, due to the influence of the muscles. Unloading the hip joint allows you to expand the joint space, this creates an optimal environment for the restoration of the femoral head [19]. The circulation of synovial fluid and the nutrition of articular cartilage improves. In the apparatus, the articular surface and epiphysis are protected from the forces acting on the thigh, and the risk of deformation of the femoral head and the collapse of newly formed vessels are also reduced. In our case, rapid revascularization of the femoral epiphysis was observed in the interval of one to three months (Figure 2). This phenomenon was observed in studies by Volpon et al. [20]. According to Ilizarov's descriptions, unloading of the hip joint causes angiogenesis around the entire joint, active histogenesis occurs not only in the bone, but also in the soft tissue area [21]. According to the literature, 77.8% of patients have satisfactory treatment results for hip relief [22]. In our observation, the operated joint according to the classification of the outcome of the disease corresponds to class II according to Stulberg, this corresponds to the results of other authors. We came to the conclusion that when the hip joint was unloaded, the time of the stage of resorption and remodeling of the femoral head was shortened. The course of the rehabilitation period did not differ from the duration of treatment with the use of similar devices [23,24].

There are studies evaluating an apparatus with an articulating mechanism for unloading the hip joint, where the patient could perform passive movements in the joint, the duration of treatment using this technique ranged from 4 to 7 months [25]. W++e came to the conclusion that the presence of mobility in the hip joint during hardware treatment is not a significant fragment in the unloading of the hip joint. Mandatory therapeutic factors are the centered position of the head in the cavity, decompression of the hip joint, and improvement of local blood supply [26-29].

Thus, reconstructive surgery on the proximal femur is a priority. Reorientation of the femoral head in the cavity, restoration of the normal anatomy of the hip joint can

provide not only centering and full "coverage" of the femoral head, but also relieve pressure on the affected area. Subject to the availability of high-quality metal structures, practical experience of the surgeon, such operations are relatively less traumatic, do not require plaster immobilization, and provide the possibility of early, full-fledged rehabilitation. At the same time, they do not exclude the possibility of further reconstruction of the pelvic bones in dysplastic acetabulum formation [30-32].

Several studies emphasize that outcomes in LCPD are significantly influenced by patient age at onset, the extent of femoral head involvement, and the duration of the disease before intervention. In our study, the average age at onset (8.5–9 years) placed patients in a higher-risk group for residual deformities. Nevertheless, the use of distraction treatment demonstrated substantial improvement in function and structure.

The epiphyseal index was used as a radiological marker to evaluate morphological recovery of the femoral head. A significant increase in this index postoperatively in the distraction group supports its validity as an indicator of treatment success. Future protocols may benefit from incorporating dynamic monitoring of the epiphyseal index to guide treatment modifications during follow-up.

Although short-term functional and radiological outcomes are promising, LCPD is a condition with potential long-term sequelae, including early-onset osteoarthritis. Our findings emphasize the need for longitudinal cohort studies with follow-up beyond skeletal maturity to assess the durability of structural outcomes and correlate them with the eventual need for hip arthroplasty in adulthood.

Unloading the hip joint using an external fixation device is a relatively new treatment for Legg-Calve-Perthes disease. Space is provided for the femoral head in the joint, minimizing physical pressure and keeping synovial fluid circulating.

**Conclusions**.

The advantages of our method are the correction of shortening, the simplicity of the technique, the minimum complication rate and the short period of hospitalization. The radiographic sphericity of the femoral head and the range of motion of the hip joint are improved, and the recovery time of the disease is reduced. Hardware unloading of the hip joint can make a good contribution to the treatment of Legg-Calve-Perthes disease.

***Author Contributions**: All authors contributed equally to the writing of this manuscript.*

***Conflict of Interest:** The authors declare no conflicts of interest. This material has not been submitted to other journals and is not under consideration elsewhere.*

***Funding:** No funding was received for this study.*

***References:***

*1. Akhtyamov I., Abakarov A., Beletsky A., Bogosyan A., Sokolovsky O.* Diseases of the hip joint in children. Kazan: Center for Operational Press, 2008. P. 456.

*2. Armando O. R., Edgar H., Elba R.* Legg-Calvé-Perthes disease overview. Orphanet J Rare Dis. 2022 Mar 15;17(1):125

*3. Adam K, Manuel J.K., Andreas H.K.* Proximal femoral varus osteotomy in Legg-Calve-Perthes disease. Oper Orthop Traumatol. 2022 Oct;34(5):307-322.

*4. Aguado M., Abril J.C., Bañuelos D.M. Garcia Alonso.* Hip arthrodiastasis in Legg-Calvé-Perthes disease. Journal of Orthopaedics Surgery and Traumatology

*5. Amer A., Khanfour A.* Arthrodiastasis for late onset Perthes' disease using a simple frame and limited soft tissue release: early results. Acta Orthop Belg. 2011. 77(4). P.472–479

*6. Bankes M.,*Valgus extension osteotomy for 'hinge abduction' in Perthes' disease. The Journal of Bone & Joint Surgery British VolumeVol 82-B, No.4. 01 May 2000. Pages 548 – 554

*7. Barsukov D.* Perthes disease. Terra Medica nova, 2009, 3: pp. 24–30.

*8. Catterall A.* Perthes' disease. J. Bone Joint Surg. [Br]. 1971. N53. P.37 –53

*9. Ferguson A.,* Jr. Segmental vascular changes in the femoral head in children and adults. Clin Orthop Relat Res. 1985. 200. P.291-298.

*10. Gafarov H.* Treatment of children and adolescents with orthopedic diseases of the lower extremities. Kazan: Tatar book. publ., 1995, p.383.

*11. George H Thompson.* Salter osteotomy in Legg-Calvé-Perthes disease. 2011 Sep;31(2 Suppl): S192-198

*12. Gregosiewicz A., Okonski M., Stolecka D.* et al. Ischemia of the femoral head in Perthes' disease: is thecause intra- or extravascular? J Pediatr Orthop. 1989. 9. P.160-162.

*13. Hall A., Barker D.*The age distribution of LeggPerthes disease. An analysis using Sartwell'sincubation period model // Am J Epidemiol. 1984. 120. P. 531-536.

*14. Herring J.* Legg-Calve-Perthes Disease. In Tachdjians Pediatric Orthopaedics J.A. Herring. Elsevier Health Sciences, 2001. P. 675-679.

*15. Herring J.* et al. Perthes'disease. J. Pediatr. Orthop. 1993. N13. P.41 –45.

*16. Hosny G., El-Deeb K., Fadel M., Laklouk M.* Arthrodiastasis of the hip. J. Pediatr. Orthop. 2011. Vol. 31, Suppl. 2. P. 229-234. doi: 10.1097/ BPO.0b013e318223b45a.

*17. Ilizarov G.* The tension-stress effect on the genesis and growth of tissues. Transosseous osteosynthesis. Berlin: Springer-Verlag; 1992. P.137–255

*18. Ibrahim Y., Mohamed Ahmed A., Kersh and Hesham Fahmy.* Arthrodiastasis in the management of Perthesdisease: a systematic review. Journal of Pediatric Orthopaedics B 2019, Vol XXX No XXX, P.5-11.

*19. Ilizarov G.* A method of bone fusion in fractures and an apparatus for the implementation of this method. Description of the invention. To the author's certificate. Published in the "Bulletin of Inventions" No. 6 for 1954

*20. Krutikov N., Vinogradov A.* Legg-Calve-Perthes disease. Questions of modern pediatrics. 2015. 14. 5. P. 548-552.

*21. Karagyaur M., Makarevich P., Shevchenko E.K., Stambolsky D., Kalinina N., Parfyonova Ye.* Modern approaches to peripheral nerve regeneration after injury: the prospects of gene and cell therapy. Genes and Cells. 2017. 12(1). P. 172-177.

*22. Maxwell S., Lappin K., Kealey W., McDowell B., Cosgrove A.* Arthrodiastasis in Perthes' disease. Preliminary results. J. Bone Joint Surg. Br. 2004. Vol. 86-B. No 2. P. 244-250.

*23. Mehta J., Conybeare M., Hinves B.* et al. Protein C levels in patients with Legg-Calvé-Perthesdisease: is it a true deficiency? J Pediatr Orthop. 2006. 26. 200-203.

*24. Perthes G.* The classic: On juvenile arthritis deformans. 1910. Clin. Orthop. Relat. Res. 2012. 470 (9). 2349–2368.

*25. Perry D., Skellorn P., Bruce C.* The lognormal age of onset distribution in Perthes' disease: an analysis from a large well-defined cohort. J Bone Joint Surg Br. 2016. 98(5). pp. 110–114.

*26. Perry D., Machin D., Pope D.* et al. Racial and geographic factors in the incidence of Legg-CalvéPerthes' disease: a systematic review. Am J Epidemiol. 2012. 175. P. 159-166.

*27. Rajendra R. R, Christian M.* Chiari osteotomy in Legg-Calve-Perthes disease. J Pediatr Orthop B. 2005 Jan;14(1):1-9 Vol. 60. Issue 4. pages 243-250 (July - August 2016)

*28. Reimers J.* The stability of the hip in children.Acta Orthop. Scand. 1980. Suppl. No 184. P. 1-100.

*29. Salter R. B., Thompson G. H.* Legg-Calve-Perthes Disease: the prognostic significance of the subchondral fracture and a two-group classification of the femoral head involvement. J. Bone Joint Surg. Am. 1984; 66: 479-489

*30. Sokolovsky O., Dementsov A., Beletsky A., Brodko G.* Modeling effect of triple pelvic osteotomy on the proximal femur in Perthes disease. 2009. C. 17, No 3. P. 112-120.

*31. Stulberg S., Cooperman D., Wallensten R.* The natural history of Legg-Calvé-Perthes disease. J.Bone Joint Surg Am. 1981. Sep. 63(7). 1095-1108.

*32. Wen-Chao L, Rui-Jiang X,.* Lateral shelf acetabuloplasty for severe Legg–Calvé–Perthes disease in patients older than 8 years. 2016 Nov; 95(45): e5272

**Information about the authors:**

**Tuktiyeva Nazym**, Assistant of the Department of Traumatology and Pediatric Surgery, NCJSC «Semey Medical University», Semey, Republic of Kazakhstan; E-mail: tukti.nazym.anuarbek@gmail.com; phon: 8 (707) 694-90-06, https://orcid.org/0000-0002-4024-6705.

**Dossanov Bolatbek**, Ass. Professor of the Department of Pediatric Surgery, NCJSC «Astana Medical University», Astana, Republic of Kazakhstan; E-mail: dosanovb@mail.ru; phon:8(7051034843); https://orcid.org/0000-0001-9816-7404.

**Zhunussov Yersin**, Professor of the International Science Center of Traumatology and Orthopedics. Almaty. Republic of Kazakhstan; E-mail: ersin-surgery@mail.ru; phon: 8(777)6238923; https://orcid.org/0000-0002-1182-5257.

**Abdulvakhabov Gapsamet**, The resident of the Department of Traumatology and Pediatric Surgery, NCJSC «Semey Medical University», Semey, Republic of Kazakhstan; phon: 8 (707) 6635690; https://orcid.org/0009-0004-1097-8202.

***Correspondence author:**

**Tuktiyeva Nazym,** Assistant of the Department of Traumatology and Pediatric Surgery, NCJSC «Semey Medical University», Semey, Republic of Kazakhstan;

**Postal code:** Republic of Kazakhstan, 071400, Semey city, Ibraeva Street 113.

**E-mail:** tukti.nazym.anuarbek@gmail.com

**Phone:** +7 7076949006

Received: 04 January 2025 / Accepted: 14 May 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2025.27.3.016***

***UDC 579.842.16:615.33***

This work is licensed under a Creative Commons Attribution 4.0 International License

# ANALYSIS OF TREATMENT OUTCOMES FOR BLEEDING FROM ESOPHAGEAL AND GASTRIC VARICES

**Onlasyn T. Ibekenov[1,2,3], https://orcid.org/0000-0001-6605-6435**
**Abylai N. Baymakhanov[1], https://orcid.org/0009-0001-0344-1800**
**Aman B. Berkinbay[1], https://orcid.org/0000-0002-3973-7283**
**Yermek M. Zheldibaev[1,2], https://orcid.org/0009-0004-0216-1307**
**Makhsat K. Duisebekov[1,2], https://orcid.org/0009-0001-6697-8074**
**Nurhat B. Esenbekov[2], https://orcid.org/0009-0007-5324-2117**
**Sabit K. Iskakov[2], https://orcid.org/0009-0000-2359-9026**
**Mazhit K. Abdykadyrov[2,3], https://orcid.org/0000-0002-9518-5292**
**Erzhan S. Tulebaev[1], https://orcid.org/0009-0007-6053-787X**
**Dias D. Myrzash[1], https://orcid.org/0009-0001-7793-2338**

**[1] NJC "Kazakh National Medical University named after S.D. Asfendiyarov", Almaty, Republic of Kazakhstan;**
**[2] National Scientific Center of Surgery Named After A.N. Syzganov, Almaty, Republic of Kazakhstan;**
**[3] City Emergency Medical Care Hospital, Almaty, Republic of Kazakhstan.**

**Abstract**

**Introduction.** Bleeding from esophageal and gastric varices (EGV) is one of the most life-threatening complications of liver cirrhosis and portal hypertension, associated with high mortality, especially in cases of late diagnosis and advanced hepatic insufficiency.

**Aim.** To evaluate the clinical characteristics and treatment outcomes of patients with EGV bleeding treated at the Surgical Department of the Emergency City Hospital in Almaty from 2022 to 2024.

**Materials and Methods.** The study included 162 patients. Clinical parameters, severity of cirrhosis (Child–Pugh score), MELD index, endoscopic classification of varices (JGES), and treatment outcomes were analyzed. Descriptive statistics, Student's t-test, $\chi^2$-test, and one-way ANOVA were used. Odds ratios (OR) with 95% confidence intervals were calculated to assess risk factors for rebleeding. A p-value < 0.05 was considered statistically significant.

**Results.** Among 162 patients, males predominated (55.6%), with a mean age of 54.3 ± 11.2 years. Anemia (<70 g/L) was detected in 62.3%. II–III degree varices were diagnosed in 95.1%, and Child–Pugh classes B and C were present in 69.7%. Early ligation (<24 hours) reduced rebleeding to 2.3%, compared to 12.5% with delayed intervention (OR = 2.32); presence of red color signs (RCS) increased rebleeding risk to 17.9% (OR = 6.51). Overall mortality was 4.32%, postoperative mortality — 1.2%; all fatal outcomes occurred in patients with severe hepatic dysfunction. **Conclusions.** EGV bleeding remains a severe complication of cirrhosis requiring prompt diagnosis and active treatment. Early endoscopic ligation effectively reduces the risk of rebleeding and mortality. The presence of RCS and advanced variceal grade are significant predictors of poor prognosis.

***Keywords:*** *liver cirrhosis, portal hypertension, esophageal and gastric varices, bleeding, endoscopic ligation.*

***For citation:***

*Ibekenov O.T., Baymakhanov A.N.. Berkinbay A.B.. Zheldibaev Y.M., Duisebekov M.K.. Esenbekov N.B., Iskakov S.K., Abdykadyrov M.K., Tulebaev E.S., Myrzash D.D.* Analysis of treatment outcomes for bleeding from esophageal and gastric varices // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 143-150. *doi 10.34689/SH.2025.27.3.016*

**Резюме**

# АНАЛИЗ РЕЗУЛЬТАТОВ ЛЕЧЕНИЯ КРОВОТЕЧЕНИЙ ИЗ ВАРИКОЗНО-РАСШИРЕННЫХ ВЕН ПИЩЕВОДА И ЖЕЛУДКА

**Онласын Т. Ибекенов[1,2,3], https://orcid.org/0000-0001-6605-6435**
**Абылай Н. Баймаханов[1], https://orcid.org/0009-0001-0344-1800**
**Аман Б. Беркинбай[1], https://orcid.org/0000-0002-3973-7283**
**Ермек М. Желдибаев[1,2], https://orcid.org/0009-0004-0216-1307**
**Махсат К. Дуйсебеков[1,2], https://orcid.org/0009-0001-6697-8074**
**Нурхат Б. Есенбеков[2], https://orcid.org/0009-0007-5324-2117**

**Сабит И. Искаков[2], https://orcid.org/0009-0000-2359-9026**
**Мажит К. Абдыкадыров[2,3], ʰttps://orcid.org/0000-0002-9518-5292**
**Ержан С. Тулебаев[1], https://orcid.org/0009-0007-6053-787X**
**Диас Д. Мырзаш[1], https://orcid.org/0009-0001-7793-2338**

**[1] НАО «Казахский национальный медицинский университет имени С. Д. Асфендиярова», г. Алматы, Республика Казахстан;**
**[2] Национальный научный центр хирургии имени А.Н. Сызганова, г. Алматы, Республика Казахстан;**
**[3] КГП на ПХВ "Городская больница скорой неотложной помощи", г. Алматы, Республика Казахстан.**

**Введение.** Кровотечение из варикозно-расширенных вен (ВРВ) пищевода и желудка является одним из наиболее опасных осложнений цирроза печени и портальной гипертензии, сопровождающимся высокой летальностью при поздней диагностике и тяжёлой печёночной недостаточности.

**Цель.** Оценить клинические характеристики и результаты лечения пациентов с кровотечением из ВРВ пищевода и желудка, пролеченных в хирургическом отделении ГБСНП г. Алматы в 2022–2024 гг.

**Материалы и методы.** В исследование включены 162 пациента. Изучены клинические данные, тяжесть цирроза по шкале Child–Pugh, уровень MELD, эндоскопическая характеристика ВРВ (по классификации JGES), результатов лечения. Применялись методы описательной статистики, t-критерий Стьюдента, $\chi^2$-тест, однофакторный ANOVA. Для оценки факторов риска рецидива кровотечения рассчитывались отношения шансов (OR) с 95% доверительными интервалами. Значение $p < 0,05$ считалось статистически значимым.

**Результаты.** Среди 162 пациентов с ВРВ пищевода и желудка преобладали мужчины (55,6%), средний возраст — 54,3 ± 11,2 лет. У 62,3% пациентов выявлена анемия (<70 г/л). II–III степень ВРВ диагностирована у 95,1%, классы B и C по Child–Pugh — у 69,7%. Раннее лигирование (<24 ч) снижало рецидив до 2,3%, при ≥24 ч — до 12,5% (OR = 2,32); наличие красных маркеров (RCS) повышало риск рецидива до 17,9% (OR = 6,51). Общая летальность составила 4,32%, послеоперационная — 1,2%; все случаи летального исхода зарегистрированы при тяжёлой печёночной недостаточности.

**Выводы:** Кровотечение из ВРВ пищевода и желудка требует своевременной диагностики и активной тактики. Раннее эндоскопическое лигирование эффективно снижает риск рецидива и летальности. Наличие RCS и III степень ВРВ являются значимыми предикторами неблагоприятного течения.

***Ключевые слова:*** *цирроз печени, портальная гипертензия, варикозное расширение вен пищевода и желудка, кровотечение, эндоскопическое лигирование.*

***Для цитирования:***

*Ибекенов О.Т., Баймаханов А.Н., Беркинбай А.Б., Желдибаев Е.М., Дуйсебеков М.К., Есенбеко Н.Б., Искаков С.И., Абдыкадыров М.К., Тулебаев Е.С., Мырзаш Д.Д.* Анализ результатов лечения кровотечений из варикозно-расширенных вен пищевода и желудка // Наука и Здравоохранение. 2025. Т.27 (3), С. 143-150. doi: 10.34689/SH.2025.27.3.016

**Түйіндеме**

# ӨҢЕШ ПЕН АСҚАЗАННЫҢ ВАРИКОЗДЫК КЕҢЕЙГЕН ВЕНАЛАРЫНАН ҚАН КЕТУДІ ЕМДЕУ НӘТИЖЕЛЕРІН ТАЛДАУ

**Оңласын Т. Ибекенов[1,2,3], https://orcid.org/0000-0001-6605-6435**
**Абылай Н. Баймаханов[1], https://orcid.org/0009-0001-0344-1800**
**Аман Б. Беркінбай[1], https://orcid.org/0000-0002-3973-7283**
**Ермек М. Желдібаев[1,2], https://orcid.org/0009-0004-0216-1307**
**Махсат Қ. Дүйсебеков[1,2], https://orcid.org/0009-0001-6697-8074**
**Нұрхат Б. Есенбеков[2], https://orcid.org/0009-0007-5324-2117**
**Сабит И. Искаков[2], https://orcid.org/0009-0000-2359-9026**
**Мажит К. Абдыкадыров[2,3], https://orcid.org/0000-0002-9518-5292**
**Ержан С. Тулебаев[1], https://orcid.org/0009-0007-6053-787X**
**Диас Д. Мырзаш[1], https://orcid.org/0009-0001-7793-2338**

**[1] «С. Д. Асфендияров атындағы Қазақ ұлттық медицина университеті» КЕАҚ, Алматы қ., Қазақстан Республикасы;**
**[2] А.Н. Сызғанов атындағы Ұлттық хирургия ғылыми орталығы, Алматы қ., Қазақстан Республикасы;**
**[3] Жедел жәрдем қалалық ауруханасы, Алматы қ., Қазақстан Республикасы.**

**Кіріспе.** Өңеш пен асқазанның варикозды кеңейген веналарынан (ВКВ) туындайтын қан кету — бауыр циррозы мен портальды гипертензияның ең қауіпті асқынуларының бірі. Бұл жағдай, әсіресе диагноздың кеш қойылуында және бауыр қызметінің ауыр жеткіліксіздігі кезінде, жоғары өлім-жітіммен сипатталады.

**Мақсаты.** Алматы қалалық жедел шұғыл көмек көрсету ауруханасы хирургия бөлімінде 2022–2024 жылдар аралығында ВКВ-нан қан кету диагнозымен емделген науқастардың клиникалық сипаттамаларын және емдеу нәтижелерін бағалау.

**Материалдар мен тәсілдер.** Зерттеуге ВКВ-нан қан кеткен 162 науқас енгізілді. Клиникалық деректер, цирроздың ауырлығы (Child–Pugh шкаласы бойынша), MELD индексі, эндоскопиялық жіктеу (JGES), емдеу нәтижелері зерттелді. Деректерге сипаттамалық статистика, Стьюденттің t-критерийі, $\chi^2$-тест және бір факторлы дисперсиялық талдау (ANOVA) қолданылды. Рецидив қаупін бағалау үшін салыстырмалы қауіп көрсеткіші (OR) және 95% сенімділік аралығы есептелді. $p < 0,05$ статистикалық мәнділік ретінде қабылданды.

**Нәтижелер.** 162 науқастың ішінде ерлердің үлесі – 55,6%, орташа жасы – 54,3 ± 11,2 жас. Анемия (<70 г/л) 62,3% науқаста анықталды. II–III дәрежелі ВКВ – 95,1%, ал Child–Pugh шкаласы бойынша В және С сыныптары – 69,7%. Ерте эндоскопиялық түйіндерді байлау (<24 сағат) рецидивті 2,3%-ға дейін төмендетті, ≥24 сағатта – 12,5% (OR = 2,32); қызыл маркерлердің (RCS) болуы рецидив қаупін 17,9%-ға дейін арттырды (OR = 6,51). Жалпы өлім-жітім – 4,32%, отадан кейінгі өлім – 1,2%; барлық өлім жағдайлары ауыр бауыр жеткіліксіздігімен байланысты болды.

**Қорытындылар.** ВКВ-нан қан кету бауыр циррозының ауыр асқынуы ретінде жедел диагноз қоюды және белсенді емдеу тактикасын талап етеді. Ерте эндоскопиялық түйіндерді байлау рецидив пен өлім-жітім қаупін тиімді төмендетеді. RCS және III дәрежелі ВКВ қолайсыз болжам көрсеткіштері болып табылады.

***Түйінді сөздер:*** *бауыр циррозы, портальды гипертензия, өңеш пен асқазанның варикозды кеңейген веналары, қан кету, эндоскопиялық түйіндерді байлау*

***Дәйексөз үшін:***

*Ибекенов О.Т., Баймаханов А.Н., Беркінбай А.Б., Желдібаев Е.М., Дүйсебеков М.К., Есенбеко Н.Б., Искаков С.И., Абдыкадыров М.К., Тулебаев Е.С., Мырзаш Д.Д.* Өңеш пен асқазанның варикоздық кеңейген веналарынан қан кетуді емдеу нәтижелерін талдау // Ғылым және Денсаулық. 2025. Т.27(3), Б.143–150. doi: 10.34689/SH.2025.27.3.016

**Introduction**

Esophageal and gastric varices (EGV) represent one of the most life-threatening manifestations of portal hypertension, predominantly arising in the context of liver cirrhosis. According to the World Health Organization (WHO), varices develop in approximately 30–60% of patients with compensated cirrhosis and in 85–95% of those with decompensated disease [3, 10]. The annual risk of a first bleeding episode from EGV is estimated at 12–15%, with mortality from massive hemorrhage reaching up to 50% [12].

The pathogenesis of EGV is driven by the redistribution of portal blood flow through collateral veins due to elevated portal venous pressure (exceeding 12 mmHg). Key predictors of variceal bleeding include high-grade varices according to Paquet and Sarin classifications (grades III–IV), the presence of red signs (red wale markings, cherry red spots), advanced hepatic dysfunction (Child–Pugh class B/C, MELD >18), and rapid progression of cirrhosis [6].

Esophagogastroduodenoscopy (EGD) remains the gold standard for diagnosing EGV, enabling both visualization of variceal columns and the implementation of therapeutic interventions such as endoscopic ligation or sclerotherapy. Clinical studies have demonstrated that endoscopic band ligation reduces the 1-year rebleeding rate to 15–20%, compared to 45–50% with pharmacological therapy alone [9].

In emergency settings, during active hemorrhage, in addition to vasoactive drugs (e.g., terlipressin, octreotide), balloon tamponade using a Sengstaken–Blakemore tube is employed, achieving temporary hemostasis in 80–90% of cases. However, this technique carries significant complication risks, including aspiration pneumonia (up to 25%) and esophageal perforation (up to 10%) [5, 8, 11].

To prevent rebleeding, a combined approach is recommended: non-selective β-blockers (e.g., propranolol) in conjunction with scheduled endoscopic band ligation. This combination therapy reduces the recurrence rate to 10–12% [10]. In cases refractory to medical and endoscopic treatments, placement of a trans jugular intrahepatic portosystemic shunt (TIPS) is considered. TIPS achieves up to 90% efficacy in preventing recurrent bleeding but is associated with hepatic encephalopathy in 30–35% of cases and requires advanced technical facilities [10].

According to official statistics from the Ministry of Health of the Republic of Kazakhstan, the incidence of liver cirrhosis in 2021 was 53.1 per 100,000 population, representing a 3.77% increase compared to 2020 (51.2 per 100,000) [8]. More than 49,000 individuals are under dispensary observation for viral hepatitis in Kazakhstan, including 23,500 with hepatitis C, over 22,000 with hepatitis B, and 1,250 with hepatitis D. Cirrhosis has been confirmed in 5,948 patients [5, 8].

Variceal bleeding occurs annually in 5–15% of patients with cirrhosis. Multicenter studies have shown that 25–30% of patients with newly diagnosed EGV experience bleeding within two years. Overall, up to 70% of upper gastrointestinal bleeding episodes in cirrhotic patients are attributable to esophageal and gastric varices [7].

Despite the adoption of contemporary clinical protocols, early mortality following variceal bleeding remains high, ranging from 15% to 24%. A population-based study conducted in the United States demonstrated a decline in in-hospital mortality from 18% in 2010 to 11.5% in 2016

[3,9]. However, in resource-limited settings, mortality rates remain consistently high, largely due to delayed hospital presentation, decompensated liver function, and high incidence of infectious complications [4, 11].

Therefore, bleeding from esophageal and gastric varices remains one of the leading causes of mortality in patients with liver cirrhosis, necessitating a comprehensive approach to treatment and prevention. The present study is a retrospective analysis of clinical cases of EGV-related bleeding recorded at the City Emergency Hospital in Almaty between 2022 and 2024, aimed at evaluating the clinical course, therapeutic strategies, and outcomes of these patients.

**The objective of this study** was to analyze the clinical and laboratory characteristics, diagnostic approaches, and therapeutic strategies for esophageal and gastric variceal bleeding in patients admitted to the City Emergency Medical Care Hospital in Almaty over the past three years.

**Materials and Methods**

A retrospective analysis was conducted based on medical records of patients who received treatment for bleeding from esophageal and gastric varices at the City Emergency Medical Care Hospital in Almaty between 2022 and 2024. A total of 162 patients aged 20 to 80 years (mean age 54.3 ± 11.8 years) were included, comprising 90 males (55.6%) and 72 females (44.4%).

*Inclusion criteria* were as follows: age ≥18 years; a confirmed diagnosis of liver cirrhosis; evidence of acute upper gastrointestinal bleeding endoscopically verified as originating from esophageal or gastric varices; and the availability of complete medical documentation (hospital records, diagnostic and treatment protocols).

*Exclusion criteria* included non-variceal sources of bleeding (e.g., peptic ulcer disease, erosive gastritis, Mallory–Weiss syndrome, neoplasms), insufficient clinical or endoscopic data, and coagulopathies unrelated to hepatic pathology.

The diagnostic workup comprised assessment of presenting complaints, physical examination, and laboratory testing, including complete blood count and biochemical panel (hemoglobin, platelet count, bilirubin, ALT, AST, albumin, INR), coagulation profile, Child–Pugh classification, and MELD score calculation. Abdominal ultrasound and mandatory esophagogastroduodenoscopy (EGD) were performed in all cases.

Endoscopic evaluation of esophageal varices was performed in accordance with the Japanese JGES classification, which includes assessment of variceal form (F0–F3), color (Cb/Cr), presence of red color signs (e.g., red wale markings, cherry red spots), and extent of variceal involvement (Ls, Lm, Lg).

The therapeutic protocol included fluid resuscitation, blood transfusions, vasoactive pharmacologic agents, and endoscopic interventions such as variceal band ligation or sclerotherapy of esophageal and gastric varices. In severe cases, balloon tamponade using a Sengstaken–Blakemore tube was employed as a temporary hemostatic measure prior to definitive endoscopic therapy. All patients received antibiotic prophylaxis. Patients with hemodynamic instability were transferred to the intensive care unit. Upon stabilization, secondary prophylaxis with non-selective β-blockers was initiated.

The following parameters were analyzed: demographic data (age, sex), hemostatic and liver function indices upon admission, volume and effectiveness of hemostatic interventions, rebleeding rate, mortality and its correlation with cirrhosis severity, duration of hospitalization, and overall clinical outcomes.

Statistical analysis was performed using Microsoft Excel and SPSS Statistics version 25.0. Continuous variables were expressed as mean ± standard deviation (M ± SD). Group comparisons were conducted using the Student's t-test for normally distributed variables, the $\chi^2$ test for categorical variables, and one-way analysis of variance (ANOVA). A p-value of <0.05 was considered statistically significant.

***Ethical Considerations**:* The study was reviewed and discussed at the Department of Surgical Diseases No. 1 of the Kazakh National Medical University named after S.D. Asfendiyarov. Given the retrospective design and the use of fully anonymized patient data, formal approval from the local ethics committee was not required. The conduct of the study complied with applicable national regulations and international ethical standards.

**Results:**

Over the three-year observation period (2022–2024), a total of 162 patients with bleeding from esophageal and gastric varices (EGV) were admitted to the City Emergency Medical Care Hospital in Almaty. The highest number of cases was recorded in 2024, with 64 patients (39.5%), followed by 50 patients (30.9%) in 2023, and 48 patients (29.6%) in 2022.

An analysis of the gender and age distribution of patients with EGV-related bleeding over the study period (Table 1) revealed a moderate predominance of males, who accounted for 55.6% (n = 90) of the total cohort (n = 162). The gender distribution remained relatively stable across the years, with minor fluctuations ranging from 54.7% to 56.3% among male patients. The overall mean age of patients was 54.3 ± 11.2 years. Age dynamics were also consistent over time: 53.8 ± 10.9 years in 2022, 54.5 ± 11.5 years in 2023, and 54.7 ± 11.2 years in 2024. The age range across all years extended from 20 to 80 years (Table 1).

*Table 1.*

**Distribution of patients with esophageal and gastric variceal bleeding by sex and age, 2022–2024.**

| Year | Number of Patients | Male (n, %) | Female (n, %) | Mean Age (years) | Age Range (years) |
|---|---|---|---|---|---|
| 2022 | 48 | 27 (56.3%) | 21 (43.7%) | 53.8 ± 10.9 | 20–78 |
| 2023 | 50 | 28 (56.0%) | 22 (44.0%) | 54.5 ± 11.5 | 22–80 |
| 2024 | 64 | 35 (54.7%) | 29 (45.3%) | 54.7 ± 11.2 | 21–80 |

In 101 cases (62.3%), severe posthemorrhagic anemia was identified, with hemoglobin levels below 70 g/L, necessitating urgent transfusion therapy. The mean hemoglobin level at admission was 72.6 ± 14.8 g/L. In 15 patients (9.3%), variceal bleeding was the first clinical manifestation of previously undiagnosed liver cirrhosis, complicating timely initiation of prophylactic measures against portal hypertension-related complications.

All patients underwent endoscopic evaluation of esophageal and gastric varices upon admission, utilizing the Japanese JGES classification, which assesses variceal morphology, the presence of red color signs (RCS), and the extent of variceal involvement. According to esophagogastroduodenoscopy (EGD) findings, 145 patients (89.5%) were diagnosed with grade II or III esophageal varices. Gastric varices were detected in 17 patients (10.5%), including 10 cases (6.2%) in combination with esophageal varices. Additionally, signs of portal hypertensive gastropathy were identified in 4 female patients (2.5%).

Based on endoscopic grading, the majority of patients (n = 154; 95.1%) presented with grade II or III esophageal varices according to the JGES classification. Grade II varices were observed in 70 patients (43.2%), while grade III varices were noted in 84 patients (51.9%). Only 8 patients (4.9%) had grade I varices, underscoring the predominance of advanced portal hypertension in the study cohort. The average variceal grade was 2.47 ± 0.55.

Assessment of hepatic functional status using the Child–Pugh score revealed a predominance of classes B and C, corresponding to subcompensated and decompensated cirrhosis, respectively. Class A was documented in 49 patients (30.2%), class B in 89 patients (54.9%), and class C in 24 patients (14.8%). The mean Child–Pugh score was 7.97 ± 1.6, indicating moderate hepatic dysfunction. The additionally calculated MELD score averaged 15.2 ± 3.4 (Table 2).

*Table 2.*

**Distribution of patients by esophageal variceal grade (JGES classification) and Child–Pugh class across the study years (2022–2024).**

| Criterion | 2022 (n = 48) | 2023 (n = 50) | 2024 (n = 64) | Total (n = 162) |
|---|---|---|---|---|
| Grade I (JGES) | 3 (6.3%) | 2 (4.0%) | 3 (4.7%) | 8 (4.9%) |
| Grade II (JGES) | 20 (41.7%) | 22 (44.0%) | 28 (43.8%) | 70 (43.2%) |
| Grade III (JGES) | 25 (52.1%) | 26 (52.0%) | 33 (51.6%) | 84 (51.9%) |
| Mean JGES grade | 2.46 ± 0.58 | 2.48 ± 0.52 | 2.48 ± 0.54 | 2.47 ± 0.55 |
| Child–Pugh Class A | 16 (33.3%) | 15 (30.0%) | 18 (28.1%) | 49 (30.2%) |
| Child–Pugh Class B | 26 (54.2%) | 27 (54.0%) | 36 (56.3%) | 89 (54.9%) |
| Child–Pugh Class C | 6 (12.5%) | 8 (16.0%) | 10 (15.6%) | 24 (14.8%) |
| Mean Child–Pugh score | 7.8 ± 1.5 | 8.0 ± 1.6 | 8.1 ± 1.7 | 7.97 ± 1.6 |

**Therapeutic Interventions and Outcomes.**

Patients with bleeding from esophageal and gastric varices (n = 162) received stepwise treatment aimed at hemodynamic stabilization, bleeding control, and prevention of recurrence. Management included pharmacological, transfusion, and endoscopic interventions, selected based on the severity of the patient's condition and the nature of the bleeding episode.

Pharmacological therapy was administered to all patients and consisted of vasoactive agents (terlipressin or octreotide), proton pump inhibitors, hemostatic agents, and prophylactic antibiotics—primarily third-generation cephalosporins—to prevent infectious complications. Treatment was initiated within the first hours of hospital admission.

Transfusion therapy was performed in 106 patients (65.4%) using packed red blood cells (PRBC) and fresh frozen plasma (FFP). The mean transfused volume was 2.1 ± 1.4 units of PRBC and 2.6 ± 1.9 units of FFP. Indications included hemoglobin levels <70 g/L, signs of hypovolemia, and reduced prothrombin index.

Endoscopic variceal ligation (EVL) was performed in 89 patients (54.9%), including 78 patients (48.1%) with esophageal varices and 12 patients (7.4%) with gastric varices. Of these, 65 patients (73.0%) underwent EVL within the first 24 hours of hospitalization (mean time: 16.4 ± 4.7 hours), while 24 patients (27.0%) underwent the procedure on the second day. In cases of ongoing active bleeding, the procedure was performed under intravenous anesthesia in the intensive care unit (ICU) to ensure hemodynamic stabilization, reduce the risk of aspiration, improve visualization, and enhance procedural safety.

The ligation procedure was conducted using a multiband ligator (Wilson-Cook) with a 10-ring latex cartridge, allowing for effective ligation of multiple variceal columns in a single session.

Sclerotherapy, as an alternative endoscopic hemostatic technique, was employed in 17 patients (10.5%) beginning in April 2023, primarily in cases where ligation was technically unfeasible—such as with highly tortuous varices, massive bleeding, limited endoscopic visibility, or gastric varices, which are often more challenging to manage via ligation.

Balloon tamponade using a Sengstaken–Blakemore tube was utilized in 29 patients (17.9%) for massive ongoing hemorrhage when endoscopic hemostasis was not feasible or technically limited. The mean duration of tamponade was 12.5 ± 3.2 hours.

Due to the severity of their condition, 54 patients (33.3%) were immediately transferred from the emergency department to the ICU. Indications for ICU admission included hemodynamic instability, significant hypovolemia, severe anemia, and coagulopathy. In the ICU, patients received intensive fluid and transfusion therapy, vasopressor support, correction of coagulopathies, and continuous monitoring of vital parameters. The mean ICU stay was 2.9 ± 1.7 days.

Over the three-year study period (2022–2024), complications, rebleeding rates, and survival outcomes were analyzed among the 162 patients. The in-hospital rebleeding rate was 2.5% (n = 4). Within 12 months, recurrent bleeding occurred in 11 patients (6.8%), all of whom underwent repeated EVL, while an additional 18 patients (11.1%) received conservative pharmacologic therapy.

The overall mortality rate was 4.32% (n = 7), with all deaths occurring in patients with advanced decompensation (Child–Pugh class B/C), elevated MELD scores, and ICU admission. The primary causes of death were progressive hepatic-renal failure, hepatorenal syndrome, and infectious complications. Annual mortality distribution was as follows: 2 of 48 patients (4.2%) in 2022, 4 of 50 patients (8.0%) in 2023, and 1 of 64 patients (1.56%) in 2024. No statistically significant upward trend in mortality was observed ($p > 0.05$).

Post-endoscopic procedural mortality—defined as death following EVL or sclerotherapy—was 1.2% (n = 2), with one case each in 2022 and 2023. No procedure-related deaths were recorded in 2024.

The overall procedural intervention rate was 65.4% (n = 106), including endoscopic variceal ligation in 89 patients (54.9%) and sclerotherapy in 17 patients (10.5%) (Table 3).

*Table 3.*

**Distribution of complications among patients with esophageal and gastric variceal bleeding by year of observation (2022–2024).**

| Complication | 2022 (n = 48) | 2023 (n = 50) | 2024 (n = 64) | Total (n = 162) |
|---|---|---|---|---|
| Rebleeding within 12 months | 4 (8.3%) | 4 (8.0%) | 3 (4.7%) | 11 (6.8%) |
| Overall mortality | 2 (4.2%) | 4 (8.0%) | 1 (1.56%) | 7 (4.32%) |
| Post-procedural mortality | 1 (2.1%) | 1 (2.0%) | 0 (0.0%) | 2 (1.2%) |

**Risk Factor Analysis for Rebleeding from Esophageal and Gastric Varices**. An analysis of risk factors for rebleeding among patients with esophageal and gastric variceal hemorrhage (n = 162) revealed the significant prognostic impact of endoscopic findings and timing of intervention. The presence of red color signs (RCS) was associated with the highest risk of rebleeding, observed in 17.9% of patients, with an odds ratio (OR) of 6.51. Among patients with grade III esophageal or gastric varices, the rebleeding rate was 7.7% (OR = 1.32). Delayed endoscopic intervention (ligation performed ≥24 hours after admission) was also associated with an increased risk of recurrence—12.5% of such cases experienced rebleeding (OR = 2.32). A higher MELD score (≥15) was linked to rebleeding in 8.2% of cases (OR = 1.50).

In contrast, patients with Child–Pugh class B/C had a lower recurrence rate of 6.0%, and those who did not undergo ligation had a recurrence rate of 6.8%, both with lower predictive value (OR <2). These findings emphasize the need for close monitoring of patients with unfavorable endoscopic features and advanced liver dysfunction (Table 4).

*Table 4.*

**Risk Factors for Rebleeding from Esophageal and Gastric Varices.**

| Risk Factor | Rebleeding (n, %) | No Rebleeding (n, %) | OR (Odds Ratio) |
|---|---|---|---|
| Grade III esophageal/gastric varices | 6 (7.7%) | 72 (92.3%) | 1.32 |
| Presence of red color signs (RCS) | 7 (17.9%) | 32 (82.1%) | 6.51 |
| Child–Pugh class B/C | 5 (6.0%) | 79 (94.0%) | 0.76 |
| MELD score ≥15 | 6 (8.2%) | 67 (91.8%) | 1.50 |
| Ligation performed ≥24 hours | 3 (12.5%) | 21 (87.5%) | 2.32 |
| No ligation performed | 5 (6.8%) | 68 (93.2%) | 1.29 |

**Discussion**

The results of our study highlight the critical importance of timely diagnosis and intervention in the management of variceal bleeding among patients with liver cirrhosis. The data show that the vast majority of patients (95.1%) were admitted with advanced grade II–III esophageal and gastric varices, as classified by the Japanese JGES system.

A pivotal prognostic factor identified in our cohort was the timing of endoscopic hemostasis. Early ligation performed within the first 24 hours was associated with the lowest risk of rebleeding (2.3%) and zero postprocedural mortality, whereas delayed intervention (≥24 hours) was linked to a twofold increase in rebleeding risk (12.5%; OR = 2.32). These findings align with current recommendations from the JGES and Baveno VII consensus, both of which emphasize the necessity of performing endoscopic therapy within the first 24 hours following presentation [10, 11].

The presence of red color signs (RCS) warrants particular attention as a marker of high bleeding risk. In our study, patients with RCS exhibited a rebleeding rate of 17.9% (OR = 6.51), markedly higher than in those without such signs. This finding is consistent with the results reported by Trofimov et al. and Liu et al. [6, 12], which also emphasized the high prognostic value of endoscopic features, particularly RCS, in predicting adverse outcomes.

Assessment of hepatic function revealed that the most unfavorable clinical outcomes—including an overall mortality rate of 4.32%—were primarily observed in patients with decompensated cirrhosis (Child–Pugh classes B/C and MELD ≥15). These results are corroborated by studies conducted by Mandal et al. and

Danpanichkul et al. [4, 7], which also identified hepatic decompensation as the principal predictor of mortality in cases of variceal hemorrhage.

Of note, in 9.3% of cases, the bleeding episode represented the first clinical manifestation of previously undiagnosed cirrhosis, underscoring a significant gap in early detection of liver disease in Kazakhstan. According to data from the World Health Organization (WHO) [5] and the Ministry of Health of the Republic of Kazakhstan [8], the prevalence of chronic liver diseases remains high in the region—particularly among working-age men—a trend that is reflected in our study cohort (male proportion: 55.6%).

The overall mortality rate of 4.32%, including a postprocedural mortality of 1.2%, appears acceptable when compared to international benchmarks, which range from 3% to 7% depending on the severity of cirrhosis and the presence of complications [4, 11].

In summary, the principal factors associated with rebleeding and mortality in this study were the presence of red color signs (OR = 6.51), grade III varices (OR = 1.32), delayed endoscopic intervention (≥24 hours; OR = 2.32), and MELD score ≥15 (OR = 1.50). These findings underscore the necessity for an individualized management strategy for variceal hemorrhage, including early endoscopic diagnosis, proactive use of variceal ligation for grade II–III varices, and rigorous control of risk factors in patients with advanced cirrhosis.

This study has several limitations, including its retrospective and single-center design, potential gaps in medical documentation, the absence of a standardized treatment protocol, limited sample sizes in certain subgroups (e.g., patients with grade I varices), and the lack of long-term survival data beyond one year. Nevertheless, the study possesses substantial strengths, including a robust sample size (n = 162) over a three-year period, use of validated scoring systems (Child–Pugh, MELD, JGES), comprehensive evaluation of endoscopic intervention effectiveness in real-world clinical settings, and reliable statistical analysis with odds ratio (OR) calculations and significance testing, thereby enhancing the scientific and clinical relevance of the findings.

**Conclusions**

1. Among the 162 patients with esophageal and gastric varices, males predominated (55.6%), with a mean age of 54.3 ± 11.2 years; anemia with hemoglobin levels <70 g/L was detected in 62.3% of cases.

2. Grade II–III varices were diagnosed in 95.1% of patients; Child–Pugh classes B and C accounted for 69.7%, and the mean MELD score was 15.2 ± 3.4.

3. Early ligation (<24 hours) reduced the rebleeding rate to 2.3%, while delayed ligation (≥24 hours) was associated with a higher recurrence rate of 12.5% (OR = 2.32); the presence of red color signs (RCS) increased the risk of rebleeding to 17.9% (OR = 6.51).

4. The overall mortality rate was 4.32%, and postprocedural mortality was 1.2%; all fatal outcomes occurred in patients with severe hepatic decompensation.

Bleeding from esophageal and gastric varices remains a life-threatening complication of liver cirrhosis, carrying a significant risk of mortality. The present analysis demonstrates that most patients present with advanced portal hypertension and impaired hepatic function. Early endoscopic variceal ligation (<24 hours) was identified as the most effective method for achieving hemostasis and preventing rebleeding. The presence of red color signs and higher variceal grade per JGES classification were significantly associated with an increased risk of rebleeding. These findings underscore the importance of timely diagnosis, early intervention, and risk stratification in patients with variceal bleeding in the setting of liver cirrhosis.

***Study Limitations:*** *The single-center nature of the study may limit its generalizability, and the absence of long-term follow-up data restricts the assessment of post-discharge outcomes.*

***Author Contributions:*** *All authors contributed equally to the writing of this manuscript.*

***Conflict of Interest:*** *The authors declare no conflicts of interest. This material has not been submitted to other journals and is not under consideration elsewhere.*

***Funding:*** *No funding was received for this study. Literature:*

***Literature:***

1. *Ames J.B.*, *Djerboua M.*, *Terrault N.A.*, *Booth C.M.*, *Flemming J.A.* Rising healthcare costs and utilization among young adults with cirrhosis in Ontario: a population-based study. Can J Gastroenterol Hepatol. 2022. 2022. P. 6175913. https://doi.org/10.1155/2022/6175913

2. *Bhusal M.*, *Pathak R.*, *Kafle Bhandari B.*, *Jha A.*, *Hamal R.*, *Koirala D.* et al. Liver cirrhosis among young adults admitted to the department of gastroenterology in a tertiary care centre: a descriptive cross-sectional study. JNMA J Nepal Med Assoc. 2023. 61(258). P. 115–118. https://doi.org/10.31729/jnma.8016

3. *Chooklin S.M.*, *Chuklin S.S.*, *Posivnych M.M.*, *Krystopchuk S.A.* Esophageal and stomach varices: physiological and anatomical features of formation. Ukr J Clin Surg. 2023. 90(1). P. 57–63. https://doi.org/10.26779/2786-832X.2023.1.57

4. *Danpanichkul P.*, *Ng C.H.*, *Tan D.J.H.*, *Wijarnpreecha K.*, *Huang D.Q.*, *Noureddin M.* et al. The global burden of alcohol-associated cirrhosis and cancer in young and middle-aged adults. Clin Gastroenterol Hepatol. 2024. 22(9). P. 1947–1949.e3. https://doi.org/10.1016/j.cgh.2024.02.011

5. European Health Information Gateway. Chronic liver diseases and cirrhosis per 100 000 population. WHO.int [Internet]. https://gateway.euro.who.int

6. *Liu H.*, *Chen P.*, *Jiang B.*, *Li F.*, *Han T.* The value of platelet parameters and related scoring system in predicting esophageal varices and collateral veins in patients with liver cirrhosis. J Clin Lab Anal. 2021. 35(3). P. e23694. https://doi.org/10.1002/jcla.23694

7. *Mandal A.K.*, *Paudel M.S.*, *Kc S.*, *Chaudhary S.*, *Paudel B.N.*, *Poudyal N.S.* et al. Factors predicting mortality of acute variceal bleeding in liver cirrhosis. JNMA J Nepal Med Assoc. 2018. 56(209). P. 493–496. https://doi.org/10.31729/jnma.3408

8. Ministry of Health of Kazakhstan. Kazakhstan ranks among the leaders in hepatitis control. Gov.kz [Internet]. https://www.gov.kz/memleket/entities/dsm

9. *Moon A.M.*, *Webb G.J.*, *Aloman C.*, *Armstrong M.J.*, *Cargill T.*, *Dhanasekaran R.* et al. High mortality rates for SARS-CoV-2 infection in patients with pre-existing chronic liver disease and cirrhosis: preliminary results from an international registry. J Hepatol. 2020. 73(3). P. 705–708. https://doi.org/10.1016/j.jhep.2020.05.013

10. *Pallio S.*, *Melita G.*, *Shahini E.*, *Vitello A.*, *Sinagra E.*, *Lattanzi B.* et al. Diagnosis and management of esophagogastric varices. Diagnostics. 2023. 13(6). P. 1031. https://doi.org/10.3390/diagnostics13061031

11. *Rajesh S.*, *George T.*, *Philips C.A.*, *Ahamed R.*, *Kumbar S.*, *Mohan N.* et al. Transjugular intrahepatic portosystemic shunt in cirrhosis: An exhaustive critical update. World J Gastroenterol. 2020. 26(37). P. 5561–5596. https://doi.org/10.3748/wjg.v26.i37.5561

12. *Trofimov M.V.*, *Korpusenko V.G.*, *Muntyan S.O.*, *Kuznetsov G.E.*, *Gromov V.V.* Clinical and statistical aspects of the development and course of bleeding from varicose veins of the esophagus in patients with portal hypertension. Kharkiv Surg School. 2021. (1). P. 46–51. https://doi.org/10.37699/2308-7005.1.2021.09

**Information about authors:**

**Onlasyn Ibekenov -** Candidate of Medical Sciences, Highest Category Surgeon, Head of the Strategic Block at the National Scientific Center of Surgery Named After A.N. Syzganov, Almaty, Republic of Kazakhstan; E-mail: onlasin72@mail.ru; Tel.: 8 707 740 8039, ORCID: 0000-0001-6605-6435

**Abylai Baymakhanov -** Candidate of Medical Sciences, Associate Professor, Dean of the Faculty of Postgraduate Education at NJC "Kazakh National Medical University named after S.D. Asfendiyarov, Professor of the Department of Surgical Diseases №1, Almaty, Republic of Kazakhstan; E-mail: baimakhanov.a@kaznmu.kz; Tel.: 8 701 759 4017, ORCID: 0009-0001-0344-1800

**Aman Berkinbay -** Surgical Resident (2nd year), NJC "Kazakh National Medical University named after S.D. Asfendiyarov, Almaty, Republic of Kazakhstan; E-mail: aman_98e@mail.ru; Tel.: 8 708 172 1280, ORCID: 0000-0002-3973-7283

**Yermek Zheldibaev -** Deputy Director for Surgery at the City Emergency Medical Care Hospital, Highest Category Surgeon, Almaty, Republic of Kazakhstan; E-mail: er.med@mail.ru; Tel.: 8 707 527 7792, ORCID: 0009-0004-0216-1307

**Makhsat Duisebekov -** Head of the Surgery Department, Hepatobiliary Surgeon at the City Emergency Medical Care Hospital, Almaty, Republic of Kazakhstan; E-mail: makhsatduisebekov@yandex.kz; Tel.: 8 701 745 2616, ORCID: 0009-0001-6697-8074

**Nurhat Esenbekov -** Highest Category Surgeon at the City Emergency Medical Care Hospital, Almaty, Republic of Kazakhstan; E-mail: esenbekovnurhat4@gmail.com; Tel.: 8 747 171 7273, ORCID: 0009-0007-5324-2117

**Sabit Iskakov -** Endoscopic surgeon, at the City Emergency Medical Care Hospital, Almaty, Republic of Kazakhstan; E-mail: sabit.iskakov@mail.ru, Tel.: 8 707 787 8045, ORCID: 0009-0000-2359-9026

**Mazhit Abdykadyrov** - Endoscopic surgeon, at the City Emergency Medical Care Hospital, Almaty, Republic of Kazakhstan; E-mail: abdykadyrov.m@gmail.com, Tel.: 8 707 105 0100, ORCID: 0000-0002-9518-5292

**Erzhan Tulebaev -** Surgical Resident (2nd year), NJC "Kazakh National Medical University named after S.D. Asfendiyarov, Almaty, Republic of Kazakhstan; E-mail: 1995_erzhan@mail.ru; Tel.: 8 747 222 0213, ORCID: 0009-0007-6053-787X

**Dias Myrzash -** Surgical Resident (2nd year), NJC "Kazakh National Medical University named after S.D. Asfendiyarov, Almaty, Republic of Kazakhstan; E-mail: diasmyrzash@gmail.com; Tel.: 8 705 857 4858, ORCID: 0009-0001-7793-2338

**Corresponding author:**

**Onlasyn Ibekenov -** Candidate of Medical Sciences, Highest Category Surgeon, Head of the Strategic Block at the National Scientific Center of Surgery Named After A.N. Syzganov, Almaty, Republic of Kazakhstan; ORCID: 0000-0001-6605-6435

**E-mail:** onlasin72@mail.ru;

**Phone number:** +7 701 740 80 39

Received: 07 April 2025 / Accepted: 30 May 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2025.27.3.017***

***UDC 616-079.3:616.211-002***

This work is licensed under a Creative Commons Attribution 4.0 International License

# EVALUATION OF THE EFFECTIVENESS OF MOLECULAR ALLERGY DIAGNOSTIC METHODS IN THE PERSONALIZED MANAGEMENT OF PATIENTS WITH ALLERGIC RHINITIS

**Sabina R. Valiyeva[1], https://orcid.org/0000-0003-0767-1993**
**Natalya E. Glushkova[2], https://orcid.org/0000-0003-1400-8436**
**Zhanar K. Buribayeva[1], https://orcid.org/0000-0003-3871-8002**
**Aigulsum K. Izekenova[3], https://orcid.org/0000-0003-3850-8689**

**[1] Kazakhstan Medical University "KSPH" Almaty, Republic of Kazakhstan;**
**[2] Al-Farabi Kazakh National University, Almaty, Republic of Kazakhstan;**
**[3] NCJSC "Asfendiyarov Kazakh National Medical University", Almaty, Republic of Kazakhstan.**

**Abstract**

**Introduction:** Allergic rhinitis (AR) is a common IgE-mediated condition that significantly reduces quality of life. Conventional diagnostic methods do not always allow for the accurate identification of causative allergens, especially in cases of polysensitization.

**Objective:** A comparative evaluation of the effectiveness of two molecular allergy diagnostic methods—ImmunoCAP and immunochemiluminescent assay (ICLA)—in patients with allergic rhinitis.

**Methods:** A retrospective study involving 60 patients with confirmed AR was conducted. Sensitivity, specificity, predictive values, and overall diagnostic performance of the methods were analyzed. Pearson's chi-squared test, ROC analysis, and calculation of AUC were applied.

**Results:** ImmunoCAP demonstrated a sensitivity of 87.8% and an AUC of 0.88. ICLA showed higher specificity (61.3%) and an AUC of 0.79. PPV was comparable (66.7% vs. 65.7%), whereas NPV was higher for ICLA (76.0% vs. 16.7%). The differences between the methods were statistically significant (p = 0.001).

**Conclusions:** Both methods are valuable tools in the diagnosis of AR. ImmunoCAP is preferable for the initial detection of sensitization, while ICLA is more suitable for confirming clinically relevant allergy and minimizing false-positive results.

***Keywords:*** *Allergic rhinitis, IgE, allergy diagnostics, ICLA, ImmunoCAP, personalized medicine.*

***For citation:***

*Valiyeva S.R., Glushkova N.E., Buribayeva Zh.K., Izekenova A.K.* Evaluation of the effectiveness of molecular allergy diagnostic methods in the personalized management of patients with allergic rhinitis // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 151-156. *doi 10.34689/SH.2025.27.3.017*

**Резюме**

# ОЦЕНКА ЭФФЕКТИВНОСТИ МЕТОДОВ МОЛЕКУЛЯРНОЙ АЛЛЕРГОДИАГНОСТИКИ В ПЕРСОНАЛИЗИРОВАННОМ ВЕДЕНИИ ПАЦИЕНТОВ С АЛЛЕРГИЧЕСКИМ РИНИТОМ

**Сабина Р. Валиева[1], https://orcid.org/0000-0003-0767-1993**
**Наталья Е. Глушкова[2], https://orcid.org/0000-0003-1400-8436**
**Жанар К. Бурибаева[1], https://orcid.org/0000-0003-3871-8002**
**Айгульсум К. Изекенова[3], https://orcid.org/0000-0003-3850-8689**

**[1] Казахстанский медицинский университет «ВШОЗ», г. Алматы, Республика Казахстан;**
**[2] Казахский национальный университет имени Аль-Фараби, г. Алматы, Республика Казахстан;**
**[3] НАО «Казахский Национальный медицинский университет им. С.Д. Асфендиярова», г. Алматы, Республика Казахстан.**

**Введение:** Аллергический ринит (АР) — распространённое IgE-опосредованное заболевание, существенно снижающее качество жизни. Традиционные методы диагностики не всегда позволяют точно определить причинно-значимые аллергены, особенно при полисенсибилизации.

**Цель:** Сравнительная оценка эффективности молекулярных методов диагностики аллергии ImmunoCAP и иммунохемилюминесцентного анализа (ИХЛА) у пациентов с аллергическим ринитом.

**Методы:** Ретроспективное исследование с участием 60 пациентов с подтверждённым АР. Проанализированы чувствительность, специфичность, прогностические значения и диагностическая эффективность методов. Применялись $\chi^2$-критерий, ROC-анализ и расчёт AUC.

**Результаты:** Чувствительность ImmunoCAP составила 87,8%, AUC – 0,88. ИХЛА показал большую специфичность (61,3%) и AUC – 0,79. PPV был сопоставимым (66,7% vs. 65,7%), тогда как NPV выше у ИХЛА (76,0% vs. 16,7%). Различия между методами статистически значимы (p = 0,001).

**Выводы:** Оба метода являются ценными инструментами диагностики АР. ImmunoCAP предпочтителен при первичном выявлении сенсибилизации, ИХЛА — для подтверждения клинически значимой аллергии и снижения количества ложноположительных результатов.

***Ключевые слова:*** *Аллергический ринит, IgE, аллергологическая диагностика, ИХЛА, ImmunoCAP, персонализированная медицина.*

***Для цитирования:***

*Валиева С.Р., Глушкова Н.Е., Бурибаева Ж.К., Изекенова А.К.* Оценка эффективности методов молекулярной аллергодиагностики в персонализированном ведении пациентов с аллергическим ринитом // Наука и Здравоохранение. 2025. Т.27 (3), С. 151-156. doi: 10.34689/SH.2025.27.3.017

**Түйіндеме**

# АЛЛЕРГИЯЛЫҚ РИНИТІ БАР НАУҚАСТАРДЫ ЖЕКЕ БАСҚАРУДАҒЫ МОЛЕКУЛАЛЫҚ ДИАГНОСТИКАЛЫҚ ӘДІСТЕРДІҢ ТИІМДІЛІГІН БАҒАЛАУ

**Сабина Р. Валиева[1], https://orcid.org/0000-0003-0767-1993**
**Наталья Е. Глушкова[2], https://orcid.org/0000-0003-1400-8436**
**Жанар К. Бурибаева[1], https://orcid.org/0000-0003-3871-8002**
**Айгульсум К. Изекенова[3], https://orcid.org/0000-0003-3850-8689**

**[1] "University Medical Center" корпоративтік қоры, Астана қ., Қазақстан Республикасы;**
**[2] Назарбаев Университеті, Астана қ., Қазақстан Республикасы**
**[3] «С.Д.Асфендияров атындағы Қазақ ұлттық медицина университеті» КеАҚ, Алматы қ., Қазақстан Республикасы.**

**Кіріспе:** Аллергиялық ринит – IgE-делдалды созылмалы қабыну ауруы. Көп жағдайда дәстүрлі диагностикалық әдістер себепші аллергенді дәл анықтауға мүмкіндік бермейді.

**Зерттеу мақсаты:** Аллергиялық ринитпен ауыратын науқастарда ImmunoCAP және иммунды-хемилюминесценттік талдау (ИХЛА) әдістерінің диагностикалық тиімділігін салыстырып бағалау.

**Зерттеу әдістері:** Алматы қаласындағы клиникада 60 науқасқа ретроспективті зерттеу жүргізілді. ROC-анализ, $\chi^2$-сынамасы, AUC, диагностикалық көрсеткіштер есептелді.

**Нәтижелері:** ImmunoCAP сезімталдығы – 87,8%, AUC – 0,88. ИХЛА спецификалығы – 61,3%, AUC – 0,79. PPV салыстырмалы (66,7% пен 65,7%), ал NPV ИХЛА-да жоғары (76,0% пен 16,7%). Айырмашылықтар статистикалық тұрғыдан маңызды (p = 0,001).

**Қорытынды:** Екі әдіс те аллергиялық ринитті диагностикалауда құнды. ImmunoCAP бастапқы скринингке лайық, ал ИХЛА нақты сенсибилизацияны растау үшін тиімді.

***Түйінді сөздер:*** *Аллергиялық ринит, IgE, аллергия диагностикасы, ИХЛА, ImmunoCAP, жекешелендірілген медицина.*

***Дәйексөз үшін:***

*Валиева С.Р., Глушкова Н.Е., Ьурибаева Ж.К., Изекенова А.К.* Аллергиялық риниті бар науқастарды жеке басқарудағы молекулалық диагностикалық әдістердің тиімділігін бағалау // Ғылым және Денсаулық. 2025. Т.27 (3), Б. 151–156. doi: 10.34689/SH.2025.27.3.017

**Introduction**

Allergic rhinitis (AR) is a chronic inflammatory disorder of the nasal mucosa caused by an IgE-mediated response to inhaled allergens. Globally, the prevalence of AR reaches 25–30% and continues to rise, especially under conditions of urbanization and environmental degradation [1]. AR significantly reduces patients' quality of life, is associated with sleep disturbances, decreased work productivity, and may serve as a predictor for the development of bronchial asthma and other respiratory diseases [2].

Conventional diagnostic approaches include clinical history, physical examination, skin prick testing, and total IgE assessment. However, these methods do not always allow for the accurate identification of causative allergens or

the sensitization profile. The relevance of more precise diagnostic tools increases, particularly in cases of polysensitization or cross-reactivity [3].

The development of molecular allergy diagnostics based on the detection of allergen-specific IgE to individual molecular components has enabled the implementation of personalized management strategies in patients with AR. Specifically, ImmunoCAP (a fluorescence immunoassay) and immunochemiluminescent assay (ICLA) are among the main technologies used for the quantitative measurement of specific IgE [4]. The personalized molecular approach in allergology allows for the precise identification of clinically relevant sensitizations and optimization of allergen-specific immunotherapy (AIT), reducing the risk of treatment inefficacy [5]. These technologies represent a paradigm shift from empirical approaches to precision diagnostics in allergology.

Currently, ImmunoCAP is more widely recognized as the “gold standard” in molecular diagnostics, whereas ICLA is increasingly utilized in clinical practice due to its availability, automation, and high reproducibility. However, there is a lack of studies comparing the performance of these methods in real-world clinical settings for the diagnosis of AR [6]. Therefore, the comparative effectiveness of ImmunoCAP and ICLA remains a matter of debate [7],[8]. Some studies suggest that ImmunoCAP may overestimate the clinical relevance of sensitization, while ICLA may be more suitable for confirming AR diagnosis [9],[10].

**The aim of this study** was to evaluate the diagnostic effectiveness of two molecular allergy diagnostic methods - ImmunoCAP and immunochemiluminescent assay (ICLA) - in the personalized management of patients with allergic rhinitis and to perform a comparative analysis.

**Research objectives:** to determine the sensitivity, specificity, and predictive values of molecular allergy diagnostics using ImmunoCAP and ICLA in patients with allergic rhinitis;

**Materials and Methods**

A retrospective descriptive study was conducted in an outpatient setting at the *Prima Medical Group* clinic (Almaty, Kazakhstan) from October 2023 to September 2024. The study analyzed outpatient records of patients referred for molecular allergy diagnostics using ImmunoCAP and immunochemiluminescent assay (ICLA) for the evaluation of diagnostic performance. A total of 60 patient records were selected, with patient ages ranging from 18 to 60 years, all meeting international ARIA criteria for the diagnosis of allergic rhinitis. The study population was formed using a continuous sampling method and included patients with a confirmed diagnosis of AR who sought medical care between 2022 and 2023.

*Inclusion criteria* were: age ≥18 years, confirmed sensitization based on patient history, skin testing and/or the presence of allergen-specific IgE (sIgE) antibodies, and availability of both ImmunoCAP and ICLA test results.

*Exclusion criteria* included decompensated chronic or autoimmune diseases and uncontrolled comorbid bronchial asthma. All patients were instructed to discontinue antihistamines at least 5–7 days prior to testing to minimize interference with the results. Blood samples were collected in the morning hours following a light fasting period to reduce variability in IgE levels. Both assays were performed in accordance with the manufacturers’ protocols and internal laboratory quality standards.

Seven inhalant allergen extracts were used for testing: birch, ragweed, house dust mite (*Dermatophagoides pteronyssinus*), mold (*Alternaria alternata*), cat epithelium, timothy grass, and mugwort. The ImmunoCAP method was performed using the Phadia 250 analyzer (Thermo Fisher Scientific), while ICLA testing was performed using the Immulite 2000 analyzer (Siemens). The measurement range for both methods was 0.1–100 kU/L, with a cutoff value of 0.35 kU/L.

Data were processed using IBM SPSS Statistics software. Descriptive statistics were used (mean (M), standard deviation (SD), median (Me), mode (Mo)), along with Pearson’s $\chi^2$ test and ROC analysis. The significance threshold was set at $p < 0.05$. Confidence intervals (95% CI) were reported. The following diagnostic metrics were calculated: sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and likelihood ratios.

*Ethical Considerations*

The study was conducted in accordance with ethical standards and the principles of the Declaration of Helsinki. The study was approved by the local Ethics Committee of Kazakhstan Medical University “KSPH” (Protocol No. 18/23, dated September 25, 2023). No personal identifying information was disclosed.

**Results**

The study included 60 patients diagnosed with allergic rhinitis, of whom 36 (60.0%) were women and 24 (40.0%) were men. The mean age of the patients was 35.0 ± 11.2 years (95% CI: 32.1–37.9).

*Table 1.*

**General demographic characteristics of the sample.**

| Parameter | Value |
|---|---|
| Number of patients | 60 |
| Female, n (%) | 36 (60,0 %) |
| Male, n (%) | 24 (40,0 %) |
| Mean age, n (%) | 35.0 ± 11.2 (95 % ДИ: 32.1–37.9) |

The diagnostic performance of the ImmunoCAP and ICLA methods was assessed using the following indicators: sensitivity, specificity, positive and negative predictive values, and overall diagnostic efficiency.

*Table 2.*

**Comparative diagnostic performance of the methods.**

| Indicator | ImmunoCAP | ICLA |
|---|---|---|
| True positives (TP), n | 36 | 23 |
| False positives (FP), n | 18 | 12 |
| False negatives (FN), n | 5 | 6 |
| True negatives (TN), n | 1 | 19 |
| Sensitivity (%) | 87.8 | 79.3 |
| Specificity (%) | 51.3 | 61.3 |
| Positive predictive value (%) | 66.7 | 65.7 |
| Negative predictive value (%) | 16.7 | 76.0 |
| Diagnostic efficiency (%) | 61.7 | 70.0 |

The mean level of specific IgE measured by ImmunoCAP was 40.3 ± 9.8 kU/L (95% CI: 38.1–42.5) (Figure 1).

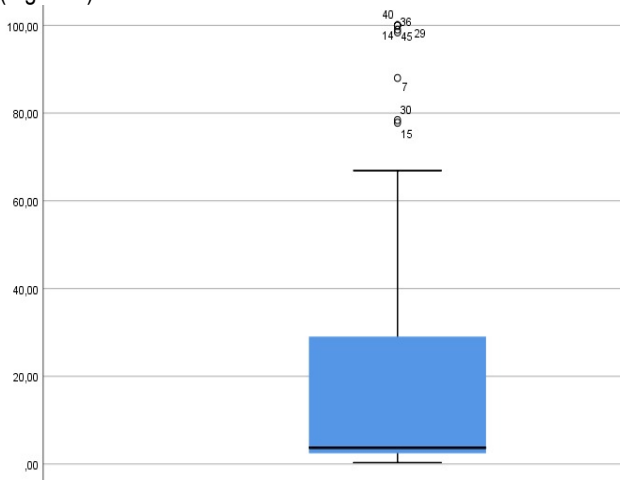



**Figure 1. Distribution of specific IgE levels using the ImmunoCAP method.**

The mean level of specific IgE by ICLA was 36.0 ± 10.4 kU/L (95% CI: 33.7–38.3) (see figure 2).

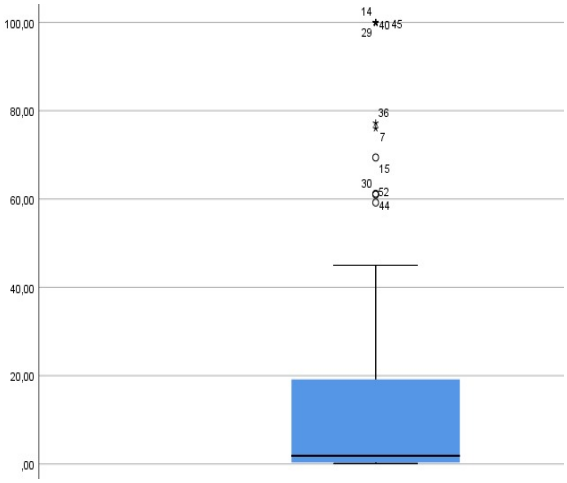



**Figure 2. Distribution of specific IgE levels using the ICLA method.**

**The area under the ROC curve (AUC)** was 0.88 for ImmunoCAP and 0.79 for ICLA, indicating high and good diagnostic accuracy, respectively (see figure 3). The difference was statistically significant based on Pearson's $\chi^2$ test ($\chi^2 = 12.4$; df = 1; p = 0.001). Both methods showed acceptable diagnostic utility for allergic rhinitis. ImmunoCAP demonstrated higher sensitivity, while ICLA had greater specificity. The advantage of ICLA was its higher diagnostic efficiency and a lower number of false-positive results.

Sensitivity and specificity values were further stratified by individual allergens, revealing that ImmunoCAP showed the highest sensitivity for house dust mite and birch pollen, whereas ICLA demonstrated superior specificity for mugwort and cat epithelium allergens. This suggests a possible allergen-dependent performance profile.

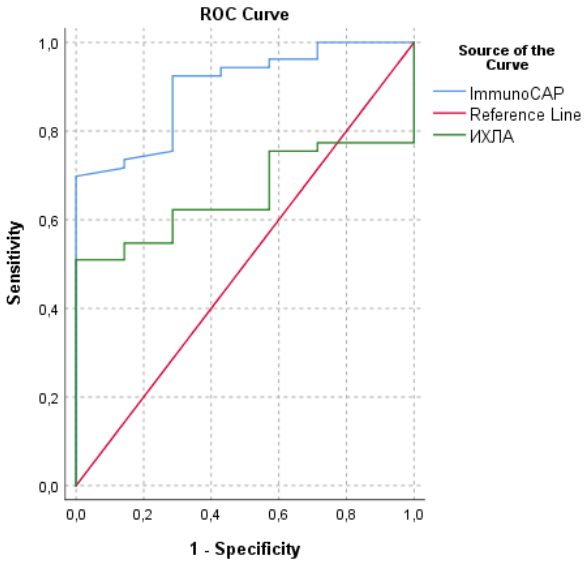



**Figure 3. Comparison of method sensitivity and specificity (ROC curves).**

## Discussion

Allergic rhinitis is characterized by the progressive nature of the pathological process, including the risk of complications and development of more severe disease forms such as bronchial asthma [11]. Patients with allergic rhinitis often experience cognitive impairments, sleep disturbances, daytime fatigue, irritability, and depressive symptoms, all of which substantially reduce quality of life and interfere with daily functioning [12].

Prick tests and skin allergy testing are traditionally used for diagnosing AR. However, the results of skin tests may be unreliable due to multiple factors, leading to false-positive or false-negative outcomes [13]. This necessitates the application of more precise laboratory methods to objectively confirm allergic sensitization—namely, molecular allergy diagnostics [14]. Thus, in this study we compared two modern molecular diagnostic methods—ImmunoCAP and immunochemiluminescent assay (ICLA)—to assess their diagnostic effectiveness in managing patients with allergic rhinitis.

### Comparison of Sensitivity and Specificity

The results of this study showed that ImmunoCAP had higher sensitivity (87.8%), whereas ICLA demonstrated greater specificity (61.3%). These findings align with data from Korean researchers, where ImmunoCAP also exhibited superior sensitivity compared to other methods for specific IgE detection [7]. At the same time, recent data suggest that the innovative NOVEOS method using chemiluminescence provides high specificity (96.2%) and may serve as a reliable tool for diagnosing AR, offering comparable results to ImmunoCAP with a significantly smaller sample volume [15].

According to our data, the high sensitivity of ImmunoCAP was associated with an increased number of false-positive results (18 cases), which could lead to overdiagnosis of sensitization. In contrast, the higher specificity of ICLA helped reduce false positives, though it slightly increased the likelihood of false-negative results (6 cases). The choice of diagnostic method should be guided by the clinical context: ImmunoCAP is preferable in cases of polysensitization, while ICLA is more appropriate for confirming clinically relevant allergy [5].

It is important to note that differences in sensitivity and specificity may be due to the technical characteristics of the

assays: fluorescence-based detection (ImmunoCAP) yields stable signals measurable with high sensitivity, but lower concentrations of IgE can lead to higher background noise. Meanwhile, chemiluminescent reactions generate strong signals even at low IgE concentrations, providing more accurate detection in such cases [16].

**Predictive Value of the Tests**

An important measure of a diagnostic method's effectiveness is its **positive predictive value (PPV)** and **negative predictive value (NPV)**. In our study, the PPV for ImmunoCAP was 66.7%, and for ICLA it was 65.7%, indicating similar capabilities of both methods in predicting the presence of sensitization. However, the NPV was significantly higher for ICLA (76.0% vs. 16.7% for ImmunoCAP), highlighting its advantage in ruling out allergic rhinitis. These findings are consistent with those of a German study, in which ImmunoCAP also demonstrated a higher PPV but was inferior to alternative methods in terms of NPV [17].

**ROC Curve Analysis**

The diagnostic accuracy of the methods was evaluated using ROC analysis. The **area under the ROC curve (AUC)** for ImmunoCAP was 0.88, indicating high predictive capability. Meanwhile, the AUC for ICLA was 0.79, also reflecting good diagnostic accuracy and the method's utility in differential diagnosis [18]. The differences between the methods were statistically significant ($p = 0.001$), underscoring the importance of choosing the appropriate method based on the clinical context. These results are consistent with prior studies showing higher AUC values for ImmunoCAP compared to other diagnostic tools for allergic rhinitis [19].

**Clinical Applications of the Methods**

Several studies suggest that combining both methods may enhance diagnostic precision, especially in patients with polysensitization. It is recommended to use ImmunoCAP for initial screening, and ICLA for confirmatory diagnostics [20],[21]. However, given its relatively high sensitivity, ImmunoCAP can be considered a suitable method for primary testing in AR patients with complex clinical presentations or inconclusive skin test results. On the other hand, ICLA—with its higher specificity and strong NPV—is preferable for confirming allergen sensitization. Accordingly, molecular allergy diagnostics should be selected based on individual patient characteristics [3].

Both single-component molecular diagnostic methods have clear clinical value. The choice between them should depend on the diagnostic objective and the need for a personalized approach in managing allergic rhinitis.

Our study has several limitations. First, the retrospective design limits the ability to establish causal relationships between molecular diagnostic results and clinical manifestations of allergic rhinitis. Second, the relatively small sample size and single-center nature of the study restrict the generalizability of the findings. Moreover, the use of a limited allergen panel may not fully reflect the spectrum of sensitization, and the lack of comparison with other diagnostic methods also constrains interpretation. These factors highlight further multicenter prospective studies are warranted to validate the diagnostic accuracy of ImmunoCAP and ICLA in diverse patient populations. Integration of molecular diagnostics with emerging biomarkers and digital health tools may enhance personalized allergy management. Additionally, long-term studies assessing the predictive value of these methods for treatment response and disease progression are needed. Moreover, as the burden of allergic diseases continues to grow globally, incorporating precise diagnostic tools such as ImmunoCAP and ICLA into national clinical guidelines could improve early detection and targeted interventions. These methods may also play a role in public health surveillance by identifying regional sensitization patterns and guiding preventive strategies in high-risk populations.

**Conclusion**

This study demonstrated that the ImmunoCAP method has higher sensitivity (87.8%) in detecting sensitization in patients with allergic rhinitis, making it particularly effective in complex diagnostic cases. The immunochemiluminescent assay (ICLA) showed greater specificity (61.3%) and a higher negative predictive value (76.0%), confirming its utility in verifying AR diagnosis and minimizing false-positive results. ROC curve analysis revealed statistically significant differences between the two methods ($p = 0.001$), with ImmunoCAP showing superior diagnostic accuracy (AUC = 0.88) compared to ICLA (AUC = 0.79). Both methods are valuable tools in the diagnosis of allergic rhinitis; however, their application should be justified by clinical context: ImmunoCAP is suitable for screening, while ICLA is preferable for confirmation and reduction of overdiagnosis.

Further studies are needed to investigate the prognostic value of molecular allergy diagnostics in long-term patient monitoring, as well as their effectiveness in personalized allergen-specific immunotherapy planning.

***Author Contributions**: All authors contributed equally to the writing of this manuscript.*

***Conflict of Interest:** The authors declare no conflicts of interest. This material has not been submitted to other journals and is not under consideration elsewhere.*

***Funding:** No funding was received for this study.*

***References:***

1. Global Atlas of Allergic Rhinitis and Chronic Rhinosinusitis. – EAACI, 2025. – 112 p.

*2. Nugmanova D., Tulebayev K., Akhmetzhanov A.* The prevalence of allergic rhinitis in CIS countries. Dubai Medical Journal. 2021. Vol. 4, No. 2. P. 81–92.

*3. Bousquet J., Khaltaev N., Cruz A.A.* et al. Allergic Rhinitis and its Impact on Asthma (ARIA) update. Journal of Allergy and Clinical Immunology. 2008. Vol. 122, Suppl. 1. P. S1–S84.

*4. Canonica G.W., Ansotegui I.J., Pawankar R.* et al. Molecular-based allergy diagnostics. World Allergy Organization Journal. 2013. Vol. 6, No. 1. Article 17.

*5. González-Pérez A., Rodríguez-González M., López-Valero M.* et al. Precision allergy molecular diagnosis (PAMD@) in allergen immunotherapy selection. Current Issues in Molecular Biology. 2023. Vol. 45, No. 2. P. 518–523.

*6. Park K.H., Song C.H., Kim T.B.* et al. Comparison of ImmunoCAP and Immulite 2000 for detection of specific IgE in allergic diseases. Annals of Laboratory Medicine. 2018. Vol. 38. P. 23–31.

*7. Apoil P., Trouche-Estival B., Vitte J.* NOVEOS (Hycor) demonstrates better clinical performance than ImmunoCAP™. Authorea Preprints. 2023. 14 p.

*8. Wang Y., Ren Y., Zhang Y.* Component resolved diagnostics for cow's milk allergy in children: a systematic review. Authorea Preprints. 2023. 20 p.

*9. Davies J.M., Pralong C., Tickner J.* Nanofluidic point-of-care IgE test for rapid diagnosis of allergic rhinitis. Annals of Allergy, Asthma & Immunology. 2024. P. 2–5.

*10. Riccio A.M., De Ferrari L., Chiappori A.* Molecular diagnosis and precision medicine in allergy management. Clinical Chemistry and Laboratory Medicine. 2016. P.30–33.

*11. Potapova O., Ivanov A., Smirnova T.* Validation of NOVEOS CLIA for allergic rhinitis diagnostics: comparison with ImmunoCAP. Allergy. 2021. Vol.76, No. 5. P. 332–338.

*12. Morjaria J.B., Caruso M., Emma R., Russo C., Polosa R.* Treatment of allergic rhinitis as a strategy for preventing asthma. Current Allergy and Asthma Reports. 2018. Vol. 18, No. 4. DOI: 10.1007/s11882-018-0781-y.

*13. Ozdoganoglu T., Songu M., Inancli H.M.* Quality of life in allergic rhinitis. Therapeutic Advances in Respiratory Disease. 2011. – DOI: 10.1177/1753465811424425.

*14. Peters R.L., Gurrin L.C., Allen K.J.* The predictive value of skin prick testing for challenge-proven food allergy: a systematic review. Pediatric Allergy and Immunology. 2012. Vol. 23, No. 4. P. 347–352. DOI: 10.1111/j.1399-3038.2011.01237.x.

15. NOVEOS and ImmunoCAP have similar performances for diagnosing food allergies. The Journal of Allergy and Clinical Immunology: In Practice. 2024. Vol. 12, No. 6. P. 1605–1613.e5. – DOI: 10.1016/j.jaip.2024.02.037.

*16. Hao Y., Yang Y., Zhao H., Chen Y., Zuo T.* Multi-omics in allergic rhinitis: mechanism dissection and precision medicine. Clinical Reviews in Allergy & Immunology. 2025. Springer. P. 7–9.

*17. Darsow U., Brockow K., Pfab F., Jakob T.* et al. Heterogeneity of molecular sensitization profiles in grass pollen allergy – implications for immunotherapy? Clinical & Experimental Allergy. 2014. Vol. 44, No. 5. P. 658–668. – DOI: 10.1111/cea.12303.

*18. Chinthrajah R.S., Goyard S., Balbino B., Lyu S.C.* et al. A highly sensitive bioluminescent method for measuring allergen-specific IgE in microliter samples. Allergy. 2020. DOI: 10.1111/all.14365.

*19. Keshavarz B., Platts-Mills T.A.E., Wilson J.M.* The use of microarray and other multiplex technologies in the diagnosis of allergy. Annals of Allergy, Asthma & Immunology. 2021. P. 14–17.

*20. Taka S., Arsenis C., Skevaki C.* Fundamentals of laboratory diagnostics in allergology. Allergo Journal International. 2025. P. 20–23.

*21. Trenti T., Scacchetti A.T.* Laboratory diagnostics in allergic diseases. Clinical Laboratory Medicine Textbook. Springer, 2024. P. 11–14.

**Information about the authors:**

**Valiyeva Sabina Radikovna** – Master's student in Medicine, Kazakhstan Medical University "Higher School of Public Health" (KSPH); allergist-immunologist and general practitioner, ENT Clinic Prima Medical Group, Almaty, Kazakhstan; Phone: +7 777 132 45 96, E-mail: svalieva52@gmail.com, ORCID: https://orcid.org/0000-0003-0767-1993

**Glushkova Natalya Egorovna** – PhD, Professor of the Department of Epidemiology, Biostatistics and Evidence-Based Medicine, Al-Farabi Kazakh National University; Director of the Health Research Institute, Almaty, Kazakhstan; Phone: +7 702 803 2508, E-mail: GlushkovaNatalyaE@gmail.com, ORCID: https://orcid.org/0000-0003-1400-8436

**Buribayeva Zhanar Kuanyshbekovna** – Doctor of Medical Sciences, Professor, Head of the Department of Epidemiology, Evidence-Based Medicine and Biostatistics, Kazakhstan Medical University "Higher School of Public Health" (KSPH), Almaty, Kazakhstan; Phone: +7 701 351 2033, E-mail: mm-antai@mail.ru, ORCID: https://orcid.org/0000-0003-3871-8002

**Izekenova Aigulsum Kulyntayevna** – PhD, Associate Professor of the Department of Epidemiology with the Course of HIV and Infection Control, Asfendiyarov Kazakh National Medical University, Almaty, Kazakhstan; Phone: +7 701 299 5159, E-mail: Izekenova.a@kaznmu.kz, ORCID: https://orcid.org/0000-0003-3850-8689

**Corresponding author:**

**Valieva Sabina Radikovna—** 2nd-year Master's student in Medicine, Kazakhstan Medical University "KSPH" Republic of Kazakhstan.

**Postal code:** Republic of Kazakhstan, 050060, Almaty St. Utepova 19a.

**E-mail:** svalieva52@gmail.com

**Phone:** +7 777 132 45 96

Received: 18 January 2025 / Accepted: 14 April 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2025.27.3.018***

***UDC 616-036.21***

This work is licensed under a Creative Commons Attribution 4.0 International License

# ANALYSIS OF CLINICAL AND EPIDEMIOLOGICAL FEATURES OF HERPESVIRUS REACTIVATION IN INDIVIDUALS WITH A HISTORY OF COVID-19

**Akerke K. Janzakova[1], https://orcid.org/0009-0001-1838-2524**
**Janara K. Buribaeva[1], https://orcid.org/0000-0003-3871-8002**
**Vitaliy B. Kamhen[1], https://orcid.org/0000-0003-4105-4008**
**Baurzhan B. Janzakov[2], https://orcid.org/0009-0008-3298-0601**
**Aigulsym K. Izekenova[3], https://orcid.org/0000-0003-3850-8689**
**Saule T. Doskojaeva[4], https://orcid.org/0000-0001-6016-6713**
**Gaukhar K. Kurmanova[5], https://orcid.org/0000-0001-6098-7829**
**Anna L. Shin[5], https://orcid.org/0000-0001-9911-8233**

**[1]"Kazakhstan Medical University "Higher School of Public Health", Almaty, Kazakhstan;**
**[2]"Kazakhstan-Russian Medical University", Almaty, Kazakhstan.**
**[3]"S.D. Asfendiyarov Kazakh National Medical University", Almaty, Kazakhstan;**
**[4]"International Scientific Research Institute of Postgraduate Education", Almaty, Kazakhstan;**
**[5]"Kazakh National University named after Al-Farabi", Almaty, Kazakhstan;**

**Abstract**

**Introduction.** Herpesvirus reactivation in patients with a history of Coronavirus disease (COVID-19) is an increasingly recognized problem that may exacerbate the clinical manifestations of post-COVID syndrome. Reactivation of latent viruses such as herpes simplex virus (HSV), Epstein–Barr virus (EBV), and cytomegalovirus (CMV) has been frequently observed, but the clinical and epidemiological features of this phenomenon remain insufficiently studied.

**Objective.** To investigate the clinical and epidemiological characteristics of herpesvirus reactivation (CMV, EBV, HSV) in patients after COVID-19, based on a comprehensive analysis of symptoms and laboratory findings.

**Methods.** A retrospective analytical case–control study was conducted, including 80 patients, of whom 40 comprised the main group with a confirmed history of COVID-19, and 40 formed the control group without any indication of previous COVID-19. The analysis included the assessment of clinical symptoms, results of specific immunological testing by enzyme-linked immunosorbent assay (ELISA) for IgG and IgM antibodies to herpesviruses, as well as laboratory parameters, including complete blood count and biochemical profile. Statistical analysis was performed using nonparametric tests, including the Mann–Whitney U test and Pearson's chi-square test. Statistical significance was set at $p < 0.05$.

**Results.** Cytomegalovirus was the most frequently reactivated herpesvirus (30%). Reactivation occurred significantly more often in patients with moderate to severe COVID-19 compared to those with mild disease (*75% vs. 33.3%; p = 0.036*). Patients with reactivation more frequently presented with peripheral lymphadenopathy (*85% vs. 47.5%; p = 0.0009*) and febrile fever (*25% vs. 5%; p = 0.028*). Serological testing revealed elevated IgG titers with high optical density and absence of IgM, indicating reactivation. CRP ($p = 0.002$) and blood glucose ($p = 0.035$) levels were also significantly higher in the reactivation group.

**Conclusion.** The study identified a range of clinical and laboratory features associated with herpesvirus reactivation in patients following COVID-19. These findings highlight the relevance of comprehensive post-COVID assessment, considering potential interactions between SARS-CoV-2 and latent viruses, and support the inclusion of herpesvirus screening in post-COVID monitoring protocols.

***Keywords:*** *post-COVID syndrome; herpesvirus infections; risk factors; COVID-19; viral reactivation.*

***For citation:***

*Janzakova A.K., Buribaeva J.K., Kamhen V.B., Janzakov B.B., Izekenova A.K., Doskojaeva S.T., Kurmanova G.K., Shin A.L.* Analysis of Clinical and Epidemiological Features of Herpesvirus Reactivation in Individuals with a History of COVID-19 // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 157-164. *doi 10.34689/SH.2025.27.3.018*

**Резюме**

# АНАЛИЗ КЛИНИКО-ЭПИДЕМИОЛОГИЧЕСКИХ ПРИЗНАКОВ РЕАКТИВАЦИИ ГЕРПЕСВИРУСОВ У ЛИЦ, ПЕРЕНЁСШИХ COVID-19

**Акерке К. Джанзакова[1],** https://orcid.org/0009-0001-1838-2524
**Жанар К. Бурибаева[1],** https://orcid.org/0000-0003-3871-8002
**Виталий Б. Камхен[1],** https://orcid.org/0000-0003-4105-4008
**Бауржан Б. Джанзаков[2]** https://orcid.org/0009-0008-3298-0601
**Айгульсум К. Изекенова[3],** https://orcid.org/0000-0003-3850-8689
**Сауле Т. Доскожаева[4],** https://orcid.org/0000-0001-6016-6713
**Гаухар М. Курманова[5],** https://orcid.org/0000-0001-6098-7829
**Анна Л. Шин[5],** https://orcid.org/0000-0001-9911-8233

[1] Казахстанский медицинский университет «Высшая школа общественного здравоохранения», г. Алматы, Республика Казахстан;
[2]«Казахский–Российский медицинский университет», г. Алматы, Республика Казахстан.
[3] «Казахский национальный медицинский университет им. Асфендиярова», г. Алматы, Республика Казахстан;
[4] «Научно-исследовательский Международный институт последипломного образования», г. Алматы, Республика Казахстан;
[5] «Казахский национальный университет им. Аль-Фараби», г. Алматы, Республика Казахстан;

**Введение:** Реактивация герпесвирусных инфекций у пациентов, перенёсших COVID-19, рассматривается как одно из потенциальных осложнений постковидного периода, способное усиливать системную воспалительную реакцию и пролонгировать клинические проявления. Наиболее часто в этом контексте обсуждаются вирус простого герпеса (ВПГ), вирус Эпштейна–Барр (ВЭБ) и цитомегаловирус (ЦМВ), способные к реактивации на фоне иммунной дисрегуляции, индуцированной SARS-CoV-2.

**Цель исследования:** Изучить клинико-эпидемиологические особенности реактивации герпесвирусных инфекций (ЦМВ, ВПГ, ВЭБ) у пациентов после перенесённой коронавирусной инфекции на основе комплексного анализа симптоматики, лабораторных данных.

**Методы:** Проведено ретроспективное аналитическое исследование по типу «случай–контроль» с включением 80 пациентов, из которых 40 составили основную группу с подтверждённой в анамнезе COVID-19, а 40- контрольную группу без указаний на перенесённый COVID-19. Статистическая обработка данных проводилась с применением непараметрических методов, включая критерий Манна–Уитни и $\chi^2$ Пирсона; уровень значимости считался статистически достоверным при $p < 0,05$.

**Результаты:** В ходе анализа установлено, что реактивация герпесвирусных инфекций достоверно чаще наблюдалась у пациентов, перенёсших COVID-19 средней и тяжёлой степени тяжести, по сравнению с пациентами, перенёсшими лёгкую форму заболевания (75% против 33,3%). В клинической картине таких пациентов значительно чаще регистрировались признаки периферической лимфоаденопатии (85% против 47,5%) и фебрильной лихорадки (25% против 5%). По данным серологического обследования выявлено преобладание высоких уровней IgG с увеличенной оптической плотностью и сниженной авидностью, что соответствует признакам реактивации латентной герпесвирусной инфекции.

**Выводы:** Проведённое исследование позволило выделить ряд клинико-эпидемиологических и лабораторных особенностей, ассоциированных с реактивацией герпесвирусных инфекций у пациентов после перенесённого COVID-19. Установлена актуальность комплексной оценки состояния пациентов в постковидном периоде с учётом возможного взаимодействия SARS-CoV-2 с латентными вирусами. Полученные данные могут служить основанием для дальнейших исследований в данном направлении и целесообразности внедрения скрининга на герпесвирусные инфекции в практику постковидного мониторинга.

***Ключевые слова:*** *постковидный синдром; герпесвирусные инфекции; факторы риска, COVID-19, реактивация вирусов.*

***Для цитирования:***

*Джанзакова А.К., Бурибаева Ж.К., Камхен В.Б., Джанзаков Б.Б., Изекенова А.К., Доскожаева С.Т., Курманова Г.М., Шин А.Л.* Анализ клинико-эпидемиологических признаков реактивации герпесвирусов у лиц, перенёсших COVID-19 // Наука и Здравоохранение. 2025. Т.27 (3), С. 157-164. doi: 10.34689/SH.2025.27.3.018

**Түйіндеме**

# COVID-19-ДАН КЕЙІНГІ ГЕРПЕСВИРУС ИНФЕКЦИЯЛАРЫНЫҢ РЕАКТИВАЦИЯСЫНЫҢ КЛИНИКО-ЭПИДЕМИОЛОГИЯЛЫҚ БЕЛГІЛЕРІН ТАЛДАУ

**Акерке К. Джанзакова[1], https://orcid.org/0009-0001-1838-2524**
**Жанар К. Бурибаева[1], https://orcid.org/0000-0003-3871-8002**
**Виталий Б. Камхен[1], https://orcid.org/0000-0003-4105-4008**
**Бауржан Б. Джанзаков[2] https://orcid.org/0009-0008-3298-0601**
**Айгульсум К. Изекенова[3], https://orcid.org/0000-0003-3850-8689**
**Сауле Т. Доскожаева[4], https://orcid.org/0000-0001-6016-6713**
**Гаухар М. Курманова[5], https://orcid.org/0000-0001-6098-7829**
**Анна Л. Шин[5], https://orcid.org/0000-0001-9911-8233**

**[1] «Қоғамдық денсаулық сақтау жоғары мектебі» медицина университеті, Алматы қ., Қазақстан Республикасы;**
**[2] Қазақстан-Ресей медициналық университеті», Алматы қ., Қазақстан Республикасы.**
**[3] «С.Ж.Асфендияров атындағы Қазақ Ұлттық медицина университеті», Алматы қ., Қазақстан Республикасы;**
**[4] «Дипломнан кейінгі білім беру жөніндегі халықаралық ғылыми-зерттеу институты», Алматы қ., Қазақстан Республикасы;**
**[5] «Әль-Фараби атындағы Қазақ ұлттық университеті», Алматы қ., Қазақстан Республикасы;**

**Кіріспе:** COVID-19-бен ауырған науқастарда герпесвирус инфекцияларының реактивациясы постковид кезеңінің ықтимал асқынуларының бірі ретінде қарастырылады. Бұл жағдай жүйелік қабыну реакциясын күшейтіп, клиникалық белгілердің ұзақ сақталуына әкелуі мүмкін. Бұл контексте жиі қозғалатын вирус түрлеріне жай герпес вирусы (ЖГВ), Эпштейн–Барр вирусы (ЭББ) және цитомегаловирус (ЦМВ) жатады, олар иммундық дисрегуляция жағдайында реактивацияға қабілетті.

**Зерттеудің мақсаты:** COVID-19-бен ауырған науқастарда герпесвирус инфекцияларының (ЦМВ, ЖГВ, ЭББ) реактивациясының клиникалық-эпидемиологиялық ерекшеліктерін симптоматика мен зертханалық мәліметтердің кешенді талдауы негізінде зерттеу.

**Әдістер:** «Жағдай–бақылау» типіндегі ретроспективті аналитикалық зерттеу жүргізілді. Жалпы 80 пациент қамтылды: олардың 40-ы анамнезінде COVID-19 диагнозы қойылған негізгі топты, ал 40-ы бұрын коронавирус инфекциясын бастан өткермеген бақылау тобын құрады. Статистикалық өңдеу Манн–Уитни критерийі мен Пирсонның $\chi^2$ критерийін қолдану арқылы жүргізілді; $p < 0,05$ мәні статистикалық мәнділік ретінде қабылданды.

**Нәтижелер:** Зерттеу нәтижесінде герпесвирус инфекцияларының реактивациясы COVID-19-дың орташа және ауыр түрімен ауырған науқастарда жеңіл түрімен ауырғандарға қарағанда жиірек тіркелгені анықталды (75% қарсы 33,3%). Реактивация тобына жататын науқастарда шеткергі лимфаденопатия (85% қарсы 47,5%) және фебрильді қызба (25% қарсы 5%) едәуір жиі кездесті. Серологиялық зерттеу барысында IgG деңгейінің жоғарылауы, оптикалық тығыздықтың артуы және төмен авидтілік анықталды, бұл жасырын вирустың реактивациясын көрсетеді.

**Қорытынды:** Зерттеу барысында COVID-19-дан кейінгі кезеңде герпесвирус инфекцияларының реактивациясымен байланысты бірқатар клиникалық, эпидемиологиялық және зертханалық ерекшеліктер анықталды. Бұл жағдай SARS-CoV-2 мен латентті вирустардың өзара әрекеттесу мүмкіндігін ескере отырып, постковидтық науқастардың жағдайын кешенді бағалаудың маңыздылығын көрсетеді. Алынған деректер осы бағыттағы әрі қарайғы зерттеулерге негіз бола алады және герпесвирус инфекцияларына скрининг жүргізудің постковидтық мониторинг тәжірибесіне енгізілуінің орынды екенін дәлелдейді.

***Түйін сөздер:*** *постковид синдромы; герпесвирус инфекциялары; қауіп факторлары; COVID-19; вирустардың реактивациясы.*

***Дәйексөз үшін:***

*Джанзакова А.К., Бурибаева Ж.К., Камхен В.Б., Джанзаков Б.Б., Изекенова А.К., Доскожаева С.Т., Курманова Г.М., Шин А.Л.* COVID-19-дан кейінгі герпесвирус инфекцияларының реактивациясының клинико-эпидемиологиялық белгілерін талдау // Ғылым және Денсаулық. 2025. Т.27 (3), Б. 157-164. doi: 10.34689/SH.2025.27.3.018

**Introduction.**

COVID-19, caused by the SARS-CoV-2 virus, has emerged as one of the most significant global medical and social challenges of the past decade. Its acute course, along with persistent post-viral inflammation following recovery, contributes to a sustained disruption of immune homeostasis, which may promote the reactivation of latent viruses, including members of the Herpesviridae family [4–6].

Against this background, infections caused by herpesviruses have gained particular relevance, given their prominent role in clinical practice, especially in individuals with underlying immune dysregulation. The latent nature of herpesviruses, their persistence in the host organism, and their ability to reactivate under stressful or immunosuppressive conditions contribute to a wide spectrum of clinical manifestations [1–3].

In recent years, the reactivation of herpesvirus infections following COVID-19 has drawn increasing attention from researchers. According to S.K. Dunmire et al., EBV reactivation may occur as early as the incubation period of COVID-19, triggered by immune restructuring [7]. Similar mechanisms have been observed for CMV, particularly in immunocompromised populations [8–9]. Studies by K. Luzuriaga and J.L. Sullivan emphasize that latent virus reactivation may not only exacerbate the course of the primary illness but also mimic systemic manifestations of COVID-19-associated damage [10].

Post-COVID syndrome is a clinical and pathophysiological condition persisting in a subset of patients after recovery from SARS-CoV-2 infection. It is characterized by a wide range of symptoms, most commonly involving the cardiorespiratory and neuropsychiatric systems, along with signs of immune dysregulation. According to current evidence, the pathogenesis of this condition involves chronic immune activation, cytokine profile dysregulation, the development of autoimmune processes, and functional impairments of epithelial and endothelial cells. Persistent viral components or virus-induced immune surveillance disruption play a crucial role, creating favorable conditions for the reactivation of latent infections, including herpesviruses. These reactivated viruses may, in turn, aggravate the course of post-COVID syndrome by intensifying systemic inflammation and impairing the restoration of immune homeostasis.

Clinical observations have described cases of reactivation of herpes simplex virus, CMV, and EBV following both severe and mild COVID-19 [11–13]. According to several authors, the reactivation of latent viral infections is driven not only by weakened T-cell immune surveillance but also by the direct impact of SARS-CoV-2 on immune cells, including lymphocyte apoptosis and the activation of proinflammatory cytokines [14–15].

Serological studies have demonstrated elevated antibody titers against herpesviruses in patients with post-COVID syndrome, reflecting a reactivation-type immune response, characterized by high-avidity positive IgG and negative IgM [16–17]. Clinically, such patients may report persistent fatigue, sleep disturbances, low-grade fever, and headaches or abdominal pain, complicating differential diagnosis from post-COVID sequelae [18–20].

Despite the abundance of case reports, there is a lack of systematized data on the clinical and epidemiological features of herpesvirus reactivation in patients recovering from COVID-19, particularly in regional populations. This highlights the need for a comprehensive analysis encompassing epidemiological parameters, clinical manifestations, laboratory findings, and immunological markers in this group of patients.

**Aim of the Study.** To analyze the clinical and epidemiological features of reactivation of chronic herpesvirus infections in patients who have recovered from coronavirus infection.

**Objectives**

1. To describe the clinical polymorphism and frequency of major complaints associated with herpesvirus reactivation during the post-COVID period.

2. To analyze laboratory and immunological indicators in patients with active herpesvirus infection following COVID-19.

**Materials and Methods.** This study employed a retrospective analytical observational case–control design aimed at investigating the clinical and epidemiological characteristics of herpesvirus reactivation in patients with a history of coronavirus infection. A total of 80 patients who received treatment between 2021 and 2024 at *City Clinical Hospital No. 7 and the S. Zhekenov City Clinical Infectious Diseases Hospital* (Almaty) were included in the study.

The main group consisted of 40 patients with a confirmed history of COVID-19, diagnosed based on clinical and epidemiological data and confirmed by laboratory testing (PCR and/or serological analysis). The control group included 40 patients with no history of manifest COVID-19, no laboratory confirmation, and no signs indicative of prior SARS-CoV-2 infection. Patient selection was performed through the analysis of medical records, considering epidemiological history, clinical presentation, and laboratory data.

*Inclusion criteria* encompassed patients aged 18 years and older, with complete medical information regarding COVID-19, as well as available serological and molecular genetic testing data for herpesvirus infections (CMV, EBV, HSV types 1 and 2).

*Exclusion criteria* included patients with immunodeficiency conditions, malignant neoplasms, ongoing immunosuppressive therapy, and pregnancy.

Depending on the presence of a prior COVID-19 infection and laboratory-confirmed herpesvirus infection, patients were categorized into four groups, including a control group. The control group comprised individuals who had neither COVID-19 nor herpesvirus infection.

In this study, herpesvirus reactivation was determined based on a combination of clinical and laboratory findings. Clinical criteria included the presence of at least three of the following symptoms: low-grade fever, general weakness, malaise, loss of appetite, headache, catarrhal symptoms, skin rashes, joint pain, lymphadenopathy, hepatomegaly, or splenomegaly.

Laboratory signs of reactivation included high titers of specific IgG antibodies with low avidity and/or detection of herpesvirus DNA in biological specimens (blood, saliva, urine) by PCR. Patients meeting at least one laboratory criterion in combination with clinical symptoms were classified as probable cases of latent herpesvirus reactivation.

*Statistical analysis* was conducted using IBM SPSS Statistics version 26.0. The Mann–Whitney U test was used to assess differences between independent groups. Associations between categorical variables were evaluated using Pearson's chi-square ($\chi^2$) test. A *p-value of <0.05* was considered statistically significant. For key comparisons, 95% confidence intervals and effect sizes were additionally calculated. The analysis addressed variables such as the type of herpesvirus infection, COVID-19 severity, clinical symptom severity, and laboratory parameters. The choice of statistical methods was based on data type and research objectives, adhering to the principles of scientific validity and reproducibility.

*Ethical Considerations.* The study was conducted in accordance with ethical standards and the principles of the Declaration of Helsinki. The study was approved by the local Ethics Committee of Kazakhstan Medical University "KSPH" (Protocol No. 1 dated January 15, 2024). No personal identifying information was disclosed.

**Results.**

The study included 80 patients with a mean age of 41.6 years. Women comprised the majority of the sample-63.8% (n = 51), while men accounted for 36.2% (n = 29). The main group consisted of 40 patients with a confirmed history of COVID-19, while the control group included 40 patients (50% of the total sample) without clinical manifestations typical of COVID-19 in their medical history. The distribution of patients based on a history of coronavirus infection was balanced. Among those with a history of SARS-CoV-2 infection, the majority had experienced a mild form of the disease-60% (n = 24). Moderate and severe courses were reported in 20% (n = 8) of cases each (Figure 1).

Among patients with a history of COVID-19, herpesvirus reactivation was observed at a comparable frequency in both females and males, suggesting no significant gender-based association with this phenomenon. However, age-related analysis revealed an increased frequency of reactivation in individuals aged 30–50 years, as well as in those over 60 years of age. These findings may indicate age-dependent variations in immune surveillance over latent viral infections, particularly under conditions of virus-induced immune dysregulation following SARS-CoV-2 infection (Figure 1).

The most pronounced differences between patients with and without reactivation were noted when analyzing the severity of prior COVID-19. Reactivation occurred significantly more often in individuals who experienced moderate to severe forms of COVID-19, whereas cases of reactivation were considerably less frequent among those with mild disease. These data support the hypothesis that intense viral inflammation and immune exhaustion associated with severe COVID-19 may contribute to a loss of immune control over persistent herpesviruses, facilitating their subsequent reactivation.

Among the patients who had previously contracted COVID-19, 60% (24) experienced a mild form of the disease, 20% (8) had a moderate course, and 20% (8) had a severe course. Herpesvirus reactivation was observed in 33.3% (8) of patients with mild COVID-19, in 75% (6) of those with a moderate course, and in 75% (6) of those with a severe course. The overall frequency of herpesvirus reactivation was 50% (20). (Table 1).

A chi-square analysis demonstrated a statistically significant association between the severity of COVID-19 and the frequency of herpesvirus reactivation *($\chi^2 = 6.67$; $p = 0.036$)*. These findings suggest that a more severe course of coronavirus infection may be associated with an increased likelihood of latent virus reactivation, likely due to pronounced immune dysregulation.

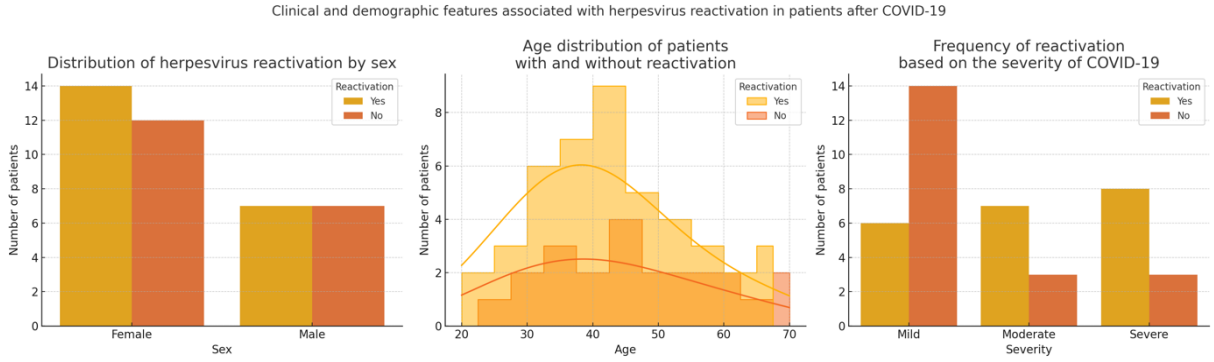



***Figure 1. Clinical and demographic features associated with herpesvirus reactivation in patients after COVID-19.***

*Table 1.*

**Frequency of herpesvirus reactivation depending on the severity of COVID-19.**

| COVID-19 Severity | Reactivation Present % (n) | No Reactivation % (n) | Total % (n) |
|---|---|---|---|
| Mild | 33,3% (8) | 66,7% (16) | 60%(24) |
| Moderate | 76% (6) | 25% (2) | 20%(8) |
| Severe | 76% (6) | 25% (2) | 20%(8) |
| **Total** | 50% (20) | 50% (20) | 100%(40) |

*Note: $\chi^2 = 6.67$; $p = 0.036$ (Pearson's chi-square test).*

When comparing laboratory parameters between patients with and without herpesvirus reactivation using the Mann–Whitney test, statistically significant differences were observed at a significance level of $p < 0.05$. The most pronounced differences were found in the levels of specific antibodies to herpesviruses. For instance, IgG levels to CMV were significantly higher in patients showing signs of reactivation ($p < 0.001$), indicating activation of the humoral

immune response. Similarly, markedly elevated levels of IgG to EBV and HSV types 1 and 2 ($p < 0.001$ *and* $p = 0.001$, respectively) suggest potential activity of latent viral infections during or following COVID-19.

In addition to serological differences, patients with reactivation demonstrated significantly higher levels of C-reactive protein ($p = 0.002$), indicating a systemic inflammatory response. Elevated blood glucose levels ($p = 0.035$) also reached statistical significance, potentially reflecting secondary metabolic disturbances developing in the context of chronic inflammation or viral persistence. (Figure 2).

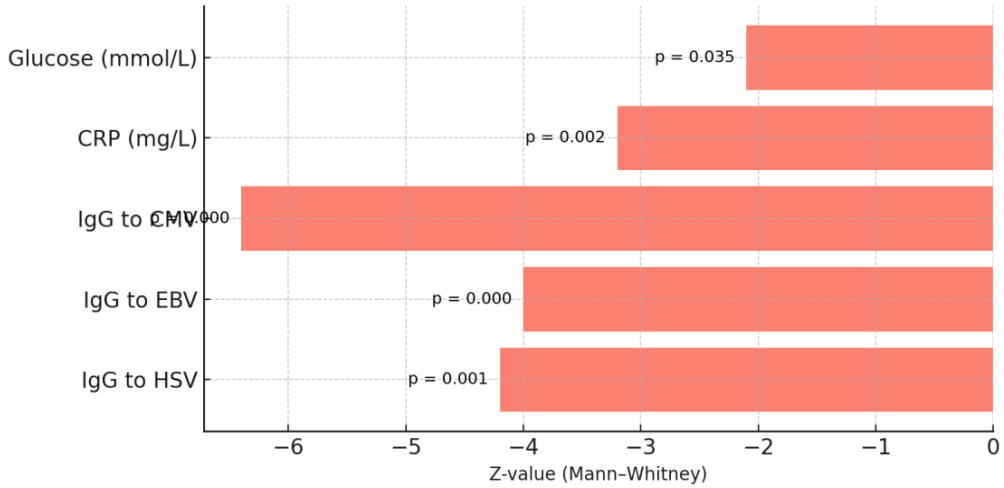



**Figure 2. Statistically significant differences in laboratory parameters between patients with and without herpesvirus reactivation.**

All reported parameters had p-values below the predetermined threshold of 0.05, supporting the interpretation that these differences are statistically significant and potentially clinically relevant.

A comparative analysis of the frequency of clinical symptoms between patients with herpesvirus reactivation and those without signs of herpesvirus infection revealed marked differences across several parameters. Patients in the reactivation group more frequently reported symptoms such as weakness, malaise, low-grade fever, loss of appetite, headache, and catarrhal manifestations. In addition, this subgroup showed a higher prevalence of skin rashes, lymphadenopathy, joint pain, and signs of hepatomegaly. Complaints related to the cardiovascular and gastrointestinal systems, as well as respiratory symptoms-including cough-were also more common in this group. In contrast, clinical manifestations were significantly less frequent among patients without herpesvirus infection. (Figure 3).

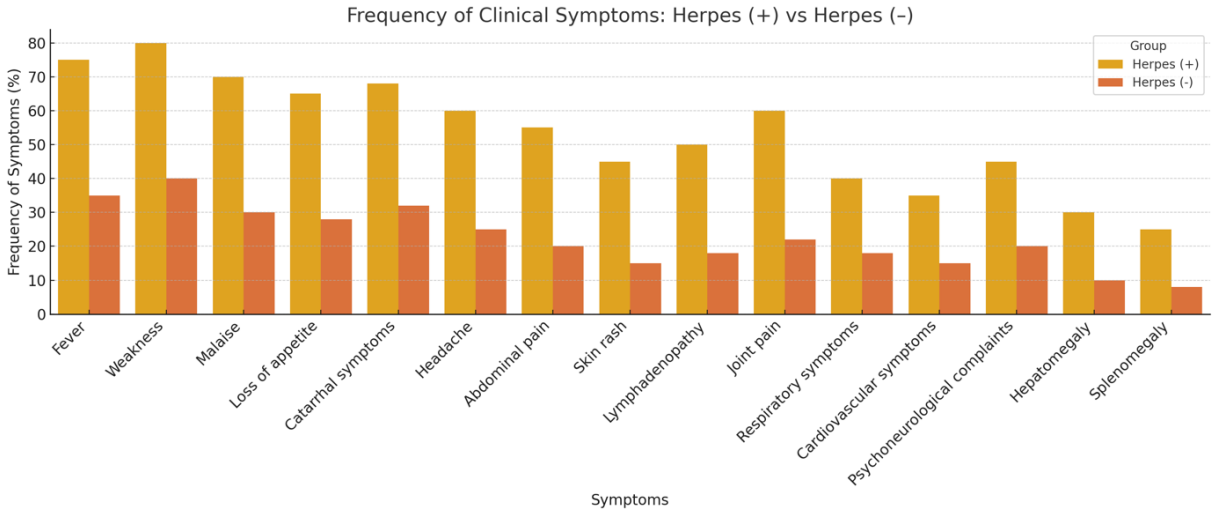



**Figure 3. Frequency of clinical symptoms in patients with and without herpesvirus reactivation.**

**Discussion**

The findings of this study underscore the clinical relevance of herpesvirus reactivation in patients with a history of COVID-19. The identified clinical, laboratory, and immunological features point to a strong pathogenetic link between SARS-CoV-2 and herpesviruses-particularly CMV, EBV, and HSV.

The mechanisms underlying herpesvirus activation in the post-COVID period have been discussed in several studies. Immune dysregulation plays a central role, including T-cell apoptosis, reduced antibody avidity, cytokine imbalance, and increased expression of HLA class II molecules [6, 8, 10]. These factors contribute to the

reactivation of latent viruses, enhancing both inflammatory and neurotropic effects [7, 11, 14].

According to S.K. Dunmire and K.A. Hogquist, EBV reactivation frequently occurs even under moderate immunosuppression and may present with nonspecific somatic symptoms such as asthenia, low-grade fever, and myalgia [7]. Similar manifestations were observed in our study among patients with combined COVID-19 and herpesvirus infection, regardless of COVID-19 severity. Epidemiological studies [3, 5, 12] indicate that CMV is the most common herpesvirus reactivation in the context of secondary immunodeficiency. This was confirmed in our analysis: CMV accounted for 30% of all reactivation cases in COVID-positive patients, while EBV and HSV were less frequently detected. In contrast, patients in the control group (without COVID-19) more often exhibited herpesvirus coinfections (e.g., CMV + EBV, CMV + HSV), consistent with previously published findings [1, 15].

Serological profiles of patients indicated predominantly reactivation-type responses-characterized by high titers of specific IgG antibodies with low avidity and/or PCR positivity. These findings align with the results of De Paschale and Clerici, who highlighted the diagnostic value of antibody avidity as a marker of chronic or reactivated infection [16].

Immunologically, patients with herpesvirus reactivation after COVID-19 showed elevated platelet levels, neutrophilic shift, and decreased lymphocyte counts, which support the hypothesis of subclinical inflammation maintained by both residual SARS-CoV-2 activity and reactivated herpesviruses [9, 13, 17].

The polymorphic nature of clinical symptoms observed in this cohort is in agreement with the data presented by James and Kimberlin, who described the systemic but often indolent manifestations of herpesvirus reactivation. The most commonly reported symptoms included low-grade fever, general weakness, reduced productivity, headaches, and muscle pain. In some cases, lymphadenopathy and herpetic rashes on the skin or mucous membranes were also reported. Several patients described sleep disturbances, irritability, and emotional instability. In more pronounced cases, the clinical picture resembled a mononucleosis-like syndrome with pharyngitis and signs of hepatomegaly [11].

Importantly, the results of this study support the hypothesis of a multifactorial nature of post-COVID syndrome, in which herpesviruses act as cofactors that modulate both the duration and intensity of symptoms. According to the work of Luzuriaga and Sullivan,reactivation of latent viruses may play a decisive role in the development of prolonged post-infectious conditions.

The identified features of herpesvirus reactivation in patients recovering from COVID-19 are consistent with previously described mechanisms of viral interaction. These findings highlight the importance of immunological monitoring and support the inclusion of herpesvirus status in the diagnostic and follow-up strategies for individuals with post-COVID syndrome.

**Conclusion.** This study provides a comprehensive overview of herpesvirus reactivation in patients recovering from COVID-19, revealing significant differences in clinical symptoms, laboratory findings, and serological profiles compared to individuals without prior COVID-19.

Herpesvirus reactivation was more common among COVID-19 survivors, with isolated CMV infections being predominant. In contrast, coinfections involving HSV and EBV were more frequently observed in patients without COVID-19. Clinical symptoms in the reactivation group were more diverse and severe, particularly asthenic, abdominal, and vascular complaints, suggesting a potential contribution of herpesviruses to the persistence or severity of post-COVID syndrome. Laboratory and serological analyses confirmed signs of immune dysregulation and reactivation of latent infections. These findings support the need to include herpesvirus screening in post-COVID care algorithms, even in the absence of overt clinical signs. Further studies on SARS-CoV-2 and Herpesviridae interactions are essential to clarify their role in post-viral pathogenesis and to guide personalized management strategies. This area of research requires continued investigation, particularly in relation to long-term immune alterations, viral persistence, and their implications for clinical outcomes in diverse patient populations.

***Literature:***

1.*Jeffery-Smith A., Riddell A.* Herpesviruses. Medicine (UK). 1996. Vol. 49. P. 780–784. https://doi.org/10.1016/j.mpmed.2021.09.011

2. *Lan K., Luo M.H.* Herpesviruses: epidemiology, pathogenesis, and interventions. Virol Sin. 2017. Vol. 32. P. 347–348. https://doi.org/10.1007/S12250-017-4108-2

3. *Manicklal S., Emery V.C., Lazzarotto T.* et al. The "Silent" Global Burden of Congenital Cytomegalovirus. Clin Microbiol Rev. 2013. Vol. 26(1). P. 86–102. https://doi.org/10.1128/CMR.00062-12

4. *Luzuriaga K., Sullivan J.L. In*fectious Mononucleosis. N Engl J Med. 2010. Vol. 362. P. 1993–2000. https://doi.org/10.1056/NEJMCP1001116

5. *Zhang W.J., Wu L.Q., Wang J.* et al. Epstein-Barr-virus-associated hepatitis with aplastic anemia: A case report. World J Clin Cases. 2022. Vol. 10(23). P. 8242–8248. https://doi.org/10.12998/WJCC.V10.I23.8242

6. *James S.H., Kimberlin D.W.* Neonatal Herpes Simplex Virus Infection. Infect Dis Clin North Am. 2015. Vol. 29(3). P. 391–400. https://doi.org/10.1016/j.idc.2015.05.001

7. *Dunmire S.K., Verghese P.S., Balfour H.H.* Primary Epstein-Barr Virus Infection. J Clin Virol. 2018. Vol. 102. P. 84–92. https://doi.org/10.1016/j.jcv.2018.03.001

8. *De Paschale M., Clerici P.* Serological diagnosis of Epstein-Barr virus infection: Problems and solutions. World J Virol. 2012. Vol. 1(1). P. 31–43. https://doi.org/10.5501/wjv.v1.i1.31

9. *Rivera L.B., Boppana S.B., Fowler K.B.,* et al. Predictors of Hearing Loss in Children with Congenital Cytomegalovirus Infection. *Pediatrics.* 2002. Vol. 110(4). P. 762–767. https://doi.org/10.1542/peds.110.4.762

10. *Salisbury S., Embil J.A.* Graves disease following congenital cytomegalovirus infection. J Pediatr. 1978. Vol. 92. P.954–955. https://doi.org/10.1016/S0022-3476(78)80373-4

11. *Razonable R.R., Hayden R.T.* Clinical utility of viral load in management of cytomegalovirus infection after solid

organ transplantation. Clin Microbiol Rev. 2013. Vol. 26. P. 703–727. https://doi.org/10.1128/CMR.00015-13

12. *Corey L., Spear P.G.* Infections with Herpes Simplex Viruses. N Engl J Med. 1986. Vol. 314. P. 686–691. https://doi.org/10.1056/NEJM198603133141105

13. *Rea T.D., Russo J.E., Katon W.* et al. Prospective study of the natural history of infectious mononucleosis caused by Epstein-Barr virus. J Am Board Fam Pract. 2001. Vol. 14. P. 234–242.

14. *Evans A.S., Neiderman J.C., Cenabre L.C.* et al. A Prospective Evaluation of Heterophile and EBV-Specific IgM Antibody Tests // *J Infect Dis.* – 1975. – Vol. 132(5). – P. 546–554. https://doi.org/10.1093/infdis/132.5.546

15. *Raborn G.W., McGaw W.T., Grace M.* et al. Herpes labialis treatment with acyclovir 5% // *Oral Surg Oral Med Oral Pathol.* – 1989. – Vol. 67(6). – P. 676–679. https://doi.org/10.1016/0030-4220(89)90007-8

16. *Sauerbrei A.* Optimal management of genital herpes: current perspectives // *Infect Drug Resist.* – 2016. – Vol. 9. – P. 129–141. https://doi.org/10.2147/IDR.S96164

17. *Gagelmann N., Ljungman P., Styczynski J., Kröger N.* Antiviral agents for CMV prophylaxis: a meta-analysis // *Biol Blood Marrow Transplant.* – 2018. – Vol. 24(11). – P. 2101–2109. https://doi.org/10.1016/j.bbmt.2018.05.017

18. *Razonable R.R., Paya C.V., Smith T.F.* Laboratory in Diagnosis of CMV in Transplant Recipients // *J Clin Microbiol.* – 2002. – Vol. 40(3). – P. 746–752. https://doi.org/10.1128/jcm.40.3.746-752.2002

19. *Raynor E.M., Martin H.L., Poehlein E.* et al. Maternal CMV and Childhood Hearing Loss // *Laryngoscope Investig Otolaryngol.* – 2022. – Vol. 7. – P. 1626–1633. https://doi.org/10.1002/lio2.904

20. *Alanio C., Verma A., Mathew D.* et al. Cytomegalovirus Latency and COVID-19 Hospitalization // *J Infect Dis.* – 2022. – Vol. 226. – P. 463–473. https://doi.org/10.1093/infdis/jiac020Information about authors:

**Information about the authors:**

**Akerke Janzakova** – MD, Infectious disease specialist, Master's student in "Medicine", Kazakh Medical University "Higher School of Public Health" (HSPH), Phone: +77025399377, Email: janzakova.akerke01@gmail.com, ORCID: https://orcid.org/0009-0001-1838-2524,Almaty,Kazakhstan;

**Janara Buribaeva,** Doctor of Medical Sciences, Head of the Department of "Epidemiology, Evidence-based Medicine and Biostatistics", Kazakh Medical University "KSPH", Phone: +77013512033, Email: mm-antai@mail.ru, ORCID: https://orcid.org/0000-0003-3871-8002, Almaty, Republic of Kazakhstan

**Vitaliy Kamhen -** MD, Associate Professor, Department of "Epidemiology, Evidence-based Medicine and Biostatistics", Kazakh Medical University "KSPH", Phone: +7 777 824 9733, Email: kamchen.v.b@gmail.com, ORCID: https://orcid.org/0000-0003-4105-4008, Almaty, Republic of Kazakhstan

**Baurzhan Janzakov -** MD, MSc, Assistant, department of "Surgical diseases", Kazakhstan-Russian Medical University", Phone: +7 7021752568, Email: maladca@inbox.ru, ORCID: https://orcid.org/0009-0008-3298-0601, Almaty, Kazakhstan**.**

**Aigulsym Izekenova –** MD, Associate Professor, S.D. Asfendiyarov Kazakh National Medical University", Phone: 87012995159, Email: izekenova.a@kaznmu.kz, ORCID: https://orcid.org/0000-0003-3850-8689, Almaty, Kazakhstan**.**

**Saule Doskojaeva -** Doctor of Medical Sciences, Professor, International Scientific Research Institute of Postgraduate Education", Phone: +7 702 256 6576 Email: sdoskojaeva@mail.ru ORCID: https://orcid.org/0000-0001-6016-6713, Almaty, Kazakhstan**.**

**Gaukhar Kurmanova -** Doctor of Medical Sciences, Professor, Head of the Department of "Clinical Disciplines", Kazakh National University named after Al-Farabi,

Phone: +7 775 259 2299E-mail: gaukhar.kurmanova2000@gmail.com, ORCID: https://orcid.org/0000-0001-6098-7829, Almaty, Republic of Kazakhstan

**Anna Shin -** Doctor of Medical Sciences, PhD, Department of "Clinical Disciplines", Kazakh National University named after Al-Farabi, Phone: +7 777 320 0677, E-mail: annashin86@gmail.com, ORCID: https://orcid.org/ 0000-0001-9911-8233, Almaty, Republic of Kazakhstan

**Corresponding author:**

**Akerke Janzakova -** 2nd-year Master's student in Medicine, Kazakhstan Medical University "KSPH"; current position: Infectionist, General Practitioner, Clinic Hospital #7, Almaty, Kazakhstan.

**Address:** Utepov St 19A, Almaty 050060

**Phone:** +7 702 539 93 77

**E-mail:** janzakova.akerke01@gmail.com

Received: 09 April 2025 / Accepted: 02 June 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2025.27.3.019***

***UDC 0623.454.86.(574.41)***

This work is licensed under a Creative Commons Attribution 4.0 International License

# RADIATION EXPOSURE IN THE SEMIPALATINSK REGION: TRANSGENERATIONAL RISKS AND DOSIMETRY APPROACHES

**Altay Dyussupov[1], https://orcid.org/0000-0003-0875-1020**
**Nailya Chaizhunussova[1]*, https://orcid.org/0000-0002-6660-7118**
**Assel Baibussinova[1], https://orcid.org/0000-0003-3447-6245**
**Meruyert Massabayeva[1], https://orcid.org/0000-0001-8240-361X**
**Madina Abenova[1], https://orcid.org/0000-0002-4219-5737**
**Lyudmila Pivina[1], https://orcid.org/0000-0002-8035-4866**
**Andrey Orekhov[1], https://orcid.org/0000-0001-7201-1399**
**Zhanargul Smailova[1], https://orcid.org/ 0000-0002-4513-4614**
**Dinara Mukanova[1], https://orcid.org/ 0000-0001-5186-2346**
**Murat Lepesbayev[2], https://orcid.org/0009-0006-9810-9232**
**Rauan Kissina[1], https://orcid.org/0000-0002-1849-5596**
**Tokzhan Akhmadiyeva[1], https://orcid.org/ 0009-0001-4806-2329**
**Galiya Alibayeva[3], https://orcid.org/0000-0002-1503-4663**
**Saulesh Apbassova[1], https://orcid.org/0000-0001-6981-5441**
**Gulshara Abdildinova[4], https://orcid.org/0000-0003-0543-9568**
**Asset Izdenov[5], https://orcid.org/0000-0002-7162-4529**
**Raushan Dosmagambetova[6], https://orcid.org/0000-0002-8792-5449**
**Dariya Shabdarbayeva[1], https://orcid.org/0000-0003-0200-1763**

**[1] Semey Medical University, Semey, Republic of Kazakhstan.**
**[2]Forensic Examination Center of the Abai Region, Semey, Kazakhstan**
**[3]Semey Hospital of Emergency Medical Care, Semey, Kazakhstan**
**[4]Hospital of the Medical Center of the Presidential Administration of the Republic of Kazakhstan, Astana, Kazakhstan;**
**[5]Department of Medical Education, Ministry of Healthcare of the Republic of Kazakhstan, Astana, Kazakhstan**
**[6]Karaganda Medical University, Karaganda, Kazakhstan;**

**Summary**

**Abstract:** The Semipalatinsk Nuclear Test Site (SNTS) in Kazakhstan was the site of extensive nuclear testing during the Soviet era, leading to long-term environmental contamination and potential health effects for exposed populations.

**Aim:** Analysis of existing studies on radiation dosimetry and health effects of radiation exposure in the affected regions.

**Search strategy:** Relevant literature was identified through searches in PubMed, Scopus, and Web of Science databases. The search covered studies published up to January 2025 using the following key terms: “Semipalatinsk nuclear test site”, “radiation exposure”, “biodosimetry”, “transgenerational effects”, and “radiation-induced mutations”. No date or language restrictions were applied at the search stage. A total of 74 records were initially retrieved. After duplicate removal, 70 articles were screened based on title and abstract. The full text of 45 articles was reviewed for eligibility, and 39 publications were selected based on their relevance to the objectives of this review.

**Results:** The article discusses key biodosimetric methods, including electron paramagnetic resonance (EPR), fluorescence in situ hybridization (FISH), and glycophorin A (GPA) assays, which have been used to estimate radiation exposure. Studies indicate increased mutation rates, potential transgenerational effects, and a heightened risk of oncological diseases among exposed populations. Despite decades of research, uncertainties remain regarding radiation exposure's long-term genetic and epigenetic consequences.

**Conclusions:** This review highlights the necessity for further investigations using advanced molecular techniques to clarify the impact of radiation on future generations and improve radioprotection strategies.

***Keywords:*** *Semipalatinsk Nuclear Test Site, radiation exposure, biodosimetry, transgenerational effects, health risks, radiation-induced mutations*

***For citation:*** Dyussupov A., Chaizhunussova N., Baibussinova A., Massabayeva M., Abenova M., Pivina L., Orekhov A., Smailova Zh., Mukanova D., Lepesbayev M., Kissina R., Akhmadiyeva T., Alibayeva G., Apbassova S., Abdildinova G., Izdenov A., Dosmagambetova R., Shabdarbayeva D. Radiation Exposure in the Semipalatinsk Region: Transgenerational Risks and Dosimetry Approaches // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 165-174. *doi 10.34689/SH.2025.27.3.019*

**Резюме**

# РАДИАЦИОННОЕ ВОЗДЕЙСТВИЕ В СЕМИПАЛАТИНСКОМ РЕГИОНЕ: ТРАНСГЕНЕРАЦИОННЫЕ РИСКИ И ДОЗИМЕТРИЧЕСКИЕ ПОДХОДЫ

**Алтай Дюсупов[1], https://orcid.org/0000-0003-0875-1020**
**Найля Чайжунусова[1]*, https://orcid.org/0000-0002-6660-7118**
**Асель Байбусинова[1], https://orcid.org/0000-0003-3447-6245**
**Меруерт Масабаева[1], https://orcid.org/0000-0001-8240-361X**
**Мадина Абенова[1], https://orcid.org/0000-0002-4219-5737**
**Людмила Пивина[1], https://orcid.org/ 0000-0002-8035-4866**
**Андрей Орехов[1], https://orcid.org/0000-0001-7201-1399**
**Жанаргуль Смаилова[1], https://orcid.org/ 0000-0002-4513-4614**
**Динара Муканова[1], https://orcid.org/ 0000-0001-5186-2346**
**Мурат Лепесбаев[2], https://orcid.org/0009-0006-9810-9232**
**Рауан Кисина[1], https://orcid.org/0000-0002-1849-5596**
**Токжан Ахмадиева[1], https://orcid.org/ 0009-0001-4806-2329**
**Галия Алибаева[3], https://orcid.org/0000-0002-1503-4663**
**Саулеш Апбасова[1], https://orcid.org/0000-0001-6981-5441**
**Гульшара Абдильдинова[4], https://orcid.org/0000-0003-0543-9568**
**Асет Изденов[5], https://orcid.org/0000-0003-0200-1763**
**Раушан Досмагамбетова[6], https://orcid.org/0000-0002-8792-5449**
**Дария Шабдарбаева[1], https://orcid.org/0000-0003-0200-1763**

**[1] НАО «Медицинский университет Семей», г. Семей, Республика Казахстан;**
**[2] Центр судебно-медицинской экспертизы по Абайской области, г. Семей, Республика Казахстан;**
**[3] Больница скорой медицинской помощи г. Семей, г. Семей, Республика Казахстан;**
**[4] Больница Медицинского центра при Администрации Президента Республики Казахстан, г. Астана, Республика Казахстан;**
**[5] Департамент медицинского образования Министерства здравоохранения Республики Казахстан, г. Астана, Республика Казахстан;**
**[6] Советник по науке Директора НИИ курортологии с медицинской реабилитацией, г. Астана, Республика Казахстан.**

**Введение:** Семипалатинский ядерный полигон (СЯП) в Казахстане был местом обширных ядерных испытаний в советский период, что привело к длительному загрязнению окружающей среды и потенциальным последствиям для здоровья подвергшихся облучению групп населения.

**Цель.** Анализ существующих исследований по радиационной дозиметрии и последствиям облучения для здоровья в затронутых регионах.

**Стратегия поиска:** Актуальная литература была найдена посредством поиска в базах данных PubMed, Scopus и Web of Science. Поиск охватывал публикации до января 2025 года с использованием ключевых слов: «Семипалатинский ядерный полигон», «воздействие радиации», «биодозиметрия», «трансгенерационные эффекты», «мутации, вызванные радиацией». На этапе поиска ограничения по дате и языку не применялись. Всего было отобрано 74 публикации. После удаления дубликатов было проанализировано 70 статей по названию и аннотации. Полный текст 45 публикаций был рассмотрен на предмет соответствия критериям включения, и в итоге 39 статей были включены в обзор.

**Результаты:** В статье рассматриваются ключевые методы биодозиметрии, такие как электронный парамагнитный резонанс (ЭПР), флуоресцентная гибридизация in situ (FISH) и анализ по гликофорину А (GPA), применяемые для оценки уровня радиационного воздействия. Исследования указывают на повышенный уровень мутаций, возможные трансгенерационные эффекты и увеличенный риск онкологических заболеваний у подвергшихся облучению групп населения. Несмотря на десятилетия исследований, остаются нерешённые вопросы о долгосрочных генетических и эпигенетических последствиях радиационного воздействия.

**Выводы:** Настоящий обзор подчеркивает необходимость дальнейших исследований с применением современных молекулярных методов для уточнения влияния радиации на будущие поколения и усовершенствования стратегий радиационной защиты.

***Ключевые слова:*** *Семипалатинский ядерный полигон, радиационное воздействие, биодозиметрия, трансгенерационные эффекты, риски для здоровья, мутации, вызванные радиацией*

***Для цитирования:*** *Дюсупов А., Чайжунусова Н., Байбусинова А., Масабаева М., Абенова М., Пивина Л., Орехов А., Смаилова Ж., Муканова Д., Лепесбаев М., Кисина Р., Ахмадиева Т., Алибаева Г., Апбасова С., Абдильдинова Г., Изденов А., Досмагамбетова Р., Шабдарбаева Д.* Радиационное воздействие в Семипалатинском регионе: трансгенерационные риски и дозиметрические подходы // Наука и Здравоохранение. 2025. Т.27 (3), С. 165-174. doi: 10.34689/SH.2025.27.3.019

**Түйіндеме**

# СЕМЕЙ ӨҢІРІНДЕГІ РАДИАЦИЯЛЫҚ ӘСЕР: ҰРПАҚАРАЛЫҚ ҚАУІПТЕР ЖӘНЕ ДОЗИМЕТРИЯЛЫҚ ТӘСІЛДЕР

**Алтай Дюсупов[1], https://orcid.org/0000-0003-0875-1020**
**Найля Чайжунусова[1]*, https://orcid.org/0000-0002-6660-7118**
**Асель Байбусинова[1], https://orcid.org/0000-0003-3447-6245**
**Меруерт Масабаева[1], https://orcid.org/0000-0001-8240-361X**
**Мадина Абенова[1], https://orcid.org/0000-0002-4219-5737**
**Людмила Пивина[1], https://orcid.org/ 0000-0002-8035-4866**
**Андрей Орехов[1], https://orcid.org/0000-0001-7201-1399**
**Жанаргуль Смаилова[1], https://orcid.org/ 0000-0002-4513-4614**
**Динара Муканова[1], https://orcid.org/ 0000-0001-5186-2346**
**Мурат Лепесбаев[2], https://orcid.org/0009-0006-9810-9232**
**Рауан Кисина[1], https://orcid.org/0000-0002-1849-5596**
**Токжан Ахмадиева[1], https://orcid.org/ 0009-0001-4806-2329**
**Галия Алибаева[3], https://orcid.org/0000-0002-1503-4663**
**Саулеш Апбасова[1], https://orcid.org/0000-0001-6981-5441**
**Гульшара Абдильдинова[4], https://orcid.org/0000-0003-0543-9568**
**Асет Изденов[5], https://orcid.org/0000-0003-0200-1763**
**Раушан Досмагамбетова[6], https://orcid.org/0000-0002-8792-5449**
**Дария Шабдарбаева[1], https://orcid.org/0000-0003-0200-1763**

**[1] "Семей медицина университеті" КЕАҚ, Семей қ., Қазақстан Республикасы;**
**[2] Абай облысы бойынша сот-медициналық сараптама орталығы, Семей қ., Қазақстан Республикасы;**
**[3] Жедел медициналық жәрдем көрсету бойынша Семей қалалық ауруханасы, Семей қ., Қазақстан Республикасы;**
**[4] Қазақстан Республикасы Президенті Әкімшілігінің Медициналық орталығының ауруханасы, Астана қ., Қазақстан Республикасы;**
**[5] Қазақстан Республикасы Денсаулық сақтау министрлігінің Медициналық білім беру департаменті, Астана қ., Қазақстан Республикасы;**
**[6] Медициналық реабилитациямен айналысатын курортология ғылыми-зерттеу институтының директорының ғылыми кеңесшісі, Астана қаласы, Қазақстан Республикасы.**

**Кіріспе:** Семей ядролық сынақ полигоны (СЯСП) — Кеңес дәуірінде Қазақстан аумағында орналасқан ядролық сынақтардың ауқымды аймағы болып, қоршаған ортаның ұзақ мерзімді ластануына және халықтың денсаулығына әсер ету қаупіне алып келді.

**Зерттеудің мақсаты:** зардап шеккен аймақтардағы радиациялық дозиметрия және денсаулыққа әсері жөніндегі ғылыми зерттеулерді талдайды.

**Іздеу стратегиясы:** Қатысты әдебиеттер PubMed, Scopus және Web of Science дерекқорларында ізделді. Іздеу 2025 жылдың қаңтарына дейін жарияланған еңбектерді қамтыды. Қолданылған негізгі сөздер: «Семей ядролық сынақ полигоны», «радиация әсері», «биодозиметрия», «ұрпаққа берілетін әсерлер», «радиациямен шақырылған мутациялар». Іздеу барысында жарияланған уақыты мен тілі бойынша шектеу қолданылған жоқ. Барлығы 74 мақала табылып, қайталанатындары алынып тасталған соң 70 мақала тақырыбы мен аңдатпасы бойынша сарапталды. Толық мәтінді шолу нәтижесінде 45 мақала қаралып, 39 мақала осы шолуға енгізілді.

**Нәтижелер:** Мақалада радиациялық әсерді бағалауға арналған негізгі биодозиметриялық әдістер — электрондық парамагниттік резонанс (ЭПР), флуоресцентті in situ гибридизациясы (FISH), және гликофорин A (GPA) сынақтары талданады. Зерттеулер мутация жиілігінің жоғарылауы, ықтимал ұрпақаралық әсерлер және онкологиялық аурулар қаупінің артқанын көрсетеді. Ондаған жылдарға созылған зерттеулерге қарамастан, радиацияның ұзақ мерзімді генетикалық және эпигенетикалық әсерлері туралы сұрақтар ашық күйінде қалып отыр.

**Қорытынды:** Бұл шолу радиацияның болашақ ұрпаққа әсерін нақтылау және радиациялық қауіпсіздік стратегияларын жетілдіру үшін заманауи молекулалық әдістермен қосымша зерттеулер жүргізудің өзектілігін көрсетеді.

***Түйінді сөздер:*** *Семей ядролық сынақ полигоны, радиация әсері, биодозиметрия, ұрпақаралық әсерлер, денсаулыққа қауіп, радиациялық мутациялар.*

***Дәйексөз үшін:*** *Дюсупов А., Чайжунусова Н., Байбусинова А., Масабаева М., Абенова М., Пивина Л., Орехов А., Смаилова Ж., Муканова Д., Лепесбаев М., Кисина Р., Ахмадиева Т., Алибаева Г., Апбасова С., Абдильдинова Г., Изденов А., Досмагамбетова Р., Шабдарбаева Д.* Семей өңіріндегі радиациялық әсер: ұрпақаралық қауіптер және дозиметриялық тәсілдер // Ғылым және Денсаулық. 2025. Т.27 (3), Б. 165-174. doi: 10.34689/SH.2025.27.3.019

**Introduction**

The study of the medical consequences of radiation exposure from the Semipalatinsk Nuclear Test Site (SNTS) on the population of nearby regions has been ongoing for more than 50 years, beginning with the narrative studies of the consequences of nuclear tests aimed at assessing their long-term impact on public health. However, there is still no consensus on the long-term consequences of nuclear tests for second- and third-generation individuals exposed to ionizing radiation.

Some scientists associate the increased morbidity among populations living near the SNTS with internal radiation exposure [1]. Delayed effects of radiation exposure have been identified, which may be transmitted across generations and increase the frequency of spontaneous mutations [2]. Studies confirm DNA damage in individuals exposed to low doses of radiation, consistent with cytogenetic research conducted in the region [3-6]. Additional data on the radiological effects of nuclear war, presented in the British Institute of Radiology report "The Radiological Effects of Nuclear War," indicate that long-term exposure to ionizing radiation in populations may result not only in genetic mutations but also in an increased incidence of oncological diseases, impacts on reproductive health, and reduced immune function [7]. These findings underscore the need for further investigation into the effects of radiation contamination in areas affected by nuclear testing, such as the Semipalatinsk region.

**Aim.** To analyze existing data on the effects of radiation exposure on the residents of the SNTS, including the possibility of transgenerational mutation transmission. It also involves a comparison of biodosimetry methods used to evaluate the level of radiation exposure and its long-term consequences.

**Search strategy**

This narrative literature review was conducted to summarize and critically analyze existing studies on radiation exposure and its potential transgenerational effects among populations residing near the SNTS. To ensure a structured and comprehensive approach, elements of systematic selection were incorporated into the review process.

*Literature Search*

Relevant literature was identified through searches in PubMed, Scopus, and Web of Science databases. The search covered studies published up to January 2025 using the following key terms: “Semipalatinsk nuclear test site”, “radiation exposure”, “biodosimetry”, “transgenerational effects”, and “radiation-induced mutations”. No date or language restrictions were applied at the search stage.

*Study Selection and Data Extraction*

A total of 74 records were initially retrieved. After duplicate removal, 70 articles were screened based on title and abstract. The full text of 45 articles was reviewed for eligibility, and 39 publications were selected based on their relevance to the objectives of this review.

*Articles were included if they:*

• Focused on health risks or genetic effects associated with radiation exposure in the Semipalatinsk region;

• Provided biodosimetric data (EPR, GPA, or FISH methods);

• Discussed potential transgenerational outcomes or molecular effects.

Studies were excluded if they:

• Focused solely on environmental or ecological aspects without medical or genetic endpoints;

• Lacked sufficient methodological detail;

• Did not include primary data or were non-peer-reviewed sources.

The selection process is summarized in Figure 1.

**Scope of Analysis**

Extracted data were analyzed to compare biodosimetric methodologies and their application to the Semipalatinsk population. Additionally, findings on radiation-induced mutations and possible transgenerational effects were critically evaluated across included studies.

**Biodosimetry Methods**

Three key methods were used to assess radiation exposure doses:

Electron Paramagnetic Resonance (EPR): A method for retrospective dose analysis based on tooth enamel. Both classical EPR analysis and in vivo L-band EPR (1.0–1.2 GHz) are utilized.

Glycophorin A (GPA) Assay: A method for detecting somatic mutations in erythrocytes, enabling assessment of radiation-induced cellular damage. Suitable for large-scale screening but requires individual calibration.

Fluorescence In Situ Hybridization (FISH): A cytogenetic method that identifies radiation-induced chromosomal rearrangements. It allows evaluation of long-term radiation effects even decades after exposure.

Each method has its own advantages and limitations and is applied depending on the research objectives [8].

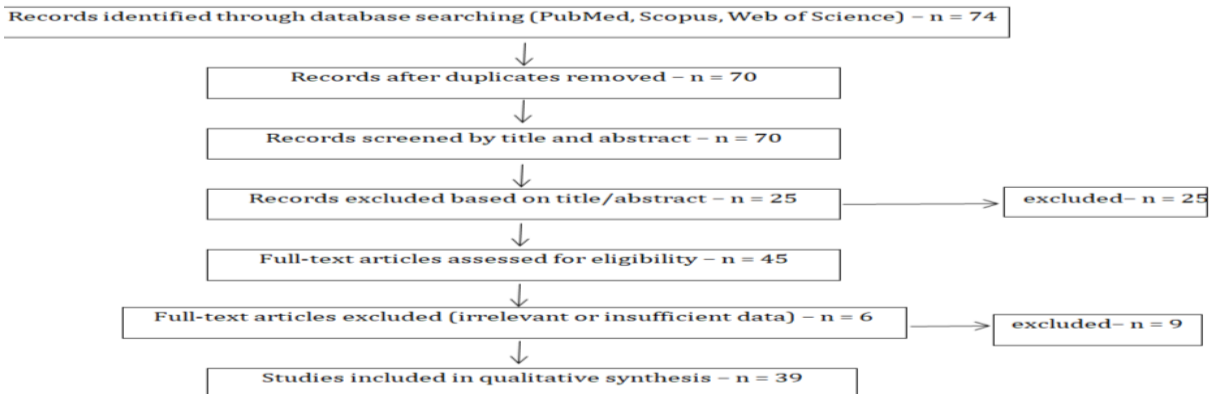



**Figure 1. PRISMA flow diagram showing the selection process of studies included in the narrative review.**

**Results**

Assessment of radiation exposure doses is a critical component of radiation biology and epidemiology. This section presents the key biodosimetry methods (Figure 1). Each biodosimetry method has its own characteristics and limitations when studying the long-term effects of radiation.

Radiobiological studies of populations living near the SNTS have identified statistically significant genetic and cellular changes in individuals exposed to chronic low-dose and acute radiation [9,10,11]. In this context, comparing biodosimetry methods and their applicability for assessing the consequences of radiation exposure in residents of nearby regions is crucial (Table 1).

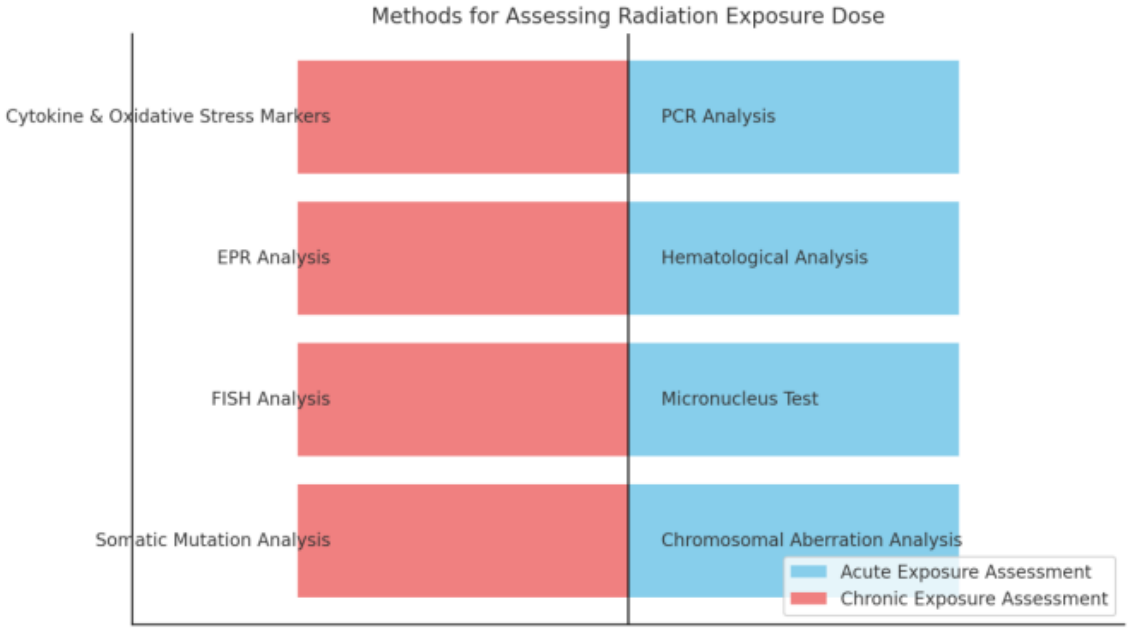



**Figure 2. Key methods for assessing radiation exposure doses.**

*Table 1.*

**Comparison of biodosimetry methods for radiation exposure at the SNTS.**

| Method | Applicability in the context of the SNTS | Limitations |
|---|---|---|
| EPR | Determination of accumulated dose, particularly in cases of acute exposure | Requires tooth extraction; not suitable for mass screening |
| GPA | Detection of somatic mutations in exposed groups | Sensitive to individual factors; requires calibration |
| FISH | Assessment of long-term genetic damage | Requires precise dosimetric correlation, but is the most informative |

The EPR method revealed accumulated radiation doses in residents of the region exposed to prolonged radionuclide exposure. EPR-based studies indicated average cumulative radiation doses ranging from 150 to 250 mSv, which is comparable to the levels observed in Chernobyl liquidators [12]. Ionizing radiation induces the formation of stable radicals in dental enamel in proportion to the dose received, making EPR an effective tool for retrospective biodosimetry, especially in cases of radiological emergencies [13–15]. However, the method requires the isolation of tooth enamel and is therefore unsuitable for mass screening. Recent technological advances have enabled in vivo EPR analysis in the L-band range (1.0–1.2 GHz), expanding its potential for rapid screening applications [15–17].

Ionizing radiation can cause mutations in human cells, which are associated with the development of cancer. To reliably and rapidly detect such mutations, the GPA was developed. It was first employed at the Lawrence Livermore National Laboratory (USA) to assess cellular damage resulting from radiation exposure. The GPA method plays a key role in biodosimetry, allowing for the fast and efficient detection of radiationinduced genetic damage.

Studies have shown that GPA correlates well with physically derived dose estimates [18,19]. The method recorded a 1.5–1.8-fold increase in the frequency of somatic mutations [9]. Due to the simplicity and speed of blood sample analysis, GPA is an effective tool for assessing genotoxic radiation exposure in large populations [20,21]. However, the results remain inconsistent, as similar studies conducted in Japan did not identify significant changes in the offspring of atomic bomb survivors [11]. Additional research, including work by Tawn et al., supports the usefulness of GPA for biodosimetry in radiation emergency scenarios [22]. Furthermore, data from Sram et al. demonstrate the successful application of GPA under conditions of chronic low-level exposure to air pollution, highlighting the method's versatility [23].

The GPA, present on the surface of erythrocytes, exists in two forms corresponding to the M and N blood groups and is associated with a gene located on chromosome 4q. Flow cytometry using fluorescent monoclonal antibodies is

employed to detect somatic mutations. The frequency of cells with a loss of the GPA allele reflects the level of radiation exposure: the higher the frequency, the higher the cumulative dose. This method is particularly useful for assessing acute radiation exposure; however, its application in cases of chronic exposure is limited due to the complexity of accounting for accumulated effects. Nevertheless, GPA remains an important tool for the individualized assessment of radiation exposure consequences [24,25].

The FISH with chromosome staining is used for retrospective dosimetry, even long after radiation exposure [26]. In radiation cytogenetics, chromosomal translocations are considered a key biological dosimeter for estimating radiation doses [27].

Studies by *Dubrov Yu.E.* (2002) and *Takeichi N.* (2006) confirmed an increased frequency of mutations in individuals exposed to radiation, suggesting the possibility of transgenerational transmission of radiation-induced changes [9,28]. FISH analysis has demonstrated high sensitivity to radiation-induced chromosomal rearrangements in exposed populations. According to Salomaa et al. (2002), the level of chromosomal translocations in residents of areas adjacent to the Semipalatinsk Test Site corresponded to doses of approximately 180 mSv [10]. This is comparable to findings from studies on Chernobyl liquidators and individuals affected by nuclear testing on the Marshall Islands [29]

**Transgenerational effects in populations exposed to radiation**

Studies on the impact of radiation from the Semipalatinsk Test Site (STS) on second and third generations remain inconclusive. An analysis of mutations in the offspring of exposed residents revealed an increased level of genetic instability [10]. However, similar studies conducted in Japan [11] did not find significant radiation-induced mutations in the descendants of individuals exposed to ionizing radiation, suggesting the possible influence of other factors such as background mutations or differences in radiation dose. Nevertheless, Japanese researchers continue to pursue investigations in this area [36–38].

Epigenetic studies have identified altered gene expression in the descendants of radiation-exposed individuals, indicating potential radiation effects at the level of genome regulation [26]. Research on the offspring of Chernobyl cleanup workers has also produced mixed results—some studies confirm the presence of mutations, while others do not [19,22,30,34,35]. This further emphasizes the need for longitudinal studies utilizing nextgeneration sequencing (NGS).

Thus, current data indicate that the FISH and GPA methods are the most informative for assessing the effects of radiation exposure among populations near the STS. However, evidence of transgenerational effects remains contradictory and calls for additional molecular genetic research, including NGS and epigenetic analysis.

**Discussion**

Radiobiological consequences for the population of the Semipalatinsk region

The SNTS was the site of 456 nuclear explosions conducted between 1949 and 1989. These tests led to significant environmental radioactive contamination and long-term exposure of the local population to low-dose ionizing radiation. Research confirms that residents of the region were subjected to both acute and chronic radiation exposure, which has manifested in increased frequencies of both somatic and hereditary mutations [9,10,27].

Various biodosimetry methods are employed to assess these consequences, with the most widely used being the EPR, GPA and FISH methods. Each method has its own advantages and specific applications.

The EPR allows for retrospective assessment of accumulated radiation doses. For example, studies by *Tolstykh et al.* (2000) indicated that the average dose, calculated from the dental enamel of residents of East Kazakhstan, ranged from 150 to 250 mSv, comparable to doses received by Chernobyl liquidators [12]. However, widespread application of this method is limited due to the scarce availability of the required biological material (teeth).

The GPA assay enables the assessment of somatic mutation frequency. Several studies have reported a 1.5–1.8-fold increase in mutation frequency among residents of the Semipalatinsk region compared to control groups [9]. Nonetheless, other studies have not consistently confirmed this trend, which may be attributed to individual population characteristics and differences in radiation doses [28].

The FISH is considered the most precise method for studying the long-term effects of radiation. According to *Salomaa et al.* (2002), the frequency of stable chromosomal aberrations (translocations) in residents of East Kazakhstan significantly exceeded control values and corresponded to doses of approximately 180 mSv [10]. These results are consistent with findings from studies of Chernobyl liquidators and atomic bomb survivors in Japan [27], confirming the high sensitivity of the method to chronic exposure and the reliability of FISH for retrospective dose estimation and analysis of long-term genetic effects of radiation. Its application, particularly when combined with other cytogenetic and molecular-genetic techniques, allows for a more accurate assessment of both individual and population level radiation risks.

Each of the biodosimetry methods discussed has its own value. EPR is suitable for ret-rospective dose assessment but is limited by the availability of biological material. The GPA assay helps detect somatic mutations, although results are sometimes inconclusive. FISH, in turn, provides high accuracy in studying the delayed effects of radiation exposure but requires calibration to account for the conditions of chronic exposure.

*Transgenerational Effects in the Context of the SNTS*

One of the key unresolved questions is the possibility of transmitting radiationinduced mutations to the descendants of populations exposed to radiation in areas surrounding the SNTS. Studies investigating this phenomenon have produced inconsistent results.

For instance, *Dubrov* (2002) reported a significant increase in mutation frequency among the children of irradiated parents living in areas contaminated by radionuclide fallout [9]. In contrast, a similar study by Cologne et al. (2022) found no statistically significant differences in the offspring of atomic bomb survivors in Japan, raising doubts about the universality of this phenomenon [28].

The situation concerning the descendants of Chernobyl residents also remains controversial. While some studies confirm the heritability of radiation-induced mutations [9], others [22] do not find significant changes, and more recent whole-genome sequencing research [31, 32] has not detected a statistically significant increase in the number of de novo mutations among the offspring of exposed individuals. These discrepancies may be due to differences in radiation doses and exposure conditions and highlight the need for further investigation.

An additional perspective is provided by the analysis of epigenetic changes. Studies of populations residing in radiation-contaminated areas, including Fukushima, have revealed gene expression modifications that may be linked to radiation exposure. This suggests that even in the absence of structural DNA changes, radiation may affect future generations through epigenetic mechanisms [24].

Despite numerous investigations, the data on transgenerational effects of radiation remain contradictory. A comparative analysis of three key regions SNTS, Chernobyl, and Japan shows variation in outcomes (Table 2). These differences can be attributed to the diversity of radiation doses, population characteristics, and methodological variations across studies.

*Table 2.*

**Critical analysis of contradictions.**

| Region | Confirmed mutations | Negative findings | Research characteristics |
|---|---|---|---|
| SNTS | Dubrov (2002): increased mutation frequency in descendants | Several studies found no mutations in the second generation | Chronic exposure; limited sample sizes |
| Chernobyl | Jensen et al. (1995): increase in GPA mutations | Bebeshko et al.: no statistically significant effects | Methodological and dosimetric inconsistencies |
| Japan | Kyoizumi et al. (1987): isolated mutations in A-bomb survivors | Cologne et al. (2022): no mutations in offspring | Background mutations and relatively lower radiation doses |

The data obtained do not provide a definitive answer regarding the transgenerational effects of radiation exposure in the context of the SNTS. To more accurately assess the impact of radiation on heritable changes, further molecular-genetic studies are needed, including next-generation sequencing (NGS) and epigenetic analysis.

Despite significant progress in the field of biodosimetry, the present study has revealed several limitations. First, many studies rely on retrospective radiation dose assessments, which introduce uncertainties due to limited access to historical data and individual variability in radiosensitivity. Second, biodosimetric methods such as FISH and GPA analysis are effective at detecting chromosomal aberrations but do not fully capture epi-genetic changes or the long-term biological effects of radiation that extend beyond direct DNA damage. Third, studies on transgenerational effects remain inconclusive, as most of the available data are derived from small samples and lack long-term follow-up. Finally, methodological differences across studies hinder comparative analysis and metaanalytical approaches, underscoring the need for standardization of research protocols and continued molecular-genetic investigation.

Thus, a comparative analysis of biodosimetry methods indicates that FISH and GPA are currently the most reliable for assessing radiation exposure in SNTS-affected populations. However, further calibration is required, particularly considering chronic exposure scenarios. The question of heritable mutations remains contentious, as existing studies yield conflicting results. This highlights the necessity of longitudinal monitoring and molecular-genetic analysis to identify potential long-term effects of radiation exposure on the second and third generations, given that the long-term health consequences of radiation exposure are well-documented [33, 39].

It is recommended to integrate advanced technologies such as NGS and epigenetic approaches to improve the accuracy of transgenerational effect assessments. Additionally, the development of preventive health programs for populations living in radiationaffected areas is crucial.

**Limitations:**

1. Lack of standardized dosimetric protocols complicates data comparison.
2. Insufficient long-term cohort studies of second and third generations.
3. Small sample sizes in several SNTS and Chernobyl-related studies.
4. Limited data on epigenetic effects and their underlying mechanisms.

**Conclusion**

The territories of the Abay Region adjacent to the former SNTS remain areas of elevated radiological risk. A significant portion of the population exposed to ionizing radiation during nuclear testing, as well as their second- and third-generation descendants, continue to reside in these regions.

Contemporary research confirms the potential for transgenerational effects of ionizing radiation, necessitating further investigation into the mechanisms of radiation-induced mutations and their health implications. The advancement and refinement of biodosimetry methods including FISH analysis, cytogenetic and molecular-genetic approaches, as well as mathematical modeling of radiation doses—offer promising opportunities for the assessment of both individual and population evel risks.

One of the key mechanisms proposed to explain transgenerational effects is radiationinduced genomic instability (RIGI), whereby numerous non-clonal genetic alterations occur in the descendants of irradiated cells. This phenomenon has been observed across various species,

including humans, and may persist across multiple generations, thereby increasing the risk of oncological and other diseases.

Biodosimetric methods, such as the analysis of chromosomal aberrations in peripheral blood lymphocytes - including dicentrics and micronuclei - as well as FISH analysis, enable quantitative assessment of radiation dose and identification of radiation-induced genetic damage. These techniques are especially relevant in the absence of physical dosimetry data and in cases of chronic or low-dose exposure.

Moreover, studies have demonstrated that ionizing radiation can induce epigenetic changes such as DNA methylation that may also be transmitted to offspring and impact their health. Thus, the integration of cytogenetic, molecular-genetic, and epigenetic approaches into biodosimetry, combined with mathematical modeling, represents a promising direction for the more precise evaluation of radiation-related risks and the development of effective public health protection strategies.

Further investigation of radiation risk among second- and third-generation individuals is a critical area of research in radiation medicine and epidemiology. Such efforts will not only enhance our understanding of the long-term consequences of ionizing radiation but also contribute to the development of targeted preventive measures and medical monitoring for affected populations. Particular emphasis should be placed on a comprehensive approach that includes molecular-genetic, epigenetic, and bioinformatic methods of analysis.

***Author Contributions:*** **A.D.** led the review, was the first reviewer, developed and under took the search strategy, and analysed and organised the data. **A.B.** and **M.M., M.A.** acted as the reviewer and **N.Ch.** with **D.Sh.** acted as third reviewer to resolve any conficts during screening. **A.O., Zh.S., M.L., R.K., T.A., G.A., S.A., G.A., A.I., R.D..** participated in data extraction and quality assessment of the included studies. **M.L., R.K., T.A.** gave direction and critical comments. **A.B., N.Ch., M.M, A.O.** wrote the manuscript and prepared tables, figures, and supplementary files. **M.A., L.P.** check translating. All authors named provided their expertise in reviewing the final manuscript and content.

***Conflict of interest:*** *No conflict of interest declared.*

***Publication information:*** *The authors declare that this material has not been previously submitted for publication in other journals.*

***Funding:*** *This research has been funded by the Science Committee of Science and Higher Education of the Ministry of Kazakhstan (Grant No. BR28512329).*

***Literature:***

1. *Tanaka K., Iida S., Takeichi N., et al.* Unstable-type chromosome aberrations in lymphocytes from individuals living near Semipalatinsk nuclear test site. J Radiat Res. 2006. 47(Suppl A):A159-A164. https://doi.org/10.1269/jrr.47.a159

2. *Little J.B.* Radiation carcinogenesis. Int J Radiat Biol. 1998. 74:663-671.

3. *Chenal C., Legue F., Nourgalieva K.* Delayed effects of low level acute irradiation and chronic environmental radioactive contamination on DNA lymphocytes of people living in Dolon, a settlement located in the vicinity of the Semipalatinsk nuclear test site (Kazakhstan). Sci Total Environ. 2006.369(1-3):91-98. https://doi.org/10.1016/j.scitotenv.2006.05.003

4. *Östling O., Johanson KJ.* Microelectrophoretic study of radiation-induced DNA damages in individual mammalian cells. Biochem Biophys Res Commun. 1984;123(1):291-298.

5. *Gusev B.I., et al.* The Semipalatinsk nuclear test site: a first assessment of the radiological situation and the test-related radiation doses in the surrounding territories. Radiat Environ Biophys. 1997;36(4):281-292.

6. *Simon S.L., Baverstock K.F., Lindholm C., et al.* A summary of evidence on radiation exposures received near to the Semipalatinsk nuclear weapons test site in Kazakhstan. Health Phys. 2003;84(6):718-725. https://doi.org/10.1097/00004032-200306000-00004

7. British Institute of Radiology. The radiological effects of nuclear war: Report of a British Institute of Radiology Working Party. Br J Radiol. 1983;56(663):147-170. https://doi.org/10.1259/0007-1285-56-663-147

8. *Salomaa S., Lindholm C., Tankimanova M.K., et al.* Stable chromosome aberrations in the lymphocytes of a popu-lation living in the vicinity of the Semipalatinsk nuclear test site. Radiat Res. 2002;158(5):591-596. https://doi.org/10.1667/0033-7587(2002)158

9. *Dubrova Y.E., Bersimbaev R.I., Djansugurova L.B., et al.* Nuclear weapons tests and human germline mutation rate. Science. 2002;295(5557):1037. https://doi.org/10.1126/science.1068102

10. *Takada J., Hoshi M., Rozenson R.I., et al.* Environmental radiation dose in Semipalatinsk area near nuclear test site. Health Phys. 1997;73(3):524-527.

11. *Cologne J., Sugiyama H., Hamasaki K., et al.* Chromosome aberrations among atomic-bomb survivors exposed in utero. Radiat Environ Biophys. 2022;61(1):59-72. https://doi.org/10.1007/s00411-021-00960-4

12. *Tolstykh E.I., Degteva M.O., Kozheurov V.P., et al.* Strontium metabolism in teeth and enamel dose assessment: analysis of the Techa river data. Radiat Environ Biophys. 2000;39(3):161-171.

13. *Brady J.M., Aarestad N.O., Swartz H.M.* In vivo dosimetry by electron spin resonance spectroscopy. Health Phys. 1968;15(1):43-47.

14. *Ikeya M., Ishii H.* Atomic bomb and accident dosimetry with ESR: natural rocks and human tooth in-vivo spec-trometer. Int J Radiat Appl Instrum A. 1989;40(10-12):1021-1027.

15. *Swartz H.M., Flood A.B., Williams B.B., et al.* Electron paramagnetic resonance dosimetry for a large-scale radiation incident. Health Phys. 2012;103(3):255-267.

16. *Miyake M., Nakai Y., Yamaguchi I., et al.* In-vivo radiation dosimetry using portable L-band EPR: on-site meas-urement of volunteers in Fukushima Prefecture, Japan. Radiat Prot Dosimetry. 2016;172(1-3):248-253. https://doi.org/10.1093/rpd/ncw214

17. *Langlois R.G., Bigbee W.L., Kyoizumi S., et al.* Evidence for increased somatic cell mutations at the glycophorin A locus in atomic bomb survivors. Science. 1987;236(4800):445-448.

18. *Kyoizumi S., Nakamura N., Hakoda M., et al.* Detection of somatic mutations at the glycophorin A locus in eryth-rocytes of atomic bomb survivors using a single beam flow sorter. Cancer Res. 1989;49(3):581-588.

19. *Jensen R.H., Langlois R.G., Bigbee W.L., et al.* Elevated frequency of glycophorin A mutations in erythrocytes from Chernobyl accident victims. Radiat Res. 1995;141(2):129-135.

20. *Straume T., Lucas J.N., Tucker J.D., et al.* Biodosimetry for a radiation worker using multiple assays. Health Phys. 1992;62(2):122-130.

21. *Albertini R.J., Hayes R.B.* Somatic cell mutations in cancer epidemiology. In: Application of Biomarkers in Cancer Epidemiology. Lyon: IARC; 1997. p. 159-184.

22. International Commission on Radiation Units and Measurements (ICRU). Retrospective Assessment of Exposures to Ionizing Radiation. Report 68. Bethesda, MD: ICRU; 2002.

23. *Zhang Y., et al.* Biomarkers of ionizing radiation exposure. Expert Rev Mol Diagn. 2010;10(4):463-474. https://doi.org/10.1586/erm.10.15

24. *Tawn E.J., Whitehouse C.A., Duff P.A.* Assessment of somatic mutations by GPA in individuals exposed to radiation. Radiation Research, 2004, 161(2), 216–223.

25. *Šrám R.J., Binková B., Rössner P., Rubes J.* Genotoxic effects of air pollution: analysis of somatic mutations in an urban population. Mutation Research, 2006, 600(1–2), 117–131

26. *Alt F.W., Zhang Y., Meng F.L., Guo C., Schwer B.* Mechanisms of programmed DNA lesions and genomic instability in the immune system. Cell. 2013;152(3):417-429. https://doi.org/10.1016/j.cell.2013.01.007

27. *Okladnikova N.D.* Chromosomal aberrations in peripheral blood lymphocytes of patients with chronic radiation sickness 25-30 years after exposure. Radiatsiya i Risk. 2000;(Special Issue):101-104. (In Russian, with English abstract).

28. *Takeichi N., Hoshi M., Iida S., et al.* Nuclear abnormalities in aspirated thyroid cells and chromosome aberrations in lymphocytes of residents near the Semipalatinsk nuclear test site. J Radiat Res. 2006;47(Suppl A):A171-A177. https://doi.org/10.1269/jrr.47.a171

29. *Stepanenko V., Kaprin A., Ivanov S., et al.* Comparison of external dose estimates using different retrospective dosimetry methods in the settlements located near Semipalatinsk Nuclear Test Site, Republic of Kazakhstan. J Radiat Res. 2024;65(1):36-46.

30. *Madiyeva M.R., Chaizhunusova N.Zh., Pivina L.M., Saimova A.Zh., Abylgazinova A.Zh., Rakhypbekov T.K.* Results of a comprehensive cytogenetic survey of the population in the eastern region of Kazakhstan. Med Zhurnal i Statyi. 2015;(2):66-72. (In Russian, with English abstract).

31. *Yeager M., Machiela M.J., Kothiyal P., et al.* Lack of transgenerational effects of ionizing radiation exposure from the Chernobyl accident. Science. 2021;372(6543):725-729. doi:10.1126/science.abg2365

32. *Chumak V., Bakhanova E., Kryuchkov V., et al.* Estimation of radiation gonadal doses for the American-Ukrainian trio study of parental irradiation in Chornobyl cleanup workers and evacuees and germline mutations in their offspring. J Radiol Prot. 2021;41(4):10.1088/1361-6498/abf0f4. Published 2021 Nov 1. doi:10.1088/1361-6498/abf0f4

33. *Kamiya K., Ozasa K., Akiba S., Niwa O., Kodama .K, Takamura N., Zaharieva E.K., Kimura Y., Wakeford R.*, Long-term effects of radiation exposure on health. Lancet 386, 469–478 (2015). doi:10.1016/S0140-6736(15)61167-9

34. *Weinberg H.S., Korol A.B., Kirzhner V.M., et al.* Very high mutation rate in offspring of Chernobyl accident liquidators. Proc Biol Sci. 2001;268(1471):1001-1005. doi:10.1098/rspb.2001.1650

35. *Kiuru A., Auvinen A., Luokkamäki M., et al.* Hereditary minisatellite mutations among the offspring of Estonian Chernobyl cleanup workers. Radiat Res. 2003;159(5):651-655. doi:10.1667/0033-7587(2003)159[0651:hmmato]2.0.co;2

36. *Nakamura N., Yoshida N., Suwa* T. Three major reasons why transgenerational effects of radiation are difficult to detect in humans. Int J Radiat Biol. 2024;100(9):1297-1311. doi:10.1080/09553002.2023.2187478

37. *Horai M,. Mishima H., Hayashida C., et al.* Detection of de novo single nucleotide variants in offspring of atom-ic-bomb survivors close to the hypocenter by whole-genome sequencing. J Hum Genet. 2018;63(3):357-363. doi:10.1038/s10038-017-0392-9

38. *Youk J., Kwon H.W., Lim J., et al.* Quantitative and qualitative mutational impact of ionizing radiation on normal cells. Cell Genom. 2024;4(2):100499. doi:10.1016/j.xgen.2024.100499

39. *Grant E.J., Furukawa K., Sakata R., et al.* Risk of death among children of atomic bomb survivors after 62 years of follow-up: a cohort study. Lancet Oncol. 2015;16(13):1316-1323. doi:10.1016/S1470-2045(15)00209-0

**Information about the authors:**

**Altay Dyussupov** - Chairman of the Board-Rector, Semey Medical University, Semey, Kazakhstan 103 Abay Street, Semey 071400, Kazakhstan, Tel: +77222522251, E-mail: altay.dyusupov@smu.edu.kz

**Nailya Chaizhunusova** - Department of Public Health, Semey Medical University 103 Abay Street, Semey 071400, Kazakhstan, Tel: +77771450100, E-mail: n.nailya@mail.ru

**Assel Baibussinova -** Epidemiology and biostatistics department, Semey Medical University, Semey, Kazakhstan, 103 Abay Street, Semey 071400, Kazakhstan, Tel: +77222522251, E-mail: assel.baibussinova@smu.edu.kz

**Meruyert Massabayeva -** Semey Medical University, Semey, Kazakhstan, 103 Abay Street, Semey 071400, Kazakhstan, Tel: +77222522251, E-mail: meruyert.massabayeva@smu.edu.kz

**Madina Abenova,** Epidemiology and biostatistics department, Semey Medical University, Semey, Kazakhstan, 103 Abay Street, Semey 071400, Kazakhstan, Tel: +77222522251, E-mail: madina.abenova@smu.edu.kz

**Lyudmila Pivina,** Department of Emergency Medicine, Semey Medical University, Semey, Kazakhstan 103 Abay Street, Semey 071400, Kazakhstan, Tel: +77222522251, E-mail: lyudmila.pivina@smu.edu.kz

**Andrey Orekhov,** Department of Therapy, Semey Medical University, Semey, Kazakhstan, 103 Abay Street, Semey 071400, Kazakhstan, Tel: +77222522251, E-mail: andrey.orekhov@smu.edu.kz

**Zhanargul Smailova,** Semey Medical University, Semey, Kazakhstan, 103 Abay Street, Semey 071400, Kazakhstan, Tel: +77222522251, E-mail: zhanargul.smailova@smu.edu.kz
**Dinara Mukanova,** Semey Medical University, Semey, Kazakhstan; 103 Abay Street, Semey 071400, Kazakhstan, Tel: +77222522251, E-mail: dinara.mukanova@smu.edu.kz
**Murat Lepesbayev,** Forensic Examination Center of the Abai Region, Semey, Kazakhstan; 3 Sechenov Street, +7 (7222) 42–23–68, Semey 071400, Kazakhstan, Tel: +77222522251, E-mail: king87ml@gmail.com
**Rauan Kissina,** Semey Medical University, Semey, Kazakhstan, 103 Abay Street, Semey 071400, Kazakhstan, Tel: +77222522251, E-mail: rauan.kisina@smu.edu.kz
**Tokzhan Akhmadiyeva,** Semey Medical University, Semey, Kazakhstan, 103 Abay Street, Semey 071400, Kazakhstan, Tel: +77222522251, E-mail: tokzhan.akhmadiyeva@smu.edu.kz
**Galiya Alibayeva,** Semey Hospital of Emergency Medical Care, Semey, Kazakhstan; 140A Michurina Street, Semey 071400, Kazakhstan, Tel: +7 (7222) 77 73 38, E-mail: galiya.5@mail.ru
**Saulesh Apbassova** - Department of Pathological Anatomy and Forensic Medicine, Semey Medical University 103 Abay Street, Semey 071400, Kazakhstan, Tel: +77079196975, E-mail: apbasova65@mail.ru
**Gulshara Abdildinova,** Hospital of the Medical Center of the Presidential Administration of the Republic of Kazakhstan, Astana, Kazakhstan, E-mail: Info@oospm.kz
**Asset Izdenov,** Department of Medical Education, Ministry of Healthcare of the Republic of Kazakhstan, Astana, Kazakhstan, Mangilik El 8 Ave., House of Ministries, 5nd entrance, 010000, Astana city, Republic of Kazakhstan ; Clerical Office, 8 (7172) 74-31-71, 74-36-95, E-mail: Asetizdenov@mail.ru
**Raushan Dosmagambetova -** Doctor of Medical Sciences, Professor, Advisor on Science to the Director of the Research Institute of Health Resort Management and Medical Rehabilitation, Astana, Republic of Kazakhstan; e-mail: dosmagambetovaraushan@gmail.com;
**Dariya Shabdarbayeva** – Doctor of Medical Sciences, Professor, Vice Rector for Science and Strategic Development", Semey Medical University", Semey, Kazakhstan, phone 8 707 365 82 71, e-mail: dariya_kz@bk.ru

**Corresponding author:**
**Nailya Chaizhunussova** – professor of Public Health department. NJSC "Semey Medical University" Semey, Republic of Kazakhstan.
**Postal code:** Republic of Kazakhstan, 071400, Semey, st. Abaya 103.
**E-mail:** nailya.chaizhunusova@smu.edu.kz;
**Mobile number:** 87771450100

Received: 29 January 2025 / Accepted: 10 June 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2025.27.3.020***

***UDC 616.69:314.172***

This work is licensed under a Creative Commons Attribution 4.0 International License

# TRENDS AND PATTERNS OF MALE REPRODUCTIVE SYSTEM DISEASES IN THE CONTEXT OF MEDICAL AND DEMOGRAPHIC INDICATORS. LITERATURE REVIEW

**Bayan B. Orazayeva[1], https://orcid.org/0009-0005-0374-7884**

**Nazym S. Iskakova[1], https://orcid.org/0000-0001-5631-5499**

**Dinara S. Serikova-Esengeldina[1], https://orcid.org/0000-0002-9470-9488**

**Nailya M. Urazalina[1], https://orcid.org/0000-0003-0200-1763**

**Aliya K. Atabaeva[1], https://orcid.org/0000-0001-7725-2255**

**Zaituna A. Khismetova[1], https://orcid.org/0000-0001-5937-3045**

**[1] NCJSC «Semey Medical University», Semey, Republic of Kazakhstan.**

**Abstract**

**Introduction:** Male infertility, affecting every sixth man worldwide [5], is a pressing and complex medical and social issue that influences national demographic indicators, the psycho-emotional well-being of individual families, and public health at large. In Kazakhstan, there is a rising incidence of congenital reproductive system pathologies in boys, declining spermogram parameters, and inadequate organization of specialized andrological care.

**Objective:** to analyze the scientific literature in order to identify the main trends and patterns of male reproductive system diseases in the context of medico-demographic indicators (male birth and fertility rates, reproductive health parameters, and socio-demographic consequences).

**Search strategy:** scientific publications from the past 10 years were reviewed through databases such as Scopus, PubMed, Web of Science, CyberLeninka, among others. Additionally, Legal information system of Regulatory Legal Acts of the Republic of Kazakhstan "Әділет" and statistical data from the Committee on Statistics of the Ministry of National Economy of the Republic of Kazakhstan were examined, including regional demographic indicators of the male population and the structure of andrological diseases.

**Research results:** key factors contributing to the rise of male infertility were identified, including a high prevalence of varicocele (up to 40% among infertile men), delayed marriage, increasing divorce rates, and limited access to andrological care. These trends are linked to changes in male lifestyles, comorbidities, and environmental deterioration. Until 2017, specialized andrological medical care in Kazakhstan was underdeveloped; since 2022, fragmented initiatives have been introduced, but coverage remains insufficient. The absence of a unified registry, comprehensive prevention programs, and coordination across healthcare system levels hampers effective solutions.

**Conclusions:** to date, male reproductive health remains one of the underexplored areas of medicine and healthcare. Literature analysis revealed the need to develop a national strategy and an organizational-functional model for the male reproductive health system, including the creation of a registry for men experiencing infertility, development of andrological services, expansion of preventive programs, and interdepartmental cooperation.

***Key words:*** *men, male reproductive health, male infertility, demography, andrology, Kazakhstan, trends, patterns, prevention.*

***For citation*:**

Orazayeva B.B., Iskakova N.S., Serikova-Esengeldina D.S., Urazalina N.M., Atabayeva A.K., Khismetova Z.A. Trends and patterns of male reproductive system diseases in the context of medical and demographic indicators. Literature review // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 175-188. *doi 10.34689/SH.2025.27.3.020*

**Резюме**

# ТЕНДЕНЦИИ И ЗАКОНОМЕРНОСТИ ЗАБОЛЕВАНИЙ РЕПРОДУКТИВНОЙ СИСТЕМЫ МУЖЧИН В КОНТЕКСТЕ МЕДИКО-ДЕМОГРАФИЧЕСКИХ ПОКАЗАТЕЛЕЙ. ОБЗОР ЛИТЕРАТУРЫ

**Баян Б. Оразаева[1], https://orcid.org/0009-0005-0374-7884**

**Назым С. Искакова[1], https://orcid.org/0000-0001-5631-5499**

**Динара С. Серикова-Есенгельдина[1], https://orcid.org/0000-0002-9470-9488**

**Найля М. Уразалина[1], https://orcid.org/0000-0003-0200-1763**

**Алия К. Атабаева[1], https://orcid.org/0000-0001-7725-2255**

**Зайтуна А. Хисметова[1], https://orcid.org/0000-0001-5937-3045**

**[1] НАО «Медицинский университет Семей», г. Семей, Республика Казахстан.**

**Введение:** Проблема мужского бесплодия, затрагивающая каждого шестого человека в мире [5] является актуальной комплексной медико-социальной проблемой, оказывающей влияние на демографические показатели стран, психоэмоциональное состояние отдельной семьи и общественное здоровье в целом. В Казахстане отмечается увеличение числа случаев врожденной патологии репродуктивной системы среди мальчиков, снижение показателей спермограммы и недостаточная организация специализированной андрологической помощи.

**Цель исследования:** анализ литературы для выявления основных тенденций и закономерностей заболеваний репродуктивной системы мужчин в контексте медико-демографических показателей (уровень рождаемости и фертильности мужчин, показатели репродуктивного здоровья, социально-демографические последствия).

**Стратегия поиска:** поиск научной литературы в базах данных Scopus, PubMed, Web of Science, CyberLeninka и др., глубиной поиска в 10 лет. Также проведен анализ информационно-правовой базы нормативных правовых актов Республики Казахстан «Әділет» (далее – ИПС НПА «Әділет») и статистических данных Комитета по статистике Министерства национальной экономики РК (МНЭ РК), региональных демографических показателей мужской популяции, структуры андрологических заболеваний.

**Результаты исследования:** среди многочисленной информации были идентифицированы ключевые факторы, способствующие росту бесплодия среди мужчин, такие как: высокая распространенность варикоцеле (до 40% у бесплодных мужчин), позднее вступление в брак, рост числа разводов, ограниченные возможности получения андрологической помощи. Эти тенденции связаны с изменением образа жизни мужчин, наличием сопутствующих заболеваний и ухудшением экологии. До 2017 года в Казахстане специализированная медицинская помощь в области андрологии была развита слабо; с 2022 года внедряются фрагментарные инициативы, однако масштабы охвата остаются недостаточными. Отсутствие единого регистра, комплексных профилактических программ и координации между звеньями системы здравоохранения затрудняют решение проблемы.

**Выводы:** на сегодняшний день репродуктивное здоровье мужчин представляет собой одну из недостаточно изученных сфер медицины и системы здравоохранения. Анализ литературы выявил необходимость разработки национальной стратегии и организационно-функциональной модели системы охраны репродуктивного здоровья мужчин, включающей создание регистра мужчин, испытывающих трудности с зачатием, развитие андрологических служб, расширение спектра профилактических программ и межведомственное взаимодействие.

***Ключевые слова:*** *мужчины, репродуктивное здоровье мужчин, мужское бесплодие, демография, андрология, Казахстан, тенденции, закономерности, профилактика.*

***Для цитирования:***

*Оразаева Б.Б., Искакова Н.С., Серикова-Есенгелдина Д.С., Уразалина Н.М., Атабаева А.К., Хисметова З.А.* Тенденции и закономерности заболеваний репродуктивной системы мужчин в контексте медико-демографических показателей. Обзор литературы // Наука и Здравоохранение. 2025. Т.27 (3), С. 175-188. doi: 10.34689/SH.2025.27.3.020

**Түйіндеме**

# МЕДИЦИНАЛЫҚ-ДЕМОГРАФИЯЛЫҚ КӨРСЕТКІШТЕР КОНТЕКСТІСІНДЕГІ ЕРЛЕРДІҢ РЕПРОДУКТИВТІК ЖҮЙЕСІ АУРУЛАРЫНЫҢ ҮРДІСТЕРІ МЕН ЗАҢДЫЛЫҚТАРЫ. ӘДЕБИЕТТІК ШОЛУ

**Баян Б. Оразаева[1], https://orcid.org/0009-0005-0374-7884**

**Назым С. Искакова[1], https://orcid.org/0000-0001-5631-5499**

**Динара С. Серикова-Есенгельдина[1], https://orcid.org/0000-0002-9470-9488**

**Найля М. Уразалина[1], https://orcid.org/0000-0003-0200-1763**

**Алия К. Атабаева[1], https://orcid.org/0000-0001-7725-2255**

**Зайтуна А. Хисметова[1], https://orcid.org/0000-0001-5937-3045**

**[1] «Семей медицина университеті» КеАҚ, Семей қ., Қазақстан Республикасы.**

**Кіріспе:** Әлемдегі әрбір алтыншы ер адамға әсер ететін ерлер бедеулігі мәселесі [5] – бұл елдердің демографиялық көрсеткіштеріне, жекелеген отбасылардың психоэмоционалдық жағдайына және жалпы қоғамдық денсаулыққа ықпал ететін өзекті әрі күрделі медициналық-әлеуметтік мәселе болып табылады. Қазақстанда ер балалар арасында репродуктивтік жүйенің туа біткен патологияларының жиілегені, спермограмма көрсеткіштерінің төмендеуі және мамандандырылған андрологиялық көмектің жеткіліксіз ұйымдастырылғаны байқалады.

**Зерттеудің мақсаты:** ерлердің репродуктивтік жүйесі ауруларының негізгі үрдістері мен заңдылықтарын медицина-демографиялық көрсеткіштер (ерлердің туу және ұрпақ әкелу деңгейі, репродуктивтік денсаулық көрсеткіштері, әлеуметтік-демографиялық салдарлар) контекстінде анықтау үшін ғылыми әдебиеттерге шолу жүргізу.

**Іздеу стратегиясы:** соңғы 10 жыл ішінде жарық көрген ғылыми әдебиеттер Scopus, PubMed, Web of Science, CyberLeninka және басқа да мәліметтер базаларында ізделді. Сонымен қатар, Қазақстан Республикасы нормативтік

құқықтық актілерінің «Әділет» ақпараттық-құқықтық жүйесі (НҚА «Әділет» АҚЖ) мен ҚР Ұлттық экономика министрлігінің статистика Комитетінің, сондай-ақ аймақтық демографиялық мәліметтер мен андрологиялық аурулар құрылымының деректері талданды.

**Зерттеу нәтижелері:** Ерлер бедеулігінің артуына әсер ететін негізгі факторлар анықталды: варикоцеленің жоғары таралуы (бедеу ерлер арасында 40%-ға дейін), некеге кеш тұру, ажырасу деңгейінің өсуі, андрологиялық көмекті алудың шектеулі мүмкіндіктері. Бұл үрдістер ерлер өмір салтының өзгеруімен, қатар жүретін аурулардың болуымен және экологияның нашарлауымен байланысты. 2017 жылға дейін Қазақстанда андрология саласында мамандандырылған медициналық көмек жеткілікті дамымаған, 2022 жылдан бастап жекелеген бастамалар қолға алына бастағанымен, олардың ауқымы жеткіліксіз. Біртұтас тіркеу жүйесінің, кешенді алдын алу бағдарламалардың және денсаулық сақтау жүйесінің барлық буындары арасындағы үйлестіктің болмауы мәселенің шешілуін қиындатады.

**Қорытынды:** Қазіргі уақытта ерлердің репродуктивтік денсаулығы медицина мен денсаулық сақтау жүйесінде жеткіліксіз зерттелген сала болып табылады. Әдебиетке жүргізілген талдау ерлердің ұрықтандыруда қиындық көріп жүргенін тіркеуге алатын ұлттық регистрді құру, андрологиялық қызметті дамыту, алдын алу бағдарламалардың аясын кеңейту және буынаралық өзара іс-қимылды қамтитын ұлттық стратегия мен ұйымдастырушылық-функционалдық модельді әзірлеу қажеттігін көрсетеді.

***Түйінді сөздер:*** *ерлер, ерлердің репродуктивтік денсаулығы, ерлер бедеулігі, демография, андрология, Қазақстан, үрдістер, заңдылықтар, алдын алу.*

***Дәйексөз үшін:***

*Оразаева Б.Б., Искакова Н.С., Серикова-Есенгельдин Д.С., Уразалина Н.М., Атабаева А.К., Хисметова З.А.* Медициналық-демографиялық көрсеткіштер контекстісіндегі ерлердің репродуктивтік жүйесі ауруларының үрдістері мен заңдылықтары. Әдебиеттік шолу // Ғылым және Денсаулық. 2025. Т.27 (3), Б. 175–188. doi: 10.34689/SH.2025.27.3.020

**Introduction.** One of the priority areas of the modern healthcare system is the protection of the population's reproductive health, as reproductive health is a key indicator of a country's demographic potential, and directly affects socio-economic development and geopolitical security [33].

The demographic processes in our country have specific features that require detailed study and an accurate understanding of the structure of family life and the formation of a healthy younger generation to ensure full and quality generational renewal. The main goal of demographic policy is to ensure sustainable population growth, promote the stabilization of family relationships as the "basic unit" of society, and foster harmonious family values. According to the National Strategy of the Republic of Kazakhstan for 2021–2025, the main threats to national security include the deterioration of the demographic situation, such as a decline in birth rates and an increase in mortality, as well as a decrease in the level and quality of the healthcare system [24].

The challenges of the modern healthcare system emphasize the need to protect men's reproductive health, as long-standing neglect of this field of medicine has led to underestimating the male factor in demographic policy. The health status of the male reproductive system directly influences population trends, demographic stability, and the overall social well-being of society.

Currently, there is a dynamic increase in the number of men with reproductive health problems [25], as well as a rise in the number of infertile marriages. This is due to both medical and socio-economic determinants. The decline in male fertility, the increasing prevalence of male reproductive system diseases, and lifestyle changes necessitate a comprehensive approach to studying and addressing this issue.

**Aim:** to analyze the scientific literature in order to identify the main trends and patterns of male reproductive system diseases in the context of medico-demographic indicators (male birth and fertility rates, reproductive health parameters, and socio-demographic consequences).

**Search Strategy:** the literature search was conducted using the following databases: Scopus, PubMed, Web of Science, Google Scholar, Cochrane Library, Oxford University Press, eLibrary, and CyberLeninka. To obtain comprehensive information, the analysis included Legal information system of Regulatory Legal Acts of the Republic of Kazakhstan "Әділет" (hereinafter referred to as LIS RLA "Әділет"). The search covered a 10-year period (from 2015 to 2025).

An analysis was conducted of documentation from the regional branch of the Abay Republican State Enterprise on the Right of Economic Management "Salidat Kairbekova National Scientific Center for Health Development" of the Ministry of Health of the Republic of Kazakhstan (hereinafter – the branch) regarding the number of men experiencing difficulties with conception (Outgoing letter № 06-01, 06-01-10/1191 dated 24.12.2024). In addition, documents from the Regional Branch of the NCJSC "State Corporation Government for Citizens" for the Abay Region were reviewed concerning the number of marriages and divorces (Outgoing letter № 169-_И dated 17.02.2025).

*Inclusion Criteria:* studies that match the stated research topic; publications meeting the criteria for depth and completeness of the search; research published in English and Russian; dissertations; articles with evidence-based findings; full-text scientific publications in open access. To ensure a comprehensive retrospective analysis, educational and methodological sources published before 2015 and thematically relevant were included in the review. Additionally, the study utilized regulatory legal acts (in particular, ministerial

orders), as well as information obtained from official sources in response to submitted information requests.

*Exclusion Criteria:* studies not corresponding to the stated topic; sources published before 2015; articles published in other languages; articles behind paywalls; dissertation abstracts; short communications, promotional and newspaper publications; conference abstracts and non-peer-reviewed analytical reports.

The literature search used the following key words and phrases: "health AND reproductive system", with a focus on the male rather than female reproductive domain (using clarifying terms such as "male reproductive health", "men's health OR male health", "men's reproduction OR male reproduction", "male infertility", "male infertility NOT female infertility", etc.), diseases of the genitourinary system AND men, public health, medical and demographic indicators, trends AND patterns.

As a result of the search, 513 sources were identified, of which 82 were selected for further analysis.

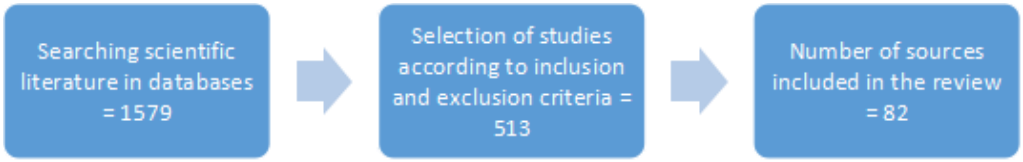



**Figure 1. Search Strategy**

**Research Results.**

According to estimates by the United Nations (UN), the current global population exceeds more than three times the population of the mid-20th century. In 1950, the world population was 2.5 billion, whereas by the end of 2022, this figure had reached 8 billion [70]. As of May 2025, the world population counter shows approximately 8.2 billion people [14]. Experts predict that within the next 30 years, the global population will increase by another 2 billion, and by the year 2080, it may reach a peak of 10.4 billion [70].

This rapid growth is explained by the increasing number of people surviving to reproductive age, as well as related factors such as increased life expectancy, intensive urban development, and expanding migration flows.

The gender composition of the global population is as follows: 50.5% of the total population are men, and 49.5% are women [14]. Globally, the sex ratio at birth is approximately 1.05 boys for every 1 girl. Overall, as of 2024, there are about 101 men for every 100 women. It is worth noting that these indicators can vary significantly depending on territorial and other factors, including political instability, population aging, and differences in life expectancy between sexes [74]. With regard to the Republic of Kazakhstan, according to the data from the Bureau of National Statistics, the population of Kazakhstan was approximately 20.3 million as of April 2025, placing it 62nd in the global ranking. Of this total, men account for 48.86%, and women account for 51.14%, respectively.

*Key Medical and Demographic Trends in Men's Health.* Based on historical demographic data repositories and population census records, the World Fertility Data database was developed, presenting information on global fertility [79].

According to World Fertility Data, the data for Kazakhstan can be interpreted as follows: from 2000 to 2018, there was a steady and progressive increase in the Total fertility rate (TFR), rising from 1.85 to 2.85. This phenomenon indicates a renewal of the population's reproductive capacity and reflects the positive influence of demographic, social, and economic factors. However, a clear trend toward delayed motherhood is observed. For example, the Mean age at childbearing (MAC) was 26.73 years in 2000, increasing to 28.51 years by 2018. This is most likely due to higher educational attainment among women, a stronger focus on professional careers, and a reassessment of life priorities.

Positive developments were also noted among adolescents aged 15 to 19. A decline in the Age-specific fertility rate (ASFR) for this group was recorded – from 33 to 24 births per 1,000 women. This is likely linked to health system reforms, including strengthened health education on reproductive health and broader access to contraceptive methods. During this period, an increase in fertility was observed among women aged 25 to 34 (from 105 in 2000 to 165 in 2018), indicating a shift in reproductive activity toward older age cohorts. Additionally, in the age groups 35–39 and 40–44, the ASFR increased by nearly 2.5 times, reflecting improvements in the quality of medical care and advances in assisted reproductive technologies (Table 1. Fertility data in Kazakhstan for the period from 2000 to 2018).

*Table 1.*

**Fertility data in Kazakhstan for the period from 2000 to 2018.**

| Age groups (years) | Indicator | Serial date in years | | | | |
|---|---|---|---|---|---|---|
| | | 2000.5 | 2005.5 | 2010.5 | 2015.5 | 2018.5 |
| 15-19 | ASFR1519 | 33.00 | 26.00 | 28.00 | 31.00 | 24.00 |
| 20-24 | ASFR2024 | 133.00 | 140.00 | 147.00 | 161.00 | 165.00 |
| 25-29 | ASFR2529 | 105.00 | 133.00 | 156.00 | 159.00 | 165.00 |
| 30-34 | ASFR3034 | 64.00 | 87.00 | 111.00 | 116.00 | 123.00 |
| 35-39 | ASFR3539 | 28.00 | 46.00 | 63.00 | 67.00 | 72.00 |
| 40-44 | ASFR4044 | 6.00 | 11.00 | 16.00 | 16.00 | 19.00 |
| 45-49 | ASFR4549 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Total | MAC | 26.73 | 27.77 | 28.32 | 28.22 | 28.51 |
| Total | TFR | 1.85 | 2.22 | 2.61 | 2.76 | 2.85 |

**Note – Indicator names: ASFR – Age-specific fertility rates, TFR – Total fertility rate, MAC – Mean age at childbearing.*

Statistical reports indicate that the average life expectancy of men worldwide is lower than that of women. This phenomenon became particularly evident in the 21st century as mortality from infectious diseases declined and cardiovascular diseases became the leading cause of death [30], [37], [82]. For example, according to a report by the Organization for Economic Co-operation and Development (OECD), in 2021 the life expectancy of women in OECD countries was 83.0 years, while for men it was 77.6 years – a gap of approximately 5.4 years on average [66]. The lowest male life expectancy is observed in Central and Eastern European countries, where the gender gap exceeds 8 years. In particular, in Latvia, men live less than 75 years, and their life expectancy at age 65 is only 12.7 years. Minor gender differences of less than three years are observed in Iceland and Norway.

Such gender differences in life expectancy are to some extent associated with the fact that men are more exposed to risk factors, including the determinant influence of unhealthy lifestyles. When discussing mortality and gender differences in disease prevalence, it is important to emphasize that men have a higher incidence of fatal outcomes than women (while women more often suffer from chronic but non-lethal diseases) [42]. Among external causes of death, the most prominent are violent deaths, suicides, and road traffic accidents. Studies by researchers from Australia and the United Kingdom indicate that the difference in life expectancy between men and women is linked to a complex interplay of biological, social, and cultural determinants [39]. The Disability-Adjusted Life Year (DALY) indicator in Kazakhstan, as well as globally, is nearly three times higher among young men than among young women due to injuries and violence [11].

Moreover, the COVID-19 pandemic significantly affected male mortality: between 2019 and 2021, life expectancy in OECD countries decreased by an average of 0.7 years. The highest reductions were recorded in Central and Eastern Europe and the United States. In the first two years of the pandemic, countries such as the Czech Republic, Hungary, Latvia, Poland, Greece, the Slovak Republic, and the United States lost as many – or even more – years of life expectancy as had been gained over the previous decade [65].

The article by *Saloni Dattani and Lucas Rodés-Guirao* presents a list of countries with both the largest and smallest gender gaps in life expectancy. As of 2021, countries with the highest gaps (over 10 years) included Russia (11.3 years), Ukraine (10.9 years), and Belarus (10.2 years). On the other hand, countries with the smallest differences (1–2 years) included Nigeria (1.3 years), Togo (1.4 years), and Bangladesh (1.7 years) [43].

As for the situation in Kazakhstan, according to data from the Ministry of Health of the Republic of Kazakhstan, in 2022 the average life expectancy of men was 9 years shorter than that of women, and men's utilization of medical services was half that of women's (according to the "Men's Health" project by the National Association of Primary Health Care) [28].

There are several reasons for this: men are more frequently exposed to harmful, hazardous, and strenuous working conditions; they have higher rates of harmful habits; they suffer from low awareness and stigmatization (cultural and social barriers); they have limited access to specialized services (e.g., andrologists, sexologists); financial barriers; a lack of systematic screening and early diagnosis; and insufficient emphasis on prevention (preventive programs are often focused on women's health, while men's health – especially reproductive health – remains on the periphery) [38], [77].

In terms of morbidity structure among men, cardiovascular diseases and heart conditions have consistently ranked first over the past 10–30 years (1990–2019) [72]. It is known that a normal level of testosterone is beneficial for men's cardiovascular health; however, its level declines with age, which may consequently contribute to deterioration of cardiovascular function. Recent studies suggest that testosterone may potentially be used in the future to treat heart failure, angina pectoris, and myocardial ischemia [63]. However, such statements require in-depth research and comprehensive analysis.

*The Problem of Population Growth.* In 2021, researchers *Christian Dudel and Sebastian Klüsener* published the results of their analysis of differentiation trends in the volume and pace of male and female fertility across 17 highly developed countries. The results demonstrated that men, in most cases, become fathers at a later age compared to women (the median age of fatherhood is 2–5 years higher). In some countries (Germany, Sweden, Japan), total male fertility exceeds female fertility by 10–50%. This phenomenon is explained by the fact that men retain reproductive potential into older age (notably, according to the WHO, reproductive age for women is defined as 15 to 49 years [6], while no specific age range is defined for men). Furthermore, it was found that male fertility is more influenced by migration processes, as men are more frequently involved in international and age-asymmetric marriages. One noteworthy feature is that male fertility is largely underestimated in most countries, as data on fathers particularly in cases of non-marital births – are often not recorded [45]. This fact complicates research, reduces the analytical reliability of data, and hinders the identification of trends and regularities.

The issue of weak population growth is not a recent development. As early as 1981, *D. Valentei and A. Kvasha* noted that 80% of families in the country had few children. Accordingly, the number of childless families has been rising: approximately one in six marriages is infertile (N.M.Pobedinsky, 1981). According to World Health Organization (WHO) estimates, around 17.5% of the population – equivalent to one in six adults – experience infertility [5]. The consequences of this are often devastating. First and foremost, infertility presents a significant sociocultural and interpersonal challenge for society [10]. The stereotype that women are always to blame in childless marriages is increasingly outdated. Modern diagnostic approaches show that infertility is attributable to the female partner in only about 50% of cases (provisionally), whereas in 45.0–52.0% of cases, infertility is associated with disorders of the male reproductive system [41], [46], [51].

The organization of proper prevention, diagnosis, and treatment of infertility is a priority and urgent task of national importance, as population reproduction directly impacts a country's national security. Male infertility should not be

viewed solely as a modern problem of medicine emerging in the late 19th century. Historical and medical records indicate that this phenomenon has always existed, although it had not previously been publicly addressed in speeches, scientific publications, or clinical reports. The absence of systematic diagnosis and monitoring of male infertility can be attributed to both limited medical capabilities in the past and the dominant sociocultural stereotype that associates reproductive dysfunction primarily with the female partner.

In the past decade, this issue has attracted increased attention from both domestic and international scientific communities. According to materials presented by the Scientific Center of Urology named after B.U.Dzharbusynov (2019), male reproductive capacity is declining, while the number of infertile couples shows a steady upward trend [13]. WHO data based on birth rate analysis suggest that in nearly every country, "about 10% of couples are unable to conceive" (WHO Chronicle, 1970). At the same time, there is a consistent downward trend in total fertility rate (TFR). Data Commons reports that in 1970, the TFR was 4.84 births per woman, whereas by 2022, it had dropped to 2.27 [7].

In Kazakhstan, according to research findings, the infertility rate is higher than in European countries, reaching up to 15% (ranging between 12.0% and 15.5%), making it a major issue for both families and society at large [34], [67]. Causes of infertility include both environmental and medical factors, such as disorders of the reproductive system and hormonal imbalances.

According to Stephen W. Leslie et al. and Calvin C. Zhao et al., the causes of male infertility can be classified by basic etiology as follows: endocrine disorders (hypogonadism in 2–5% of cases, gonadotropin deficiency); obstructive pathologies (vasectomy, cysts of the vas deferens); genetic abnormalities (Klinefelter syndrome, CFTR gene mutations, Y chromosome microdeletions); environmental and lifestyle factors (pesticide exposure, smoking, alcoholism); and idiopathic cases (approximately 10–20% of cases without an identifiable cause) [68], [81].

Undoubtedly, the role of men in infertility, sexual health, and the relationship between overall health and reproductive function is critical. According to statistical data from the Abay Region branch for 2023, 260 women were registered with conception difficulties. Of these, 149 cases were due to tubal infertility; 66 due to male-factor infertility; 11 due to anovulation; 2 due to unspecified female infertility; and 32 due to other forms of female infertility. In 2024 reports, the total number of registered women was 212, including 127 cases of tubal infertility; 44 related to male factors; 16 due to anovulation; and 25 due to other forms of female infertility.

These data reveal that infertility is still predominantly perceived as a female issue, primarily because it is the woman who typically seeks medical help first when conception difficulties arise. This is due to both the physiological characteristics of the female body and persistent social stereotypes that place the responsibility for reproduction mainly on women. Men rarely seek help from specialists regarding fertility problems, which significantly delays diagnosis and complicates the treatment of infertility in couples.

*Prevalence of Key Diseases of the Male Reproductive System.* The decline in male reproductive potential may be attributed to various factors, with the following prevalence rates (expressed in %): idiopathic infertility (30.0%) [22], varicocele (14.8%), hypogonadism (10.1%), cryptorchidism (8.4%), malignant neoplasms (7.8%), presence of antisperm antibodies (3.9%), erectile and/or ejaculatory dysfunction (2.4%), systemic diseases (2.2%), obstructive factors (2.2%), testicular tumors (1.2%), Y-chromosome deletion (0.3%) [13]. Prevalence may vary depending on the data source.

Congenital malformations of the reproductive organs are considered among the major causes of male infertility. Over the past decade, the incidence of andrological diseases among children and adolescents has increased 1.5-fold. Annually in the Russian Federation, around 500 boys are born with Klinefelter syndrome and approximately 5,000 with hypospadias. The prevalence of cryptorchidism is 30% among preterm and 4% among full-term boys, while varicocele affects 15–19.4% of adolescents aged 14–15 years [31].

Varicocele – dilation of the spermatic cord veins – is a common condition among young men and the most frequent modifiable cause of male infertility [32]. It is diagnosed in 15–40% of men with abnormal semen parameters, 32–44% of men with primary infertility, and 28–81% of men with secondary infertility [3], [49].

Official data suggest that approximately 60% of diseases affecting reproductive function develop during childhood and adolescence [59]. Domestic studies show that compared to global statistics, Kazakhstan faces significant reproductive health risks among its youth, posing a threat to public health systems [11].

In 2021, among adolescents aged 15–17 years, diseases of the genitourinary system accounted for 4% of primary morbidity, behind respiratory diseases (49%), digestive diseases (11%), injuries and poisonings (8%), skin diseases (7%), and nervous system disorders (5%). Notable sexually transmitted infections (STI) included syphilis (0.4 cases per 100,000), gonorrhea (1.6 per 100,000), trichomoniasis (3 per 100,000), and chlamydia infections (1.4 per 100,000). While STI incidence decreased 2–2.5-fold from 2016–2019, this decline slowed from 2019–2021 [11].

STIs are among the primary disruptors of reproductive health [69]. In inflammatory reproductive conditions associated with STIs or opportunistic flora, ejaculates show elevated leukocyte counts; local antibodies are produced, triggering autoimmune responses that can lead to immunologic infertility. Additionally, leukocytes release superoxide radicals that may damage spermatozoa, weakening and reducing their motility so they cannot penetrate the oocyte's zona pellucida, resulting in failed conception [27].

Male fertility depends on numerous factors, which are classified into two main categories: genetic (hereditary, e.g., Klinefelter syndrome) and acquired (lifestyle-related factors such as harmful habits, deviant behaviors, poor nutrition, stress, etc.) [31], [47].

For instance, Klinefelter syndrome (KS) is the most common chromosomal anomaly in the general male population and one of the most prevalent genetic causes of non-obstructive azoospermia (14% of men with non-obstructive azoospermia have KS [62]) and severe

oligospermia [50]. It is characterized by an additional X chromosome (47, XXY). KS occurs in approximately 1 in 500–1,000 newborn boys, making it one of the most common chromosomal deviations in men [54]. Notably, around 65% of KS cases remain undiagnosed, especially when symptoms are mild or nonspecific [61].

According to GBD 2020 Alcohol Collaborators, youth alcohol use is rising in Kazakhstan (from 34.5% to 55.6%) and globally (from 20.3% to 59.1%) [40]. Alcohol abuse causes Leydig cell atrophy and reduced numbers of mature spermatozoa, leading to conception problems and infertility in 80–85% of cases [29]. A systematic review and meta-analysis found that alcohol abuse negatively affects semen quality, particularly ejaculate volume (a reduction of 0.25 mL, 95% CI 0.07–0.42 mL) and sperm morphology (normal forms reduced by 1.87%, 95% CI 0.86–2.88%) [71].

Tobacco use (including e-cigarettes) in Kazakhstan exceeds global averages (3.3% of girls and 18.7% of boys, compared to global rates of 2.8% and 11.3%, respectively). Tobacco use among Kazakhstani boys is 1.6 times higher than the global average. E-cigarette and vaping use among youth remains at 1.0–1.4% [52]. Tobacco's harmful impact on male fertility is well documented – it is cytotoxic to spermatogenesis, suppresses testosterone production, and disrupts microcirculation, all of which are risk factors for erectile dysfunction and infertility.

A systematic review, The global prevalence of erectile dysfunction: a review, shows that cardiovascular disease (CVD) – stemming from unhealthy lifestyles – is linked to erectile dysfunction (ED). Men with ED have higher risks of overall mortality (OR = 1.26, 95% CI 1.01–1.57) and CVD mortality (OR = 1.43, 95% CI 1.00–2.05). ED prevalence ranges from 3% to 76.5%, depending on age groups and assessment methods, and is notably more common in older men due to natural aging [60].

Reproductive health issues are more common in individuals with comorbid conditions that weaken immunity (65%), as well as in men leading sedentary lifestyles and with excess body weight [26]. Numerous studies link obesity to suppressed testosterone synthesis and hypogonadism, which in turn leads to fertility problems [21], [58]. Elevated body mass index (BMI) is associated with poorer semen quality, affecting sperm volume, concentration, and motility [48].

Obesity and insulin resistance cause systemic oxidative stress that impairs sperm quality by reducing motility and increasing DNA damage. Metabolic disorders – particularly overweight and insulin resistance – are significant risk factors for male infertility [21], [57].

The scientific community increasingly calls for global sperm parameter research due to widespread declines in sperm count and/or quality, especially in Western countries [44]. Clinicians worldwide increasingly encounter patients with abnormal semen parameters [76]. According to World Population Review, as of 2025, the top 5 countries with the highest male testosterone levels are Uzbekistan (773 ng/dL), Croatia (752 ng/dL), Cameroon (731 ng/dL), Azerbaijan (694 ng/dL), and Mongolia (693 ng/dL), while Kazakhstan's level is 356 ng/dL [78].

A 2023 meta-analysis on sperm concentration (SC) and total sperm count (TSC) in males worldwide between 1973 and 2018 highlights a global decline in sperm counts affecting men across all continents. The average sperm concentration dropped by 51.6%, and since 2000 the annual decline rate doubled from 1.16% to 2.64% per year [64]. Literature reviews indicate that sperm quality decline is especially evident in the Middle East and North African regions. However, due to data heterogeneity, further research is needed [36].

*The Role of Reproductive Failure in Marital Stability.* Childless marriages represent a significant social and psychological challenge, becoming a source of chronic stress that can degrade quality of life [56] and negatively affect both the emotional state of the couple and their physiological health. Prolonged psycho-emotional tension contributes to disharmony in family-sexual relationships, sexual dysfunctions, as well as neurotic and somatic disorders, including reproductive organ dysfunction. It has been established that after a diagnosis of "infertility", partners often develop pronounced psychological issues, which under certain circumstances may lead to divorce [4]. Statistics show that for 1 in 5 Kazakhstani couples (20%), the main cause of divorce was the inability to reproduce [12].

According to data from the United Nations Statistics Division, the average age at first marriage among Kazakhstani men and women is rising. In 1979, the average age for men entering marriage was 24.1 years and for women 21.7; in 1989 it was 24.6 and 22.4; in 1999 it increased to 26.1 and 23.4; by 2009 it reached 27.6 years for men and 24.7 years for women [80].

The degradation of the family institution and crisis of family values exert destructive effects on state development. As of March 2024, Kazakhstan ranks second in the world for divorce rates, behind only the Maldives [8]. On average, over 40,000 marriages are dissolved annually in the country [1], [8].

From January to December 2023, Kazakhstan's marriage rate declined from 6.46 to 6.07 per 1,000 population. The highest rate was in the capital at 7.46 per 1,000. Among regions, Ulytau (6.76) and Almaty (6.64) had the highest, while Turkestan was lowest at 5.55. In Abay Region it stood at 5.67 per 1,000. The divorce rate in Kazakhstan was 0.84 per 1,000, down from 0.89 the previous year. The highest divorce rates were in East Kazakhstan (1.36), Karaganda (1.34), and Pavlodar (1.29) regions, while Turkestan had the lowest at 0.30. In Abay Region, it was 0.83 per 1,000 [9].

According to data from the Regional Branch of the NCJSC "State Corporation Government for Citizens" for the Abay Region, the number of marriages recorded over the last three years is rising. From July 8, 2022: 1,910 marriages; 2023: 3,220; 2024: 3,308; and by February 18, 2025: 297 marriages. Divorces have also increased: 245 (from July 8, 2022), 281 (2023), 568 (2024); and 60 divorces by February 18, 2025. Not all marriages are registered with the State Corporation (divorces are registered only by mutual consent without minor children; others go through courts and may remain unofficial), so actual divorce numbers may be higher.

From these data, we can conclude that despite the positive trend in recorded marriages, divorces are also rising. However, detailed analysis of divorce causes in Abay Region is lacking, making it difficult to identify key social, economic, and psychological factors affecting marital

stability. It is possible that infertility, affecting both women and men, is one of the drivers of divorce.

*Organization and Accessibility of Specialized Care for Men.* Male infertility is a complex problem with significant social implications. In fertility clinics, care primarily goes to women. Organizational measures to combat male infertility are insufficiently detailed. Marcia C. Inhorn and Pasquale Patrizio highlighted three key trajectories for research and intervention: controlling known causes of infertility, providing support to those experiencing conception difficulties, and promoting innovations of LCIVF (Laboratory of Clinical and Experimental In Vitro Fertilization) to improve access – including financial accessibility – and acceptability of assisted reproductive technologies (ART) [55].

There are grounds to believe that while women benefit from fairly well-developed medical support, a comparable system for men's reproductive health is effectively absent, confirming that male reproductive health remains off the medical community's radar. Research into female reproductive health is 2–3 times more prevalent than male-focused studies. The systematic review by Robab Latifnejad Roudsari, Farangis Sharifi, and Fatemeh Goudarzi (2023) describes barriers limiting men's participation in reproductive health programs, including limited access to comprehensive and quality medical services, financial constraints, personal attitudes and priorities of couples, as well as societal perceptions and cultural stereotypes. The authors emphasize the need to actively involve men in reproductive health initiatives [73].

**Discussion**

One of the key aspects of Kazakhstan's national interests, according to the National Security Strategy, is achieving and maintaining a level and quality of healthcare and social support systems that meet the needs of improving citizens' and society's well-being. Public safety aims to support natural population growth and to ensure the implementation of urgent measures aimed at countering critical demographic processes [23]. The role of men in ensuring the country's demographic sustainability is immense.

In our country, population reproduction and generational health have long been addressed mainly from the perspective of "maternal and child health protection". Men are generally left outside the scope of attention from medical professionals and health system managers. Meanwhile, this fully-fledged participant in the reproductive process exhibits – compared to women – a higher morbidity rate (including reproductive system diseases that can lead to childless marriages) and a lower average life expectancy.

At the same time, medical care in the field of male reproductive health is not separated from urological services, and the attention of urologists to these issues remains limited.

Male health clinics were first established at "Marriage and Family" consultation centers in Almaty, Karaganda, and Tselinograd on the initiative of the Kazakhstani scientist, Doctor of Medical Sciences, Professor B.U.Dzharbusynov. Also, at his initiative and under his leadership, in 1990 the first Research Institute of Urology under the Ministry of Health of the Kazakh SSR was founded on the basis of the Republican Center of Urology and Operative Nephrology under the name "The Institute of One Doctor" (Resolution of the Council of Ministers of the Kazakh SSR dated December 14, 1990, № 484) [2]. On November 11, 1996, by Resolution of the Government of the Republic of Kazakhstan № 1367, the institute was transformed into the B.U.Dzharbusynov Scientific Center of Urology under the Ministry of Health, which continues to operate to this day [13].

In 1991, the first Congress of Urologists of Kazakhstan took place, and in 1992 Kazakhstani urologists joined the European Association of Urology. The annual congresses of the European Association of Urology allocate dedicated sessions to discuss fertility issues, and all adopted updates are included in the core guidelines, which are revised every ten years.

The next step was the establishment of male infertility clinics at regional consultative polyclinics in all regional centers of the country, where registration, follow-up, diagnosis, and treatment of couples seeking medical help were carried out. These clinics provided assistance with conditions affecting family and marital relationships.

In 2008, a professional organization of sexual medicine doctors was created, which in 2011 was re-registered as the Republican Public Association (RPA) "Men's Health."

In 2013, "Centers for Men's Health and Family Longevity" (CMHFL) began operating across the country, examining more than 6,000 men. By 2014, the number of patients examined and treated exceeded 26,000 nationwide. In January 2014, the Minister of Health approved the "Regulation on the Urological Service," according to which CMHFLs were integrated into the staffing structure of primary healthcare (PHC). According to the 2016 report on the work of the "Centers for Men's Health and Family Longevity," within the framework of the "Men's Health" program, the initiatives "Men's Health Days" and "Men's Health Schools" were implemented. During the "Men's Health Days" events, 4,021 men were examined across 16 cities in Kazakhstan. However, the city of Semey remained outside the scope of attention of researchers and specialists.

Today, medical services in the field of male reproductive health are provided at the following levels: 1) Primary level – PHC specialists conduct initial diagnostics and refer the patient to a narrow specialist; 2) Secondary and tertiary levels – urologists and andrologists in specialized medical institutions conduct detailed diagnostics and targeted treatment using high-tech medical services.

Kazakhstan has a number of legislative acts regulating issues related to male reproductive health and marital-family relations [15], [16], [17], [18], [19], [20], [22]. The country also applies national standards and clinical protocols for diagnosing and treating male reproductive disorders, such as the Clinical Protocol on Male Infertility, the Standard for the Organization of Urological and Andrological Care, and the Rules for the Use of Assisted Reproductive Technologies (ART), etc.

However, despite this, there is currently no monitoring or analysis system for male reproductive health data in Kazakhstan. There is no registry system for men with fertility problems, nor any formal national databases recording male infertility cases (as in most countries, due to ethically justified approaches). Scientific foundations for organizing medical care for infertile men have not yet been developed. Nevertheless, proposals exist to create a unified

confidential registry for couples experiencing conception difficulties, which would include both men and women seeking assistance from reproductive health professionals.

By developing and implementing an electronic information platform focused on male reproductive health, men would have the opportunity to seek anonymous consultations from specialists, receive a preliminary health assessment, and obtain necessary information from official sources. This approach could significantly reduce psychological barriers and social stigma, laying the groundwork for increased trust in the healthcare system and, consequently, more frequent access by men to specialized care. This is especially important for men who are struggling with infertility but refrain from seeking medical assistance due to psychological discomfort or a lack of accessible, reliable information. Additionally, such measures could positively impact the monitoring and planning of government support programs, including in vitro fertilization (IVF) and other ART.

Typically, demographic studies focus on female fertility, but in light of today's challenges, for a more comprehensive understanding of demographic processes, it is necessary to consider male fertility as well [45]. Addressing these issues requires a comprehensive approach – taking into account genetic, environmental, social, and economic factors – including improved education and awareness among men [75], expanding access to specialized and high-tech medical services, and enhancing the quality of care provided.

**Conclusion**

The literature analysis has demonstrated the need for a comprehensive approach to the problem of male infertility. This includes organizational and functional interventions, improving the quality of diagnostics, etiopathogenetic treatment, and advancements in reconstructive and plastic surgical techniques, which could potentially lead to positive outcomes.

The World Health Organization emphasizes the critical need for scientific research in the field of reproductive health, including male reproductive health, since infertility can result in violence, divorce, social stigma, emotional stress, depression, anxiety, and low self-esteem.

The data presented above indicate significant changes in the reproductive indicators of the population, which necessitates in-depth study and the development of comprehensive measures to support reproductive health.

Typically, studies on male reproductive health are narrowly focused and examine the impact of specific pathologies. There is a noted lack of research on risk factors for male reproductive disorders, as well as on the monitoring and analysis of data related to the male reproductive system and the organization of its protection.

One of the targets of the Sustainable Development Goal "Ensure healthy lives and promote well-being for all at all ages" is to guarantee, by 2030, universal access to sexual and reproductive health services. This includes access to family planning, education, and the integration of reproductive health into national strategies and programs [35].

For effective diagnosis and treatment of reproductive disorders, standardized assessment methods should be applied. Both physical and psychological aspects must be taken into account. The development and implementation of individualized treatment plans in fertility medicine, based on a comprehensive evaluation of the patient's health status, can improve patients' sexual well-being [53].

**Conclusion:** Thus, in Kazakhstan, as in other countries, it is important to continue research in the field of male reproductive health, to develop measures aimed at supporting and protecting public health, and to enhance awareness and educational programs on reproductive health issues [44], which will ultimately contribute to improving the country's demographic situation.

The lack of effective state programs for the protection of male reproductive health and the absence of a structured mechanism for providing andrological care underscore the relevance of further research in this area.

***Author Contributions:*** *The authors equally contributed to the research and editorial work that led to the publication of this article.*

***Conflict of Interest:*** *None declared.*

***Funding:*** *This article was published with financial support from the grant-funded scientific startup project for academic staff of NCJSC "Semey Medical University" [Project title: Model of a Digital Platform for Improving the Male Reproductive Health Protection System. Implementation period: 2025–2028].*

***Publication Information:*** *The authors declare that no part of this article has been published previously or is under review elsewhere.*

***Literature:***

1. АНК: Казахстан на втором месте по числу разводов в мире [Электронный ресурс]. URL:https://24.kz/ru/news/social/675291-ank-kazakhstan-na-vtorom-meste-po-chislu-razvodov-v-mire (дата обращения: 19.03.2025).

2. Биография Б.У. Джарбусынова. Научный Центр Урологии [Электронный ресурс]. URL: https://ncu.kz/biografija-b-u-dzharbusynova/ (дата обращения: 03.04.2025).

3. *Божедомов В.А. [и др.].* Варикоцеле и репродуктивная функция: эпидемиология и риск развития бесплодия (данные обследования 3908 мужчин) // Урология. 2021. № 3. С. 122–128.

4. *Бородачева И.В.* Особенности этиологии и патогенеза невротических расстройств при мужском бесплодии 2008. С. 210.

5. ВОЗ: бесплодием страдает каждый шестой человек в мире [Электронный ресурс]. URL:https://www.who.int/ru/news/item/04-04-2023-1-in-6-people-globally-affected-by-infertility (дата обращения: 10.02.2025).

6. Женщины и здоровье [Электронный ресурс]. URL: https://www.who.int/ru/news-room/fact-sheets/detail/women-s-health (дата обращения: 16.03.2025).

7. Инициатива Мир - Демография - Data Commons [Электронный ресурс]. URL: https://datacommons.org/place/Earth?category=Demographics (дата обращения: 18.03.2025).

8. Казахстан – на втором месте в мире по разводам. Forbes.kz [Электронный ресурс]. URL: https://forbes.kz/articles/kazahstan_-_na_vtorom_meste_v_mire_po_razvodam (дата обращения: 24.03.2025).

9. Казахстан по частоте разводов уступает только Мальдивам - Ranking.kz [Электронный ресурс]. URL: https://ranking.kz/reviews/regions/kazahstan-po-chastote-razvodov-ustupaet-tolko-maldivam.html (дата обращения: 13.03.2025).

10. *Кулбаева С.Н. [и др.].* Современный взгляд на проблему бесплодного брака: обзор литературы. Репродуктивная медицина (Центральная Азия). 2024. № 1. С. 147–157.

11. *Курманова А.М. [и др.].* Показатели бремени болезней и риски для репродуктивного здоровья молодежи. Репродуктивная медицина (Центральная Азия). 2024. № 1. С. 138–146.

12. Названы основные причины разводов в казахстанских семьях. Казинформ. URL: https://www.inform.kz/ru/nazvani-osnovnie-prichini-razvodov-v-kazahstane-d0cbee (дата обращения: 06.02.2025).

13. Научный центр Урологии имени Б.У. Джарбусынова. URL: https://ncu.kz/ (дата обращения: 27.02.2025).

14. Население земли - счетчик населения мира. URL: https://countrymeters.info/ru/World (дата обращения: 03.03.2025).

15. О браке (супружестве) и семье - ИПС «Әділет». URL: https://adilet.zan.kz/rus/docs/K1100000518 (дата обращения: 02.01.2025).

16. Об утверждении правил и условий проведения вспомогательных репродуктивных методов и технологий - ИПС «Әділет». URL: https://adilet.zan.kz/rus/docs/V2000021816 (дата обращения: 13.01.2025).

17. Об утверждении правил, объема и периодичности проведения профилактических медицинских осмотров целевых групп населения, включая детей дошкольного, школьного возрастов, а также учащихся организаций технического и профессионального, послесреднего и высшего образования - ИПС «Әділет». URL: https://adilet.zan.kz/rus/docs/V2000021820 (дата обращения: 20.02.2025).

18. Об утверждении правил организации медицинской помощи по охране репродуктивного и психического здоровья несовершеннолетних в возрасте от десяти до восемнадцати лет и молодежи - ИПС «Әділет». URL: https://adilet.zan.kz/rus/docs/V2000021846 (дата обращения: 11.02.2025).

19. Об утверждении Правил проведения военно-врачебной экспертизы и Положения о комиссиях военно-врачебной экспертизы в Вооруженных Силах Республики Казахстан - ИПС «Әділет». URL: https://adilet.zan.kz/rus/docs/V2000021869/history (дата обращения: 15.01.2025).

20. Об утверждении стандарта организации оказания урологической и андрологической помощи в Республике Казахстан - ИПС «Әділет». URL: https://adilet.zan.kz/rus/docs/V2300032541 (дата обращения: 06.02.2025).

21. Ожирение, инсулинорезистентность и репродуктивное здоровье мужчины: патогенетические взаимодействия и современная патогенетическая фармакотерапия uMEDp. URL: https://umedp.ru/articles/ozhirenie_insulinorezistentnost_i_reproduktivnoe_zdorove_muzhchiny_patogeneticheskie_vzaimodeystviya.html (дата обращения: 25.01.2025).

22. О здоровье народа и системе здравоохранения - ИПС «Әділет». URL: https://adilet.zan.kz/rus/docs/K2000000360 (дата обращения: 02.02.2025.

23. О национальной безопасности Республики Казахстан - ИПС «Әділет». URL: https://adilet.zan.kz/rus/docs/Z1200000527 (дата обращения: 18.01.2025).

24. О проекте Указа Президента Республики Казахстан «Об утверждении основных направлений государственной политики Республики Казахстан в сфере официальной помощи развитию на 2021 – 2025 годы» - ИПС «Әділет». URL: https://adilet.zan.kz/rus/docs/P2100000344 (дата обращения: 25.11.2024).

25. Оценка репродуктивного потенциала мужского населения. URL:https://cyberleninka.ru/article/n/otsenka-reproduktivnogo-potentsiala-muzhskogo-naseleniya/viewer (дата обращения: 11.01.2025).

26. Просмотр «Этиологические факторы нарушения репродуктивной функции у мужчин (по данным клиники «Мать и дитя». URL: https://repromed.kz/index.php/journal/article/view/5/2 (дата обращения: 23.03.2025).

27. *Расимович А.А.* Роль инфекций, передаваемых половым путем, в формировании демографического состояния Республики Татарстан и пути его улучшения 2022. С. 321.

28. Сегодня мужским здоровьем в Казахстане никто не занимается – эксперт. Казинформ. URL: https://www.inform.kz/ru/segodnya-muzhskim-zdorov-em-v-kazahstane-nikto-ne-zanimaetsya-ekspert_a3947337 (дата обращения: 04.12.2024).

29. Сергеевич Б.Ю. Социально-гигиенические и медико-организационные аспекты совершенствования санаторно-курортного лечения пациентов с болезнями мужских половых органов 2019. С. 124.

30. Сердечно-сосудистые заболевания. URL: https://www.who.int/ru/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds) (дата обращения: 11.11.2024).

31. Современная демографическая ситуация и проблемы улучшения репродуктивного здоровья населения России. URL: https://cyberleninka.ru/article/n/sovremennaya-demograficheskaya-situatsiya-i-problemy-uluchsheniya-reproduktivnogo-zdorovya-naseleniya-rossii/viewer (дата обращения: 25.01.2025).

32. *Угли Ш.А.* Клинико-лабораторные предикторы эффективности варикоцелэктомии у мужчин с нарушением репродуктивной функции 2023. С. 131.

33. Угрозы и риски демографической безопасностИ Российской Федерации. URL: https://cyberleninka.ru/article/n/ugrozy-i-riski-demograficheskoy-bezopasnosti-rossiyskoy-federatsii/viewer (дата обращения: 06.03.2025).

34. Уровень бесплодия в Казахстане выше, чем в европейских странах. Forbes.kz. URL:

https://forbes.kz/news/newsid_296601 (дата обращения: 19.02.2025).

35. Цель 3: Обеспечение здорового образа жизни и содействие благополучию для всех в любом возрасте. Устойчивое развитие. URL: https://www.un.org/sustainabledevelopment/ru/health/ (дата обращения: 24.02.2025).

36. *Alqurna N.M., Al-Alami Z.M.* Worldwide sperm quality variations between 2000 and 2020: a scoping review. Middle East Fertility Society Journal. 2023. № 1 (28). С. 32.

37. Amini M., Zayeri F., Salehi M. Trend analysis of cardiovascular disease mortality, incidence, and mortality-to-incidence ratio: results from global burden of disease study 2017. BMC Public Health. 2021. № 1 (21). С. 401.

38. Barriers to the participation of men in reproductive health care: a systematic review and meta-synthesis | BMC Public Health | Full Text. URL: https://bmcpublichealth.biomedcentral.com/articles/10.1186/s12889-023-15692-x (дата обращения: 11.06.2025).

39. *Baum F. [и др.].* New Perspective on Why Women Live Longer Than Men: An Exploration of Power, Gender, Social Determinants, and Capitals. International Journal of Environmental Research and Public Health. 2021. № 2 (18). С. 661.

40. B*ryazka D. [и др.].* Population-level risks of alcohol consumption by amount, geography, age, sex, and year: a systematic analysis for the Global Burden of Disease Study 2020. The Lancet. 2022. № 10347 (400). С. 185–235.

41. *Chalyi M.E.C., Akhvlediani N.D.A., Kharchilava R.R.K.* Male infertility. Urologiia. 2017. (2-supplement_2017). С. 4–19.

42. *Crimmins E.M. [и др.].* Differences between Men and Women in Mortality and the Health Dimensions of the Morbidity Process. Clinical Chemistry. 2019. № 1 (65). С. 135–145.

43*. Dattani S., Rodés-Guirao L. Why do women live longer than men? Our World in Data. 2023.*

44. *De Jonge C.J. [и др.].* Current global status of male reproductive health. Human Reproduction Open. 2024. № 2 (2024). С. hoae017.

45. *Dudel C., Klüsener S.* Male–Female Fertility Differentials Across 17 High-Income Countries: Insights From A New Data Resource. European Journal of Population. 2021. № 2 (37). С. 417–441.

46. *Eisenberg M.L. [и др.].* Male infertility. Nature Reviews. Disease Primers. 2023. № 1 (9). С. 1-22, 49.

*47. Elamin I.E., Elrasheed F.E., Alameddine S.M. et al.* Male infertility: a review of medical and surgical approaches. JPTCP. *2024.*

48. *Engin-Ustun Y. [и др.].* Body Mass Index Effects Kruger's Criteria in Infertile Men. International Journal of Fertility and Sterility. 2018. № 4 (11).

49. Extended indications for varicocelectomy - PMC. URL: https://pmc.ncbi.nlm.nih.gov/articles/PMC6733372/ (дата обращения: 26.05.2025).

50. *Fainberg J., Hayden R.P., Schlegel P.N.* Fertility management of Klinefelter syndrome. Expert Review of Endocrinology & Metabolism. 2019. № 6 (14). С. 369–380.

51. *Fainberg J., Kashanian J.A.* Recent advances in understanding and managing male infertility. F1000Research. 2019. (8). С. F1000 Faculty Rev-670.

52. *Glushkova N. [и др.].* Prevalence of Smoking Various Tobacco Types in the Kazakhstani Adult Population in 2021: A Cross-Sectional Study. International Journal of Environmental Research and Public Health. 2023. № 2 (20). С. 1509.

53. *Hatzichristou D. [и др.].* Recommendations for the clinical evaluation of men and women with sexual dysfunction. The Journal of Sexual Medicine. 2010. № 1 Pt 2 (7). С. 337–348.

54. How many people are affected by or at risk for Klinefelter syndrome (KS)? | NICHD - Eunice Kennedy Shriver National Institute of Child Health and Human Development. URL: https://www.nichd.nih.gov/health/topics/klinefelter/conditioninfo/risk?utm_source (дата обращения: 11.06.2025).

55. *Inhorn M.C., Patrizio P.* Infertility around the globe: new thinking on gender, reproductive technologies and global movements in the 21st century. Human Reproduction Update. 2015. № 4 (21). С. 411–426.

56. *Jacob J.A. [и др.].* Common mental disorders, quality of life and explanatory models in men undergoing infertility treatment in a tertiary care hospital: A cross-sectional study. Journal of Psychosomatic Research. 2021. (147). С. 110536.

57. J*azayeri M. [и др.].* Underestimated Aspects in Male Infertility: Epigenetics is a New Approach in Men with Obesity or Diabetes. International Journal of Fertility and Sterility. 2021. № Online First.

58. K*ahn L.G. [и др.].* The Relation of Birth Weight and Adiposity Across the Life Course to Semen Quality in Middle Age. Epidemiology (Cambridge, Mass.). 2019. № Suppl 2 (30). С. S17–S27.

59. K*azemeini S.K. [и др.].* Causes of infertility in view of Iranian traditional medicine: A review. International Journal of Reproductive Biomedicine. 2017. № 4 (15). С. 187–194.

60. *Kessler A. [и др.].* The global prevalence of erectile dysfunction: a review. BJU International. 2019. № 4 (124). С. 587–599.

61. Klinefelter syndrome: MedlinePlus Genetics. URL: https://medlineplus.gov/genetics/condition/klinefelter-syndrome/ (дата обращения: 02.06.2025).

62. Klinefelter Syndrome. The Oncofertility Consortium. URL: https://oncofertility.msu.edu/non-malignant-conditions/klinefelter-syndrome/ (дата обращения: 02.06.2025).

63. *Kloner R.A. [и др.].* Testosterone and Cardiovascular Disease. Journal of the American College of Cardiology. 2016. № 5 (67). С. 545–557.

64. *Levine H. [и др.].* Temporal trends in sperm count: a systematic review and meta-regression analysis of samples collected globally in the 20th and 21st centuries. Human Reproduction Update. 2023. № 2 (29). С. 157–176.

65. Life expectancy at birth by sex, in years, 2023. https://datawrapper.dwcdn.net/iGZgr/4/ (дата обращения: 11.06.2025).

66. Life expectancy. OECD: https://www.oecd.org/en/publications/society-at-a-glance-2024_918d8db3-en/full-report/life-expectancy_37a61588.html (дата обращения: 19.05.2025).

67. *Lokshin V., Omar M., Karibaeva S.* Assisted

Reproductive Technologies in the Republic of Kazakhstan: A 6-Year Trend Analysis from Efficacy to Availability. Journal of Reproduction & Infertility. 2022. № 1 (23). С. 61–66.

68. Male Infertility - Male Infertility Authors Stephen W. Leslie 1 ; Taylor L. Soon-Sutton 2 ; Moien AB - Studocu [Электронный ресурс]. URL: https://www.studocu.com/row/document/kathmandu-university-school-of-medical-sciences/medicine/male-infertility/91855141 (дата обращения: 26.05.2025).

69. *Mankelkl G. [u др.].* Individual and community level factors associated with sexually transmitted infections among men in Tanzania: insights from the Tanzania demographic and health survey of 2022. BMC infectious diseases. 2024. № 1 (24). С. 580.

70. *Nations U.* Народонаселение | Организация Объединенных Наций. United Nations. URL: https://www.un.org/ru/global-issues/population (дата обращения: 18.05.2025).

71. *Ricci E. [u др.].* Semen quality and alcohol intake: a systematic review and meta-analysis. Reproductive Biomedicine Online. 2017. № 1 (34). С. 38–47.

72. *Roth G.A. [u др.].* Global Burden of Cardiovascular Diseases and Risk Factors, 1990-2019: Update From the GBD 2019 Study. Journal of the American College of Cardiology. 2020. № 25 (76). С. 2982–3021.

73. *Roudsari R.L., sharifi F., Goudarzi F.* Barriers to the participation of men in reproductive health care: a systematic review and meta-synthesis. BMC Public Health. 2023. № 1 (23). С. 818.

74. Sex ratio at birth. Our World in Data [Электронный ресурс]. URL: https://ourworldindata.org/grapher/sex-ratio-at-birth?utm_source (дата обращения: 11.06.2025).

75. *Skakkebaek N. E. [u др.].* Populations, decreasing fertility, and reproductive health. Lancet (London, England). 2019. № 10180 (393). С. 1500–1501.

76. Temporal trends in sperm count: a systematic review and meta-regression analysis | Human Reproduction Update | Oxford Academic]. URL: https://academic.oup.com/humupd/article/23/6/646/4035689 (дата обращения: 26.05.2025).

77. T*eo C.H. [u др.].* Barriers and facilitators to health screening in men: A systematic review. Social Science & Medicine (1982). 2016. (165). С. 168–176.

78. Testosterone Levels by Country 2024. URL: https://worldpopulationreview.com/country-rankings/testosterone-levels-by-country (дата обращения: 06.02.2025).

79. World Fertility Data | Population Division. URL: https://www.un.org/development/desa/pd/node/3282 (дата обращения: 18.05.2025).

80. World Marriage Data | Population Division. URL: https://www.un.org/development/desa/pd/data/world-marriage-data (дата обращения: 18.05.2025).

81. *Zhao C.C., Scott M., Eisenberg M.L.* Male Fertility as a Proxy for Health. Journal of Clinical Medicine. 2024. № 18 (13). С. 5559.

82. *Zhao E., Crimmins E.M.* Mortality and morbidity in ageing men: Biology, Lifestyle and Environment. Reviews in Endocrine & Metabolic Disorders. 2022. № 6 (23). С. 1285–1304.

***References: [1-35]***

1. ANK: Kazakhstan na vtorom meste po chislu razvodov v mire [Kazakhstan ranks second in the world in terms of the number of divorces] [Elektronnyi resurs]. URL:https://24.kz/ru/news/social/675291-ank-kazakhstan-na-vtorom-meste-po-chislu-razvodov-v-mire (accessed: 19.03.2025). [in Russian - in Kazakh]

2. Biografiya B.U. Dzharbusynova. Nauchnyi Tsentr Urologii [Biography of B. U. Dzharbusynov. Scientific Center of Urology] [Elektronnyi resurs]. URL: https://ncu.kz/biografija-b-u-dzharbusynova/ (accessed: 03.04.2025). [in Russian - in Kazakh]

3. Bozhedomov V.A. [i dr.]. Varikotsele i reproduktivnaya funktsiya: epidemiologiya i risk razvitiya besplodiya (dannye obsledovaniya 3908 muzhchin) [Varicocele and reproductive function: epidemiology and risk of infertility (data from the examination of 3908 men)]. *Urologiya* [Urology]. 2021. № 3. pp. 122–128. [in Russian]

4. Borodacheva I. V. *Osobennosti etiologii i patogeneza nevroticheskikh rasstroistv pri muzhskom besplodii* [Features of the etiology and pathogenesis of neurotic disorders in male infertility] 2008. С. 210. [in Russian]

5. *VOZ: besplodiem stradaet kazhdyi shestoi chelovek v mire* [WHO: Every sixth person in the world suffers from infertility] [Elektronnyi resurs]. URL:https://www.who.int/ru/news/item/04-04-2023-1-in-6-people-globally-affected-by-infertility (accessed: 10.02.2025). [in Russian]

6. *Zhenshchiny i zdorov'e* [Women and health] [Elektronnyi resurs]. URL: https://www.who.int/ru/news-room/fact-sheets/detail/women-s-health (accessed: 16.03.2025). [in Russian]

7. *Initsiativa Mir - Demografiya* - Data Commons [Initiative World – Demography] [Elektronnyi resurs]. URL: https://datacommons.org/place/Earth?category=Demographics (accessed: 18.03.2025). [in Russian]

8. *Kazakhstan – na vtorom meste v mire po razvodam* [Kazakhstan ranks second in the world in divorce rates]. Forbes.kz [Elektronnyi resurs]. URL: https://forbes.kz/articles/kazahstan_-_na_vtorom_meste_v_mire_po_razvodam (accessed: 24.03.2025). [in Russian - in Kazakh]

9. *Kazakhstan po chastote razvodov ustupaet tol'ko Mal'divam* [Kazakhstan ranks second after the Maldives in divorce rate] - Ranking.kz [Elektronnyi resurs]. URL: https://ranking.kz/reviews/regions/kazahstan-po-chastote-razvodov-ustupaet-tolko-maldivam.html (accessed: 13.03.2025). [in Russian - in Kazakh]

10. Kulbaeva S.N. [i dr.]. Sovremennyi vzglyad na problemu besplodnogo braka: obzor literatury [A modern view on the problem of infertility: literature review]. *Reproduktivnaya meditsina* (Tsentral'naya Aziya). 2024. № 1. С. 147–157. [in Russian]

11. Kurmanova A. M. [i dr.]. Pokazateli bremeni boleznei i riski dlya reproduktivnogo zdorov'ya molodezhi [Burden of disease indicators and risks to youth reproductive health]. *Reproduktivnaya meditsina* (Tsentral'naya Aziya). 2024. № 1. pp. 138–146. [in Russian]

12. Nazvany osnovnye prichiny razvodov v kazakhstanskikh sem'yakh [Main causes of divorce in Kazakhstani families]. *Kazinform* [Elektronnyi resurs]. URL: https://www.inform.kz/ru/nazvani-osnovnie-prichini-

razvodov-v-kazahstane-d0cbee (accessed: 06.02.2025). [in Russian - in Kazakh]

13. *Nauchnyi tsentr urologii imeni B.U. Dzharbusynova* [Scientific Center of Urology named after B. U. Dzharbusynov] [Elektronnyi resurs]. URL: https://ncu.kz/ (accessed: 27.02.2025). [in Russian - in Kazakh]

14. *Naselenie zemli - schetchik naseleniya mira* [World population counter] [Elektronnyi resurs]. URL: https://countrymeters.info/ru/World (accessed: 03.03.2025). [in Russian]

15. *O brake (supruzhestve) i sem'e* [On marriage and family] - IPS «Ədilet» [Elektronnyi resurs]. URL: https://adilet.zan.kz/rus/docs/K1100000518 (accessed: 02.01.2025). [in Russian - in Kazakh]

16. *Ob utverzhdenii pravil i uslovii provedeniya vspomogatel'nykh reproduktivnykh metodov i tekhnologii* [On approval of the rules and conditions for assisted reproductive methods and technologies] - IPS «Ədilet» [Elektronnyi resurs]. URL: https://adilet.zan.kz/rus/docs/V2000021816 (accessed: 13.01.2025). [in Russian - in Kazakh]

17. *Ob utverzhdenii pravil, ob"ema i periodichnosti provedeniya profilakticheskikh meditsinskikh osmotrov tselevykh grupp naseleniya, vklyuchaya detei doshkol'nogo, shkol'nogo vozrastov, a takzhe uchashchikhsya organizatsii tekhnicheskogo i professional'nogo, poslesrednego i vysshego obrazovaniya* [On the approval of the rules, scope, and frequency of preventive medical examinations for target population groups, including preschool and school-aged children, as well as students of technical and vocational, post-secondary, and higher education institutions] - IPS «Ədilet» [Elektronnyi resurs]. URL: https://adilet.zan.kz/rus/docs/V2000021820 (accessed: 20.02.2025). [in Russian - in Kazakh]

18. *Ob utverzhdenii pravil organizatsii meditsinskoi pomoshchi po okhrane reproduktivnogo i psikhicheskogo zdorov'ya nesovershennoletnikh v vozraste ot desyati do vosemnadtsati let i molodezhi* [On the approval of the rules for organizing medical care for the protection of reproductive and mental health of minors aged ten to eighteen and youth] - IPS «Ədilet» [Elektronnyi resurs]. URL: https://adilet.zan.kz/rus/docs/V2000021846 (accessed: 11.02.2025). [in Russian - in Kazakh]

19. *Ob utverzhdenii Pravil provedeniya voenno-vrachebnoi ekspertizy i Polozheniya o komissiyakh voenno-vrachebnoi ekspertizy v Vooruzhennykh Silakh Respubliki Kazakhstan* [On the approval of the Rules for conducting military medical examinations and the Regulation on military medical examination commissions in the Armed Forces of the Republic of Kazakhstan] - IPS «Ədilet» [Elektronnyi resurs]. URL: https://adilet.zan.kz/rus/docs/V2000021869/history (accessed: 15.01.2025). [in Russian - in Kazakh]

20. *Ob utverzhdenii standarta organizatsii okazaniya urologicheskoi i andrologicheskoi pomoshchi v Respublike Kazakhstan* [On the approval of the standard for the organization of urological and andrological care in the Republic of Kazakhstan] - IPS «Ədilet» [Elektronnyi resurs]. URL: https://adilet.zan.kz/rus/docs/V2300032541 (accessed: 06.02.2025). [in Russian - in Kazakh]

21. *Ozhirenie, insulinorezistentnost' i reproduktivnoe zdorov'e muzhchiny: patogeneticheskie vzaimodeistviya i sovremennaya patogeneticheskaya farmakoterapiya* [Obesity, insulin resistance, and male reproductive health: pathogenetic interactions and modern pathogenetic pharmacotherapy] uMEDp [Elektronnyi resurs]. URL: https://umedp.ru/articles/ozhirenie_insulinorezistentnost_i_reproduktivnoe_zdorove_muzhchiny_patogeneticheskie_vzaimodeystviya.html (accessed: 25.01.2025). [in Russian]

22. *O zdorov"e naroda i sisteme zdravookhraneniya* [On Public Health and the Healthcare System] - IPS «Ədilet» [Elektronnyi resurs]. URL: https://adilet.zan.kz/rus/docs/K2000000360 (accessed: 02.02.2025. [in Russian - in Kazakh]

23. *O natsional'noi bezopasnosti Respubliki Kazakhstan* [On the National Security of the Republic of Kazakhstan] - IPS «Ədilet» [Elektronnyi resurs]. URL: https://adilet.zan.kz/rus/docs/Z1200000527 (accessed: 18.01.2025). [in Russian - in Kazakh]

24. *O proekte Ukaza Prezidenta Respubliki Kazakhstan «Ob utverzhdenii osnovnykh napravlenii gosudarstvennoi politiki Respubliki Kazakhstan v sfere ofitsial'noi pomoshchi razvitiyu na 2021 – 2025 gody»* [On the Draft Decree of the President of the Republic of Kazakhstan «On the approval of the main directions of the state policy of the Republic of Kazakhstan in the field of official development assistance for 2021–2025»] - IPS «Ədilet» [Elektronnyi resurs]. URL: https://adilet.zan.kz/rus/docs/P2100000344 (accessed: 25.11.2024). [in Russian - in Kazakh]

25. *Otsenka reproduktivnogo potentsiala muzhskogo naseleniya* [Assessment of the reproductive potential of the male population] [Elektronnyi resurs]. URL:https://cyberleninka.ru/article/n/otsenka-reproduktivnogo-potentsiala-muzhskogo-naseleniya/viewer (accessed: 11.01.2025). [in Russian]

26. *Prosmotr «Etiologicheskie faktory narusheniya reproduktivnoi funktsii u muzhchin (po dannym kliniki „Mat' i ditya“)»* [Viewing «Etiological factors of impaired reproductive function in men (based on data from the Mother and Child clinic)»] [Elektronnyi resurs]. URL: https://repromed.kz/index.php/journal/article/view/5/2 (accessed: 23.03.2025). [in Russian]

27. Rasimovich A. A. *Rol' infektsii, peredavaemykh polovym putem, v formirovanii demograficheskogo sostoyaniya Respubliki Tatarstan i puti ego uluchsheniya* [The role of sexually transmitted infections in shaping the demographic situation of the Republic of Tatarstan and ways to improve it] 2022. C. 321. [in Russian]

28. Segodnya muzhskim zdorov'em v Kazakhstane nikto ne zanimaetsya – ekspert. *Kazinform* [Currently, no one is addressing men's health in Kazakhstan – expert] [Elektronnyi resurs]. URL: https://www.inform.kz/ru/segodnya-muzhskim-zdorov-em-v-kazahstane-nikto-ne-zanimaetsya-ekspert_a3947337 (accessed: 04.12.2024). [in Russian - in Kazakh]

29. Sergeevich B.Yu. *Sotsial'no-gigienicheskie i mediko-organizatsionnye aspekty sovershenstvovaniya sanatorno-kurortnogo lecheniya patsientov s boleznyami muzhskikh polovykh organov* [Socio-hygienic and medical-organizational aspects of improving sanatorium-resort treatment of patients with diseases of the male reproductive organs] 2019. C. 124. [in Russian]

30. *Serdechno-sosudistye zabolevaniya* [Cardiovascular diseases] [Elektronnyi resurs]. URL:

https://www.who.int/ru/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds) (accessed: 11.11.2024). [in Russian]

31. *Sovremennaya demograficheskaya situatsiya i problemy uluchsheniya reproduktivnogo zdorov'ya naseleniya Rossii* [The current demographic situation and challenges in improving the reproductive health of the population in Russia] [Elektronnyi resurs]. URL: https://cyberleninka.ru/article/n/sovremennaya-demograficheskaya-situatsiya-i-problemy-uluchsheniya-reproduktivnogo-zdorovya-naseleniya-rossii/viewer (accessed: 25.01.2025). [in Russian]

32. Ugli Sh. A. B. *Kliniko-laboratornye prediktory effektivnosti varikotselektomii u muzhchin s narusheniem reproduktivnoi funktsii* [Clinical and laboratory predictors of the effectiveness of varicocelectomy in men with impaired reproductive function] 2023. C. 131. [in Russian]

33. Ugrozy i riski demograficheskoi bezopasnosti Rossiiskoi Federatsii [Threats and risks to the demographic security of the Russian Federation] [Elektronnyi resurs]. URL: https://cyberleninka.ru/article/n/ugrozy-i-riski-demograficheskoy-bezopasnosti-rossiyskoy-federatsii/viewer (accessed: 06.03.2025). [in Russian]

34. *Uroven' besplodiya v Kazakhstane vyshe, chem v evropeiskikh stranakh* [The infertility rate in Kazakhstan is higher than in European countries] // Forbes.kz [Elektronnyi resurs]. URL: https://forbes.kz/news/newsid_296601 (accessed: 19.02.2025). [in Russian - in Kazakh]

35. *Tsel' 3: Obespechenie zdorovogo obraza zhizni i sodeistvie blagopoluchiyu dlya vsekh v lyubom vozraste* [Goal 3: Ensure healthy lives and promote well-being for all at all ages] // Ustoichivoe razvitie [Elektronnyi resurs]. URL: https://www.un.org/sustainabledevelopment/ru/health/ (accessed: 24.02.2025). [in Russian]

**Information about the authors:**

***Bayan Orazayeva** – 1st-year PhD student in Public Health, NCJSC "Semey Medical University," Semey, Republic of Kazakhstan; e-mail: borazayeva01@mail.ru; Cell phone: +77079876612; ORCID: https://orcid.org/0009-0005-0374-7884;

**Nazym Iskakova** – PhD, Lecturer at the Department of Public Health, NCJSC "Semey Medical University," Semey, Republic of Kazakhstan; e-mail: nazym.iskakova@smu.edu.kz; Cell phone: +77751030454; ORCID: https://orcid.org/0000-0001-5631-5499;

**Dinara Serikova-Esengeldina** – PhD, Lecturer at the Department of Public Health, NCJSC "Semey Medical University," Semey, Republic of Kazakhstan; e-mail: dinara.esengeldina@smu.edu.kz; Cell phone: +77785886986; ORCID: https://orcid.org/0000-0002-9470-9488;

**Nailya Urazalina** – Candidate of Medical Sciences, Associate Professor of the Department of physiological disciplines named after honored scientist of the republic of Kazakhstan, professor T.A. Nazarova, NCJSC "Semey Medical University," Semey, Republic of Kazakhstan; e-mail: hakim_15@mail.ru; Cell phone: +77779075589; ORCID: https://orcid.org/0000-0003-0200-1763;

**Aliya Atabayeva** – PhD, Lecturer at the Department of Public Health, NCJSC "Semey Medical University," Semey, Republic of Kazakhstan; e-mail: aliya.atabayeva@smu.edu.kz; Cell phone: +77753900269; ORCID: https://orcid.org/0000-0001-7725-2255;

**Zaituna Khismetova** – Candidate of Medical Sciences, Professor, Head of the Department of Public Health, NCJSC "Semey Medical University," Semey, Republic of Kazakhstan; e-mail: zaituna.khismetova@smu.edu.kz; Cell phone: +77772582681; ORCID: https://orcid.org/0000-0001-5937-3045.

**Corresponding author:**

**Bayan Bolatkalykzy Orazayeva** – 1st-year PhD student in the specialty "Public Health," Non-Profit Joint-Stock Company "Semey Medical University," Semey, Republic of Kazakhstan

**Postal code:** Republic of Kazakhstan, 070000, Abai Region, Semey city, 29-1 B. Zhamakaev Street.

**E-mail:** borazayeva01@mail.ru

**Phone:** +7 707 987 66 12

Received: 22 February 2025 / Accepted: 16 June 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2025.27.3.021***

***UDC 611.018.4:578.52-053.2-053.6***

This work is licensed under a Creative Commons Attribution 4.0 International License

# INFECTIOUS COMPLICATIONS OF UROLOGICAL INTERVENTIONS FOR UROLITHIASIS. LITERATURE REVIEW

**Ruslan B. Isakhanov[1],**

**Ulanbek Zhanbyrbekuly[2],** **https://orcid.org/0000-0003-1849-6924**

**Merkhat N. Akkaliyev[3],** **https://orcid.org/0000-0003-3122-7411**

**Maral G. Nogayeva[4],** **https://orcid.org/0000-0003-1182-5967**

**Elena G. Novikova[5],** **https://orcid.org/0000-0003-4723-0666**

**[1] NCJSC «Semey Medical University», Ust-Kamenogorsk, Republic of Kazakhstan;**
**[2] NpJSC "Astana Medical University"» Astana, Republic of Kazakhstan;**
**[3] NCJSC «Semey Medical University», Semey, Republic of Kazakhstan;**
**[4] NJSC «Kazakh National Medical University named after S.D. Asfendiyarov», Almaty, Republic of Kazakhstan;**
**[5] RMDC Clinic LLC, Novosibirsk, Russian Federation.**

**Abstract**

**Introduction**. The problem of infectious complications of urological interventions for urolithiasis is very relevant today. This is primarily due to the sharply increased number of endoscopic interventions in recent years, the uncontrolled use of antibiotics, and the increasingly significant growth of so-called multidrug-resistant strains of microorganisms.

**Purpose of the study**: to determine the main infectious complications of urological interventions for urolithiasis

**Search strategy:** A literature review of publications from the past 10 years was conducted in the PubMed, CyberLeninka, and Google Scholar databases. The main keywords included: urolithiasis, infectious complications, antibiotic resistance, and postoperative complications.

**Results:** We have reviewed the literature on this topic. Currently, scientists distinguish two main ways of penetration of microorganisms into the urinary tract: endogenous and exogenous ways. With an exogenous route of infection, the sources of UTIs are patients with purulent-septic forms of urogenital and other surgical diseases, bacteria carriers among patients and medical personnel. With the endogenous route of infection, pathogenic microorganisms penetrate the urinary tract from closely located organs (often the pelvic organs): vagina, rectum. Often, infectious complications occur at the hospital stage in patients who have undergone surgical interventions or diagnostic manipulations, including for urolithiasis. The management of patients with similar nosocomial infections of the genitourinary system (NIMPS) and infections of the surgical field (IOP) is quite difficult, since their causative agents, as a rule, are gram-negative microorganisms with increased resistance to antimicrobial drugs.

**Conclusions.** According to many researchers, the frequency of infectious and inflammatory complications after endoscopic interventions for urolithiasis depends on many factors, the main of which are the presence of an initial urinary tract infection. Therefore, patients with baseline BMI, intra- and postoperative complications during endoscopic interventions for urolithiasis should be carefully analyzed, taking into account all the risks of surgical intervention. This review of the literature touches upon the main points in the infection pathway, the main pathogens and various approaches to the treatment and prevention of infectious complications of urological interventions for urolithiasis.

***Keywords:*** *urolithiasis, infectious complications, antibiotic resistance, postoperative complications*

***For citation:***

Isakhanov R.B., Zhanbyrbekuly Ulanbek, Akkaliev M.N., Nogayeva M.G., Novikova E.G. Infectious complications of urological interventions for urolithiasis. Literature review // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 189-199. *doi 10.34689/SH.2025.27.3.021*

**Резюме**

# ИНФЕКЦИОННЫЕ ОСЛОЖНЕНИЯ УРОЛОГИЧЕСКИХ ВМЕШАТЕЛЬСТВ ПО ПОВОДУ МОЧЕКАМЕННОЙ БОЛЕЗНИ. ОБЗОР ЛИТЕРАТУРЫ.

**Руслан Б. Исаханов[1],**

**Уланбек Жаңбырбекұлы[2],** **https://orcid.org/0000-0003-1849-6924**

**Мерхат Н. Аккалиев[3],** **https://orcid.org/0000-0003-3122-7411**

**Марал Г. Ногаева[4],** **https://orcid.org/0000-0003-1182-5967**

**Елена Г. Новикова[5],** **https://orcid.org/0000-0003-4723-0666**

**[1] НАО «Медицинский университет Семей», г. Усть-Каменогорск, Республика Казахстан;**
**[2] НАО «Медицинский университет Астана», г. Астана, Республика Казахстан;**

**[3] НАО «Медицинский университет Семей», Семей, Республика Казахстан;**
**[4] НАО «Казахский национальный медицинский университет им. С.Д. Асфендиярова», г. Алматы, Республика Казахстан;**
**[5] «Клиника РМДЦ», Новосибирск, Российская Федерация.**

**Введение.** Проблема инфекционных осложнений урологических вмешательств по поводу мочекаменной болезни на сегодняшний день очень актуальна. Связано это в первую очередь, с резко возросшим за последние годы, количеством эндоскопических вмешательств, бесконтрольным приемом антибиотиков, все более значительным ростом, так называемых, полирезистентных штаммов микроорганизмов. Все это делает борьбу с послеоперационной инфекцией сложнее из года в год.

**Цель исследования:** определить основные инфекционные осложнения урологических вмешательств по поводу мочекаменной болезни

**Стратегия поиска:** Был проведен обзор литературы за последние 10 лет в базах данных PubMed, CyberLeninka и Google Scholar. Ключевые запросы: мочекаменная болезнь, инфекционные осложнения, антибиотикорезистентность, послеоперационные осложнения.

**Результаты.** В настоящее время, учеными выделяются два основных пути проникновения микроорганизмов в мочевыделительный тракт: эндогенный и экзогенный пути. При экзогенном пути инфицирования источниками ИМВП являются больные с гнойно-септическими формами урогенитальных и других хирургических заболеваний, бактерионосители среди пациентов и медицинского персонала. При эндогенном пути занесения инфекции патогенные микроорганизмы проникают в мочевыводящие пути из близко расположенных органов (зачастую органы малого таза): влагалища, прямой кишки. В свою очередь, уролитиаз почти всегда протекает в связке с инфекциями мочеполовой системы (ИМПС) или, которые могут быть как причиной, так и следствием мочекаменной болезни. Часто, инфекционные осложнения возникают на госпитальном этапе у пациентов, перенесших хирургические вмешательства или диагностические манипуляции, в том числе и по поводу уролитиаза. Ведение пациентов с подобными нозокомиальными инфекциями мочеполовой системы (НИМПС) и инфекциями операционного поля (ИОП) достаточно сложно, так как их возбудителями, как правило, являются грамотрицательные микроорганизмы с повышенной резистентностью к антимикробным препарата.

**Выводы.** По мнению многих исследователей, частота инфекционно-воспалительных осложнений после эндоскопических вмешательств по поводу уролитиаза зависит от множества факторов, основными из которых являются наличие исходной инфекции мочевых путей. Поэтому больных с наличием исходной ИМТ, интра- и послеоперационными осложнениями при выполнении эндоскопических вмешательств по поводу уролитиаза следует тщательно анализировать, учитывая все риски оперативного вмешательства. В данном обзоре литературы затронуты основные моменты в пути инфицирования, основные возбудители и различные подходы к лечению и профилактике инфекционных осложнений урологических вмешательств по поводу мочекаменной болезни

***Ключевые слова**: мочекаменная болезнь, инфекционные осложнения, антибиотикорезистентность, послеоперационные осложнения*

***Для цитирования:***

*Исаханов Р.Б., Жаңбырбекұлы Уланбек., Аккалиев М.Н., Ногаева М.Г., Новикова Е.Г.* Инфекционные осложнения урологических вмешательств по поводу мочекаменной болезни. Обзор литературы // Наука и Здравоохранение. 2025. Vol.27 (3), С.189-199. *doi 10.34689/SH.2024.27.3.021*

**Түйіндеме**

# ЗӘР ТАС АУРУЫ КЕЗІНДЕГІ УРОЛОГИЯЛЫҚ АРАЛАСУДЫҢ ИНФЕКЦИЯЛЫҚ АСҚЫНУЛАРЫ. ӘДЕБИЕТТІК ШОЛУ.

**Руслан Б. Исаханов[1],**
**Уланбек Жаңбырбекұлы[2], https://orcid.org/0000-0003-1849-6924**
**Мерхат Н. Аккалиев[3], https://orcid.org/0000-0003-3122-7411**
**Марал Г. Ногаева[4], https://orcid.org/0000-0003-1182-5967**
**Елена Г. Новикова[5], https://orcid.org/0000-0003-4723-0666**

**[1] «Семей медицина университеті» КеАҚ, Өскемен қ., Қазақстан Республикасы;**
**[2] «Астана медицина университеті» КеАҚ, Астана қ., Қазақстан Республикасы;**
**[3] «Семей медицина университеті» КеАҚ, Семей қ., Қазақстан Республикасы;**
**[4] «С. Ж. Асфендияров атындағы Қазақ ұлттық медицина университеті» ҚеАҚ, Алматы қ., Қазақстан Республикасы;**
**[5] ООО «Клиника РМДЦ», Новосибирск, Ресей Федерациясы.**

**Кіріспе.** Урологиялық араласудың инфекциялық асқынулары мәселесі бүгінгі күні өте өзекті. Бұл, ең алдымен, соңғы жылдары эндоскопиялық араласулар санының күрт артуы, антибиотиктерді бақылаусыз қолдану және микроорганизмдердің көп дәріге төзімді штаммдарының айтарлықтай өсуіне байланысты.

**Зерттеу мақсаты**: урологиялық араласудың негізгі инфекциялық асқынуларын анықтау.

**Іздеу стратегиясы:** Соңғы 10 жылдағы жарияланымдарға PubMed, CyberLeninka және Google Scholar дерекқорларын іздеу жүргізілді. Негізгі іздеу сұраулары: уролитияз, инфекциялық асқынулар, антибиотикке төзімділік және операциядан кейінгі асқынулар.

**Әдістері:** Біз осы тақырып бойынша әдебиеттерді қарастырдық. Қазіргі уақытта ғалымдар микроорганизмдердің зәр шығару жолына енуінің екі негізгі жолын ажыратады: эндогендік және экзогендік жолдар.

**Нәтижелері:** Инфекцияның экзогендік жолы кезінде ЖЖИ көздері несеп-жыныс және басқа хирургиялық аурулардың іріңді-септикалық түрлерімен ауыратын науқастар, науқастар мен медицина қызметкерлері арасында бактерия тасымалдаушылар болып табылады. Инфекцияның эндогендік жолы арқылы патогендік микроорганизмдер зәр шығару жолына жақын орналасқан мүшелерден (көбінесе жамбас мүшелерінен) енеді: қынаптан, тік ішектен. Көбінесе инфекциялық асқынулар хирургиялық араласулардан немесе диагностикалық манипуляциялардан өткен науқастарда, соның ішінде уролитияда аурухана сатысында пайда болады. Несеп-жыныс жүйесінің (NIMPS) ұқсас ауруханаішілік инфекциялары және хирургиялық өріс инфекциялары (IOP) бар науқастарды емдеу өте қиын, өйткені олардың қоздырғыштары, әдетте, микробқа қарсы препараттарға төзімділігі жоғары грам-теріс микроорганизмдер болып табылады.

**Қорытындылар.** Көптеген зерттеушілердің пікірінше, уролитияға арналған эндоскопиялық араласудан кейін инфекциялық және қабыну асқынуларының жиілігі көптеген факторларға байланысты, олардың негізгілері зәр шығару жолдарының бастапқы инфекциясының болуы. Сондықтан бастапқы BMI бар емделушілерге, уролитияға арналған эндоскопиялық араласулар кезінде операция ішілік және операциядан кейінгі асқынуларға хирургиялық араласудың барлық тәуекелдерін ескере отырsп, мұқият талдау қажет. Әдебиеттердің бұл шолуы инфекция жолындағы негізгі сәттерді, негізгі патогендерді және уролитияға арналған урологиялық араласудың инфекциялық асқынуларын емдеу мен алдын алудың әртүрлі тәсілдерін қозғайды.

***Түйінді сөздер:*** *уролития, инфекциялық асқынулар, антибиотиктерге төзімділік, операциядан кейінгі асқынулар*

***Дәйексөз үшін:***

*Исаханов Р.Б., Жаңбырбекұлы Уланбек., Аккалиев М.Н., Ногаева М.Г., Новикова Е.Г.* Зәр тас ауруы кезіндегі урологиялық араласудың инфекциялық асқынулары. Әдебиеттік шолу // Ғылым және Денсаулық сақтау. 2025. Vol.27 (3), Б. 189-199. *doi 10.34689/SH.2025.27.3.021*

**Introduction.**

The problem of infectious complications of urological interventions for urolithiasis is very relevant today. This is primarily due to the sharply increased number of endoscopic interventions in recent years, the uncontrolled use of antibiotics, the increasing growth of so-called multidrug-resistant strains of microorganisms. All this makes the fight against postoperative infection more difficult year after year.

**Objective of the study: to** determine the main infectious complications of urological interventions for urolithiasis

**Search strategy:** A literature review of the last 10 years was conducted in PubMed, CyberLeninka and Google Scholar databases. The main keywords were urolithiasis, infectious complications, antibiotic resistance and postoperative complications.

**Source Selection Algorithm.**

The source selection algorithm included:

1) literature search in PubMed, CyberLeninka, Google Scholar databases using the keywords "urolithiasis", "infectious complications", "antibiotic resistance", "postoperative complications";

2) selection of publications for the last 10 years

3) application of inclusion (description of endoscopic methods of urolithiasis treatment) and exclusion criteria (exclusion of articles with data on patients with nephrostomies, cystostomies, stent catheters);

4) final analysis and selection of relevant publications for review.

**Methods**

The aim of this literature review is to comprehensively analyse existing data on infectious complications in patients with urolithiasis undergoing endoscopic surgery. The review considers risk factors, prevalence of complications, the impact of antibiotic resistance and approaches to antibiotic prophylaxis. The scientific rationale for this review is based on the need to objectively summarise current data and identify the most significant factors affecting the outcomes of endoscopic surgery in patients with urolithiasis.

Given the specificity of the topic and the limited number of publications, authoritative and frequently used databases in medical research were selected for the search: PubMed, CyberLeninka and Google Scholar. These sources provide access to both international and domestic publications, allowing a comprehensive assessment of the problem and consideration of results from different countries and clinical settings. The depth of the search was 10 years, allowing us to focus on current approaches to the prevention and treatment of complications. However, due to the relatively small volume of publications on this topic, the review also includes earlier works, starting from 1982, which contain fundamental information related to treatment methods and concepts of antibacterial prophylaxis in urological diseases.

The review was based on strict inclusion and exclusion criteria designed to maximise the relevance of the data. The inclusion criteria included the selection of publications that included data on patients with urolithiasis who underwent endoscopic surgery such as ureteroscopy with contact laser lithotripsy, percutaneous nephrolithotripsy and retrograde intrarenal surgery. Only studies concerning infectious complications, their prevention and the role of antibiotic

resistance in these processes were included. Publications describing patients with genitourinary fistulas (e.g. nephrostomies or cystostomies) and stent catheters were excluded because their cases require specific approaches to prevention and treatment that are not the subject of this review.

To perform a structured search, key queries were developed: "urolithiasis", "infectious complications", "antibiotic resistance", "postoperative complications", as well as terms related to specific endoscopic techniques such as "ureteroscopy", "percutaneous nephrolithotripsy", "retrograde intrarenal surgery". The use of these search words allowed us to focus on publications relevant to the clinical aspects of the management and prevention of complications of endoscopic surgery.

After the initial search, 68 publications were found and further screened. The included publications were analysed according to the criteria of methodological quality, scientific significance and reliability of the data presented. Based on the analysis of publications, the information was systematised to identify the main categories for summarisation: types of infectious complications, identified risk factors, antibiotic prophylaxis regimens and their efficacy, and the impact of antibiotic resistance on treatment outcomes.

The methodology of this review is based on the concept of a systematic and structured approach that brings together disparate data and identifies significant clinical patterns. This approach not only provides a holistic picture of the state of the problem, but also contributes to the development of recommendations to improve the practice of endoscopic interventions and prevention of infectious complications in patients with urolithiasis.

**Results**

In situations of exogenous contamination, sources of urinary tract infections include individuals suffering from purulent and septic urogenital infections, as well as bacterial carriers among patients and health care workers. The transfer of pathogens in such conditions is accomplished through medical instruments, dressing materials, and direct contact with the hands of health care personnel. If the endogenous route of infection is activated, pathogens enter the urogenital tract from nearby organs such as the vagina and rectum.

Many variables affect the risk of developing urinary tract infections.

Internal factors that increase the risk of infection include anatomical abnormalities in patients, such as stenoses and fistulas, which increase the possibility of infections from the external environment. Other factors include the presence of foreign objects and stones in the body, low blood pressure, bladder and ureter hypotonia, neurogenic bladder, diabetes, immune deficiency states, post-kidney transplantation, postpartum period, complications of female childbirth, HIV infection, spinal cord injury and central nervous system damage.

In contrast to internal factors, external factors are often associated with medical procedures, including instrumental diagnostics and surgical procedures such as transurethral resection of the prostate gland, prostate biopsy, as well as the use of catheters and urinary drainage systems and other therapeutic manipulations. In addition, the use of intracavernous injections for the treatment of erectile dysfunction is also mentioned among external factors. [6].

In turn, the prevalence of urolithiasis (urolithiasis) ranges from 1% to 20% worldwide, depending on geographical, climatic, ethnic and genetic factors, and recur within the first five years in 26% of individuals with first-time stones [7,8,10].

According to *Romero V., Akpinar H., Assimos D.G.* (2010) the prevalence of urolithiasis is relatively high (>10%) and has increased by more than 37% between 1983 and 2010 in countries with a higher standard of living where a large proportion of the society follows a high-protein diet [9,11-13].

Studies of scientists *Romero V., et al.* (2010), and *Lopez M., et al.* (2010) concluded that not the least role in the pathogenesis of urolithiasis is played by changes in metabolic processes due to diseases or disorders such as obesity, diabetes, metabolic syndrome, etc. [9,10].

The expected financial cost of treating patients with urolithiasis in Germany in 2000 exceeds €500 million per year [14]; in the United States, this approximate cost in 2007 (adjusted for inflation to 2014) was $3.79 billion, then it is expected to exceed $4.5 billion per year by 2030 [15].

Urinary tract stones, if left untreated, can cause life-threatening consequences such as obstructive uremia, hypertension, acute and recurrent urinary tract infections, pyelonephritis followed by septicaemia and septicaemia, renal failure, acute and chronic renal failure (ARF and CKD) and so on [16,17].

Urolithiasis almost always occurs in conjunction with genitourinary infections (UTIs) or, which can be both a cause and a consequence of urolithiasis. Often, infectious complications occur at the hospital stage in patients who have undergone surgical interventions or diagnostic manipulations, including for urolithiasis. Management of patients with such nosocomial genitourinary infections (NIMPS) and surgical site infections (SSI) is quite difficult, as their causative agents are usually Gram-negative microorganisms with increased resistance to antimicrobials [18,19,20]. Consequently, identifying risks and developing techniques to predict severe non-infectious complications after surgery and postoperative infections may play a key role in reducing the risks and possibly preventing the occurrence of postoperative infectious complications in patients who undergo invasive procedures due to urolithiasis.

According to the research conducted by *A.Ch. Usupbaev, B.A. Kabaev and their colleagues* (2018) [24], the wide spread of infectious complications after surgical interventions in the practice of urology puts the issue of their prevention in the forefront. Such complications are especially common in patients who underwent surgery for urolithiasis, which is explained by the interaction of intrinsic and extrinsic risk factors.

The study analysed 116 episodes of postoperative complications. It was recorded that 42 of these patients, equivalent to 36.2% of the total, developed infections after surgical intervention in the aria (OH). The division of infections according to the depth of the lesion showed that 31 patients had superficial infections, 8 had deep infections, and three had infections localised in the area of the operated organ or cavity. In the remaining surgical cohort,

17 patients (14.7%) developed pyelonephritis, while 24 (20.7%) developed urethritis after surgery. The researchers identified different nosological forms of infectious complications in patients undergoing different types of urolithiasis treatment.

A number of common infectious sequelae following surgical interventions performed as part of urolithiasis therapy can be identified:

-Infections in the surgical area - 36.2% of cases,

-Acute inflammation of the urethra - 20.7%,

-Acute variant of pyelonephritis - 14.7%,

-Inflammation of perirenal fibre - 9.5%,

-Acute orchitis combined with appendiceal inflammation - 7.8%,

-Acute inflammation of the bladder - 6%,

-Purulent inflammation of the kidneys - 3.4%,

-Infectious lesion with penetration into blood - 1.7%.

The following microorganisms are the most common pathogens associated with health care services:

1.Escherichia coli - in 43% of cases,

2.Proteus - in 9.5% of cases,

3.Staphylococcus spp. including Staphylococcus aureus - in 8.3% of cases,

4.Various microorganisms - in 11.9% of cases.

A study of the pattern of resistance to beta-lactam antibiotics among members of the Enterobacteriaceae family revealed that Escherichia accounted for 63.2% of the total, Proteus 21%, and Klebsiella 15.8%.

The researchers' presentations emphasise the importance of scientific work aimed at analysing the distribution of treatment-resistant forms of microorganisms, applying more accurate and sensitive tests and monitoring these processes. Such measures contribute to improving the results of therapeutic interventions, reducing the likelihood of the spread of drug-resistant strains and reducing the incidence of healthcare-associated infections. [24].

A study of surgical outcomes performed by *F.A. Akilov and Sh.I. Giyasov (2017)* [25] revealed multiple factors that contributed to the development of postoperative pyelonephritis in 115 patients. These include the presence of primary urinary tract infection before surgery, despite preoperative preparation, as well as various problems that occurred during and after surgery.

Researchers emphasise that the chance of infection and inflammatory reactions from endoscopic urolithiasis surgery is related to both the presence of an initial urinary tract infection and the number of complications that occur during and after surgery. Those patients who already have a urinary tract infection and experience additional difficulties during and after endoscopic interventions for stone management should be considered at increased risk for postoperative infectious and inflammatory complications. Studies show that complicated pyelonephritis is a consequence of endoscopic removal of upper urinary tract stones in about 11.2% of cases.

In the majority of patients, 82.6%, complicated pyelonephritis was successfully managed with conservative treatment, while 17.4% of patients required additional invasive procedures and intensive care. This resulted in a 60% longer hospitalisation compared with the average [25].

*Ф. Sadulloev* studied the incidence of hospital-acquired infections, taking into account the severity of the primary disease, the extent and number of surgical and other urological manipulations, including invasive and endoscopic ones, as well as their regularity and duration. In addition, it analysed how individual clinical manifestations affect the overall dynamics of urinary tract infections and took into account patients' gender and age as factors within the study [26]. In a microbiological study of urine, drainage contents and wound secretions, the research team analysed the bacterial spectrum to determine the mechanisms of infection. A total of 268 chicken, wound and drainage fluid samples from 122 patients affected by hospital-acquired infections were studied, leading to the identification of more than 300 diverse microbial cultures. The diversity of causative agents of urinary tract infections was extensive, with ten predominant bacterial types identified. Among patients with infections, microorganisms from the following genera were most frequently detected:

-Escherichia - 24%,

-Proteus - 10.7 per cent,

-Ps.aeruginosa - 17.6%,

-Klebsiella - 5.8 per cent,

- totalling 58.1% of the total number of strains isolated.

-Bacteria of the Micrococcaceae family including the genera Staphylococcus, Streptococcus and Enterococcus occupied 30.9%.

-Fungi of the genus Candida, predominantly Candida albicans, were found in 3.7% of cases,

-associations of different microorganisms amounted to 3.3%,

-and other microbes accounted for up to 4%.

Infections that occurred in the hospital setting during diagnosis or treatment of patients were identified by microbiological analysis of drainage fluids, purulent secretions and urine, which revealed many bacterial strains that were not present at the time of admission. The author suggests that the underlying cause of nosocomial infection in patients suffering from urolithiasis and treated by various methods is most often Gram-negative bacteria. Among Gram-positive microorganisms, E.coli (24%) and Ps.aeruginosa (17.6%) and staphylococci (19.3%) were the most common. In most cases, Gram-negative bacteria cause inflammatory processes in the kidneys and upper urinary tract, whereas Gram-positive microorganisms are more commonly associated with lower urinary tract inflammation (26).

*M Charton, G Vallancien, B Veillon, J M Brisset* studied the bacteriological results of 126 cases of percutaneous renal stone extraction. 107 patients had sterile urine preoperatively and intentionally did not receive antibiotics prophylactically so that the mechanisms of urinary tract infection after percutaneous nephrolithotomy could be studied [27]. Of these patients, 37 (35%) had postoperative urinary tract infection, usually caused by Escherichia coli, Streptococcus or Staphylococcus aureus. The pathogen was isolated in bladder urine only in 22 cases, in the nephrostomy tube in 2 and in both localisations in 13. Eleven patients (10%) had a fever of 38.5°C or higher. All infected patients received appropriate antibiotic therapy and there were only 2 positive cultures at long-term follow-up (5%). The risk of clinical infection after percutaneous

nephrolithotomy is low, even though 35% of patients develop bacteriuria in the postoperative period, provided that a thorough preoperative bacteriological examination is performed and patients with urinary tract infection are adequately treated. These results are in favour of short-term prophylactic antibiotic therapy adapted to the bacterial ecology [27].

In modern urological practice retrograde intrarenal surgery occupies an increasing share in the treatment of kidney stones.

A research team led by *Dong Soo Kim, Koo Han Yoo, Seung Hyun Jeon, and Sang Hyub Lee* evaluated the risk factors for febrile urinary tract infections (UTIs) resulting from retrograde intrarenal surgery (RIRS) to remove kidney stones [28]. The study was based on a retrospective review of medical files of patients with renal concretions ranging in size from 10 to 30 millimetres who underwent RIRS between January 2014 and July 2017. Parameters such as age, gender, patient's body mass index, stone size and location, and duration of surgery were taken into account in the evaluation. It is noted that all surgical interventions were performed by a single surgeon and no preoperative ureteral stenting was performed. A total of 150 patients were included in the study, out of which 17 (11.3%) patients had febrile UTI after RIRC. The mean age of the patients was 56.64 ± 13.91 years, both sexes were evenly distributed. The mean stone size was 14.16 ± 5.89 mm.The mean operative time was 74.50 ± 42.56 minutes.

*Dong Soo Kim, Koo Han Yoo, Seung Hyun Jeon, Sang Hyub Lee* [28] stated that age, sex, body mass index, comorbidities, preoperative bacteriuria, hydronephrosis, kidney stone characteristics, and time of surgery were not associated with febrile UTI after retrograde intrarenal surgery. Preoperative pyuria was the only risk factor for infectious complications after retrograde intrarenal surgery.

Thus, the authors recommend careful management after RIFC, especially when preoperative urinalysis shows pyuria [28].

Hospital-acquired infection, which includes so-called catheter-associated infection, also deserves special attention. *Tsewaeng Badamsuren* points out that the main foci of hospital infections in urology are associated with activities in the dressing (54.1%) and cystoscopy (34.2%) departments [29]. The main mechanism of transmission of infections to the urinary system is still associated with catheter use, where the risk of developing infection increases depending on: Type of drainage system used and In situations where open catheterisation is used, infectious manifestations are reported in all patients by day five. In situations where a closed catheterisation system is used, infection is recorded in half of the patients on day ten and reaches one hundred percent prevalence within a month:

-In situations where open catheterisation is used, infectious manifestations are recorded in all patients by day five. In situations where a closed catheterisation system is used, infection is reported in half of the patients on day ten and reaches one hundred percent prevalence within a month.

Badamsuren also highlights factors that may contribute to the accelerated spread of catheter-associated infections:

-Catheter insertion outside of the operating theatre setting;

Catheterisation performed late in the patient's hospital stay;

-Position of the drainage catheter above the level of the bladder;

-The need to open urological drains to empty them (contamination of systems);

-Inappropriate manipulation of the drainage system;

-Practice of regular replacement of urinary catheters without strict indications.

*F.F. Ercole, T.G. Macieira, L.C. Wenceslau* emphasise that the use of intermittent catheterisation is associated with a reduction in complications and infectious processes compared with continuous catheter use [30]. Catheter removal within the first 24 hours after surgery, as well as the use of antimicrobial-treated or hydrophilic-coated catheters, helps to reduce the risk of urinary tract infection [30].

In exceptional cases, when the catheter is colonised by multiple resistant microorganisms, it may cause urosepsis due to urinary catheter infection. An American research group that studied the incidence of nosocomial infections in patients at 15 US hospitals (based on data from the Duke Infection Control Outreach Network) between 1 January 2010 and 30 June 2012 found that incidents of catheter-associated infections were the second most common after surgical infections, at 26% [31].

A study by *S.S. Bansal, P.W. Power and A.S. Sawant* shows that the risk of inflammation with subsequent urosepsis exists even in minimally invasive surgical procedures such as percutaneous nephrolithotripsy. The presence of large stones larger than 25 mm, intraoperative haemorrhages requiring blood transfusion, and surgical duration exceeding 120 minutes have been identified as factors that increase this risk. [32].

Several authors suggest that urologists should be very specific when choosing antibiotic treatment. Based on a study by *Ahmed A. Shokeir, Abdulla A. Al Ansa*ri [33], they argue that antibiotics should be administered to patients with a stented ureter as if there were clinical signs of infection and to patients with a high probability of infection. In endourological strategies, antibiotic prophylaxis is indicated in cases of contaminated stones, preoperative UTI or long-term strategies [33].

The authors *Chuan Peng, Zhaozhao Chen, Jun Xu* studied risk factors for MPS infection in patients undergoing retrograde lithotripsy of upper urinary tract stone [34]. The researchers found that Escherichia coli (62.90%) was the most common bacterium in patients with urinary tract infection. Female gender, age >50 years, diabetes mellitus, stone diameter ≥2 cm, duration of ureteral catheter placement ≥3 days, and duration of surgery ≥90 minutes were independent risk factors for postoperative urinary tract infection in patients with upper urinary tract retrograde lithotripsy. In patients undergoing retrograde lithotripsy of the upper urinary tract, countermeasures targeting these risk factors are needed to prevent and reduce postoperative urinary infection in the clinical setting [34].

*Adam Cole, Jaya Telang, Tae-Kyung Kim [35]* analysed 1817 cases of ureteroscopy from 11 hospitals. In hospitalised patients, the causative organisms were Gram-negative (61.5%), Gram-positive (19.2%), yeast (15.4%) and mixed (3.8%) microorganisms. Key elements

influencing hospitalisation due to infectious diseases included an elevated Charlson comorbidity index, previous recurrence of genitourinary tract infections, stone size, complications during surgery, and procedures in which stone fragments were not retrieved.

The authors state that one in 40 patients is re-hospitalised with an infectious complication after ureteroscopy.

In order to reduce the incidence of postoperative complications, the authors recommend urinalysis and bacteriological examination of urine in the postoperative period [35].

*Futoshi Morokuma, Eiji Sadashima, Soutaro Chikamatsu, and Tomoya Nakamura* [36] evaluated the risk of febrile urinary tract infections after ureterorenoscopic lithotripsy in patients with upper urinary tract stones. In a retrospective analysis, they examined the clinical data of 109 patients who underwent this procedure. The parameters analysed were age, sex, body mass index (BMI), mobility, presence of diabetes, duration of surgery, use of ureteral stent preoperatively, number and size of stones, their characteristics on CT scan, localisation, as well as the presence of urinary tract infection and pyelonephritis preoperatively and urine bacteriological test results. Comparisons were made between groups with different postoperative outcomes.

Postoperative infection developed in three out of 109 patients (2.8%). When comparing the two groups, low BMI was a significant risk factor.

One of the three episodes of febrile UTI was accompanied by anorexia nervosa and BMI was 11 kg/m2. As a result, the authors conclude that low BMI is a significant risk factor for urinary tract infection after ureterorenoscopy [36].

Recently, an increasing number of studies on the use of disposable ureteroscopes have appeared. *Rei Unno, Gregory Hosier, Fadl Hamouche, David B Bayne* state that urinary tract infection is a frequent complication after ureteroscopy [37]. Disposable ureteroscopes have been shown to contain bacteria despite sterilisation. It is unknown whether this characteristic was associated with a higher incidence of UTIs. The authors conducted a study comparing the incidence of postoperative UTIs after ureteroscopy for urolithiasis performed with disposable ureteroscopes versus reusable ureteroscopes. The primary outcome was postoperative urinary tract infection.

Secondary endpoints were intraoperative and postoperative outcomes, as well as the use of additional medical services postoperatively. Of the 991 patients identified, 500 (50.4%) underwent ureteroscopy using a disposable ureteroscope. The incidence of postoperative UTIs was lower in those who underwent ureteroscopic stone removal with a disposable ureteroscope compared to a reusable ureteroscope. Use of a disposable ureteroscope was associated with lower risks of postoperative UTI compared with a reusable ureteroscope. Use of a disposable ureteroscope was associated with a higher rate of stone removal compared with a reusable ureteroscope. There were no differences in operative time, overall complication rates, re-hospitalisation or emergency department visits between the two groups. Thus, the authors concluded that the use of disposable ureteroscopes resulted in a twofold reduction in the risk of UTI and an increased stone removal rate after ureteroscopy for urolithiasis compared with reusable ureteroscopes [37].

In this case report, the authors *Luca Sindolo, Francesco Berardinelli and Pietro Castellan* [38] mention a very important and unusual consequence of retrograde intrarenal surgery. The authors describe a 44-year-old woman with a single left kidney who had a history of extensive multiple sclerosis, epilepsy, bed rest and percutaneous endoscopic gastrostomy. The patient was hospitalised due to recurrent lower urinary tract infections. A follow-up computed tomography (CT) scan revealed an obstructive renal pelvic stone measuring 1.7 cm and multiple bladder stones. After cancellation of percutaneous access, RIFC was planned and performed. No intraoperative problems were found. During the postoperative period, she developed urinary tract septicaemia, which worsened her general health. The patient died of septic shock six days after RIRC despite a positive blood culture for Candida glabrata. As a result, the authors recommend that future research should be conducted in a certain direction and that the patient should be carefully preoperatively prepared [38].

In their study, *James P. Blackmoore, Neil W. Maitra, and Rajendar R. Marri* [39] sought to identify the factors most likely to increase the incidence of postoperative urosepsis within 28 days after ureteroscopy and laser fragmentation of a ureteral or kidney stone. The authors prospectively collected data from a single national health centre.

A total of 462 patients were included in the study. Thirty-four patients (7.4%) developed an episode of urosepsis within 28 days after surgery. A positive preoperative midstream urine culture was significantly associated with postoperative urosepsis in multivariate analysis despite appropriate treatment with a preoperative course of antibiotics. Presence of diabetes mellitus, presence of ischaemic heart disease, American Society of Anaesthesiologists' patient status score, bilateral URS during one session and stone volume were other variables significantly associated with postoperative infection in single factor analysis, but they ceased to be significantly associated in multivariate analysis. analysis. analysis. Subgroup analysis showed that a positive midstream urine culture in both patients with and without a preoperative ureteral stent was significantly associated with postoperative urosepsis. In matched pairs analysis, patients with a positive preoperative bacteriological culture were significantly more likely to have postoperative urosepsis compared to the control group

Based on their results, the authors concluded that a positive preoperative bacteriological culture was significantly associated with postoperative urosepsis. Patients at higher risk should be appropriately counselled preoperatively and should be the focus of vigilant postoperative follow-up. The study suggests special caution in patients with a positive preoperative urine culture [39].

According to *Marcelino Rivera , Boyd Viers , Patrick Cockerill*,[40] who analysed the case histories of 227 patients, the presence of a coral stone increases the risk of postoperative infection by more than 3 times.

*Jun Sheng, Fa Sin, Fang-Ming Chen and Zhi-Ping Wu* [40] aimed to identify risk factors that contribute to the

development of urosepsis after endoscopic ureterolithotripsy in patients without preoperative infection. Their aim was to create a more efficient and safer approach to the prevention and treatment of such complications. The authors analysed the histories of 5 patients with ureteral calculi who underwent endoscopic lithotripsy of ureteral stones with Holmium laser and developed urosepsis in the postoperative period, confirmed by clinical and laboratory findings, while they had no preoperative blood or urine infection. All 5 patients were eventually cured. The authors state that stones and surgery alone are potential factors causing urosepsis after endoscopic ureteral lithotripsy, even in the absence of infection preoperatively. Careful preoperative preparation, corrective manipulation, low-pressure irrigation, drainage and time control during surgery, as well as early diagnosis and appropriate postoperative management, are key to cure and prevention of urosepsis, especially for patients who have not had infection before surgery [41].

**Discussion of results**

Urolithiasis (urolithiasis) continues to be an important medical problem with a high prevalence, especially in countries with a high standard of living where high-protein diets are common. The increased incidence is associated with metabolic disorders such as obesity and diabetes, requiring a comprehensive treatment approach including nutritional intervention and management of comorbidities. The economically rising costs of treating urolithiasis, which are projected to be up to $4.5 billion in the US by 2030, highlight the need to optimise diagnostic and treatment methods.

One of the most serious complications of urolithiasis remains infections, especially after surgery. This requires the development of effective preventive strategies, including the fight against antibiotic resistance. Despite advanced therapies, urinary tract infections, especially pyelonephritis, remain frequent complications after surgical interventions such as ureterorenoscopy or endoscopic lithotripsy. For example, studies have shown that the risk of infections after endoscopic upper urinary tract stone removal surgery can be as high as 11.2% for complicated pyelonephritis. These data emphasise the need for early detection and effective treatment of urinary tract infections prior to surgery.

Special attention is paid to preoperative preparation. The presence of a primary urinary tract infection, even despite the preparation, may contribute to complications. The risk of infectious complications also depends on the complexity of the operation and the patient's condition. Patients with primary urinary tract infections or those who encounter difficulties during the intervention have an increased risk of developing infections.

In addition, it is important to note the impact of catheterisation on the incidence of infectious complications. The use of catheters, especially in prolonged catheterisation, significantly increases the risk of infection, which requires adherence to strict protocols for catheter insertion and use, as well as antibiotic prophylaxis. Open catheterisation increases the risk of infection in the first days after surgery, whereas a closed system causes infectious manifestations later, but with a longer period of spread.

To minimise infectious complications associated with urinary tract surgery, appropriate choice of equipment (e.g. disposable ureteroscopes, which reduce infection rates compared with reusable ones), careful preoperative diagnosis, antibiotic prophylaxis and strict postoperative monitoring are important measures. Urinary tract stones, especially coral stones, significantly increase the likelihood of urosepsis, even in the absence of infection preoperatively, which also emphasises the importance of a comprehensive approach to treatment and infection prevention.

Thus, successful treatment of urolithiasis requires a comprehensive approach that includes dietary recommendations, correction of metabolic disorders, improved medical care, and effective prevention and treatment of infectious complications.

**Conclusions**

Urolithiasis remains an important medical problem characterised by high morbidity, especially in countries with a high standard of living where high-protein diets are common. In recent decades, there has been an increase in the incidence of urolithiasis, which is associated with metabolic disorders such as obesity and diabetes. These changes require a comprehensive approach to treatment, including nutritional correction, treatment of comorbidities and the use of modern diagnostic and therapeutic methods.

Special attention should be paid to infectious complications, which are a serious problem in the surgical treatment of urolithiasis. Urinary tract infections such as pyelonephritis and urosepsis remain frequent complications after urinary tract surgery. This emphasises the need to develop effective preventive strategies such as antibiotic prophylaxis and antibiotic resistance, as well as close monitoring of patients in the postoperative period. Preoperative preparation is an important step in preventing infections, as the presence of urinary tract infection before surgery significantly increases the risk of postoperative complications. A positive preoperative bacteriological urine culture is also a risk factor for the development of infections, which requires preoperative treatment and monitoring.

In addition, the choice of medical equipment has a significant impact on the incidence of infectious complications. For example, the use of disposable ureteroscopes is associated with a lower incidence of infection compared with reusable ones, which confirms the importance of choosing quality equipment. However, even in the absence of preoperative infection, the presence of stones, especially coral stones, increases the likelihood of urosepsis, which requires special attention during preparation and surgical intervention.

An equally important problem is catheter-associated infections, which significantly increase the risk of infections in the postoperative period, especially with prolonged catheter use. In such cases, the use of antibiotic prophylaxis, preference for intermittent catheterisation and the use of antimicrobial catheters can significantly reduce the incidence of infectious complications.

Thus, successful treatment of urolithiasis and prevention of infectious complications require a comprehensive approach, including the correct choice of equipment, preoperative diagnosis, antibiotic prophylaxis and careful monitoring of the postoperative condition of patients. It is important to consider the individual risks of

each patient to minimise the likelihood of complications and improve treatment outcomes.

***Funding.*** *Not funded (as this is a literature review)*

***Conflict of Interest.*** *We confirm that we do not have any conflicting interests.*

***Authors' contributions:*** *Conceptualisation - Isakhanov R.B., Zhanbyrbekuly U., Akkaliev M.N., Nogayeva M.G., Novikova E.G.**;** methodology **-** Isakhanov R.B., Zhanbyrbekuly U., Akkaliev M.N., Nogayeva M.G., Novikova E.G**,** verification - Zhanbyrbekuly U., Akkaliev M.N., Nogayeva M.G.; formal analysis - Isakhanov R.B.**;** writing (original drafting) - Isakhanov R.B.**;** writing (review and editing) - Isakhanov R.B.*

*All authors read, agreed to the final version of the manuscript and signed the copyright transfer form.*

***Acknowledgements.*** *Alidjanov Jahongir - Justus-Liebig-Universität Gießen - urologist*

***Literature:***

1. *Abdurakhmanovich K.O.* et al. Ultrasound diagnosis of urolithiasis // Central Asian Journal of Medical and Natural Science. - 2021. - T. 2. - №. 2. - C. 18-24.

2. *Akilov F.A., Giyasov S.I.* Analysis of causes, frequency and severity of acute complicated pyelonephritis in endoscopic interventions for urolithiasis. Urology Herald. 2017;5(4):5-12. (In Russ.) Https://Doi.Org/10.21886/2308-6424-2017-5-4-5-5-12.

3. *Akilov F.A., Mukhtarov Sh.T, Giiasov Sh.I., Mirkhamidov D., Nasirov F.R., Muratova N.B. [Postoperative Infectious-Inflammatory Complications of Endoscopic Surgery for Urolithiasis].* [Postoperative Infectious-Inflammatory Complications of Endoscopic Surgery for Urolithiasis]. Urologiia. 2013. (1):89-91.

4. *Sadulloev F.S.* Nosocomial Infections in Patients with Urolithiasis in the Postoperative Period. Issled. Prakt. Med. 2015; 2(3): 25-29. DOI: 10.17709/2409-2231-2015-2-3-25-29.

5. *Sorokin I., Mamoulakis C., Miyazawa K., Rodgers A., Talati J., Lotan Y.* Epidemiology of Stone Disease across the World. World J Urol. 2017. 35 (9):1301-1320. Doi:10.1007/S00345-017-2008-6.

6. *Koza N.M.* Risk Factors and Prevention of Nosocomial Urinary Tract Infections. Perm Medical Journal. 2015. No. 1. pp. 135-140.

7. *Usupbaev A.C.* et al. Postoperative infectious complications in patients with urinary disease. Research and Practical Medicine Journal. 2018. T.5. №. 1. C. 30-37.

8. *Usupbaev A.Ch., Kabaev B.A., Imankulova A.S., Sadyrbekov N.Zh., Cholponbaev K.S., Usupbaeva A.A.* Postoperative Infectious Complications in Patients with Urinary Disease. Research'n Practical Medicine Journal (Issled. Prakt. Med.). 2018; 5(1): 30-37. DOI: 10.17709/2409-2231-2018-5-1-3.

9. *Al-Mamari S.A.* Complications of Urolithiasis. In: Urolithiasis in Clinical Practice. Springer International Publishing, Cham, 2017. Pp 121-129. Doi:10.1007/978-3-319-62437-2_8.

10. *Alexander R.T, Hemmelgarn B.R., Wiebe N., Bello A., Morgan C., Samuel S., Klarenbach S.W., Curhan G.C., Tonelli M.,* Alberta Kidney Disease N. Kidney Stones and Kidney Function Loss: A Cohort Study. BMJ. 2012. 345:E5287. Doi:10.1136/Bmj.E5287.

11. *Antonelli J.A., Maalouf N.M., Pearle M.S., Lotan Y.* Use of the National Health and Nutrition Examination Survey to Calculate the Impact of Obesity and Diabetes on Cost and Prevalence of Urolithiasis in 2030. Eur Urol. 2014. 66 (4):724-729. Doi:10.1016/j.Eururo.2014.06.036.

12. *Baboudjian M.* et al. Predictive risk factors of urinary tract infection following flexible ureteroscopy despite preoperative precautions to avoid infectious complications. World journal of urology. 2020. T. 38. C. 1253-1259.

13. *Bansal S.S., Pawar P.W., Sawant A.S., Tamhankar A.S., Patil S.R., Kasat G.V.* Predictive Factors for Fever and Sepsis Following Percutaneous Nephrolithotomy: A Review of 580 Patients. Urol Ann. 2017 Jul-Sep;9(3):230-233. Doi: 10.4103/UA.UA_166_16. PMID: 28794587; PMCID: PMC5532888.

14. *Blackmur J.P., Maitra N.U, Marri R.R., Housami F, Malki M, McIlhenny C.* Analysis of Factors' Association with Risk of Postoperative Urosepsis in Patients Undergoing Ureteroscopy for Treatment of Stone Disease. J Endourol. 2016 Sep;30(9):963-9. Doi: 10.1089/End.2016.0300. Epub 2016 Jul 13. PMID: 27317017.

15. *Bruyère F.* et al. Prosbiotate: a multicenter, prospective analysis of infectious complications after prostate biopsy. The Journal of urology. 2015. T.193. №.1. C. 145-150.

16. *Cai T.* et al. Infectious complications after laser vaporisation of urinary stones during retrograde intrarenal surgery are not associated with spreading of bacteria into irrigation fluid but with previous use of fluoroquinolones. European urology focus. 2021. T.7. №. 1. - C. 190-197.

17. *Charton M., Vallancien G., Veillon B., & Brisset J. M.* (1986). Urinary Tract Infection in Percutaneous Surgery for Renal Calculi. The Journal of Urology, 135(1), 15-17. Doi:10.1016/S0022-5347(17)45500-5.

18. *Chen Y., Feng J., Duan H., Yue Y., Zhang C., Deng T., Zeng G.* Percutaneous Nephrolithotomy versus Open Surgery for Surgical Treatment of Patients with Staghorn Stones: A Systematic Review and Meta-Analysis. 2019. PLoS One 14 (1):E0206810. Doi:10.1371/Journal.Pone.0206810.

19. *Chugh S.* et al. Predictors of urinary infections and urosepsis after ureteroscopy for stone disease: a systematic review from EAU section of urolithiasis (EULIS). Current urology reports. 2020. VOL. 21.pp. 1-8.

20. *Cindolo L., Berardinelli F., Castellan P., Castellucci R., Pellegrini F., Schips L.A.* Fatal Mycotic Sepsis after Retrograde Intrarenal Surgery: A Case Report and Literature Review. Urologia. 2017 Apr 28;84(2):106-108. Doi: 10.5301/Uro.5000173. Epub 2016 May 6. PMID: 27174535.

21. *Cole A., Telang J., Kim T.K., Swarna K, Qi.J., Dauw C., Seifman B., Abdelhady M., Roberts W., Hollingsworth J., Ghani K.R..* Michigan Urological Surgery Improvement Collaborative. Infection-Related Hospitalisation Following Ureteroscopic Stone Treatment: results from a Surgical Collaborative. BMC Urol. 2020 Nov 3;20(1):176. Doi: 10.1186/S12894-020-00720-4. PMID: 33138815; PMCID: PMC7607640.

22. *Cosic I., Cosic V.* Complicated Urinary Tract Infections in the Elderly. Acta Med Croatica. 2016. Vol. 70 (4-5). P. 249-255.

23. *Deng T., Liu B., Duan X., Cai C, Zhao Z., Zhu W., Fan J., Wu W., Zeng G* (2018) Antibiotic Prophylaxis in Ureteroscopic Lithotripsy: A Systematic Review and Meta-Analysis of Comparative Studies. BJU Int 122 (1):29-39. Doi:10.1111/Bju.14101.

24. *Ercole F.F., Macieira T.G., Wenceslau L.C., Martins A.R., Campos C.C., Chianca T.C.* Integrative Review: Evidences on the Practice of Intermittent/Indwelling Urinary Catheterisation. Rev Lat Am Enfermagem. 2013 Feb;21(1):459-68. English, Portuguese, Spanish. Doi: 10.1590/S0104-11692013000100023. PMID: 23546332.

25. *Ferraro P.M., Curhan G.C., D'Addessi A., Gambaro G.* Risk of Recurrence of Idiopathic Calcium Kidney Stones: Analysis of Data from the Literature. J Nephrol 2017. 30 (2):227-233. Doi:10.1007/S40620-016-0283-8.

26. *Fisang C.* et al. Urolithiasis-an interdisciplinary diagnostic, therapeutic and secondary preventive challenge. Deutsches Ärzteblatt International. 2015. T.112. №.6. С. 83.

27. *Gambaro G.* et al. The risk of chronic kidney disease associated with urolithiasis and its urological treatments: a review. The Journal of urology. 2017. Т. 198. №. 2. С. 268-273.

28. *Gardiner R.A., Gwynne R.A., Roberts S.A.* Perinephris Abscess. BJU Int. 2011. Vol. 107. P. 20-23.

29. *Geraghty R.M.* et al. Best practice in interventional management of urolithiasis: an update from the European Association of Urology guidelines panel for urolithiasis 2022. European Urology Focus. - 2022.

30. *Gottlieb M., Long B., Koyfman* A. The evaluation and management of urolithiasis in the ED: A review of the literature. The American journal of emergency medicine. 2018. Т. 36. №. 4. С. 699-706.

31. *Grabe M.* et al. Preoperative assessment of the patient and risk factors for infectious complications and tentative classification of surgical field contamination of urological procedures. World journal of urology. 2012. VOL. 30. P. 39-50.

32. *Hesse A., Brandle E., Wilbert D., Kohrmann K.U., Alken P.* Study on the Prevalence and Incidence of Urolithiasis in Germany Comparing the Years 1979 vs. 2000. Eur Urol 2003. 44 (6):709-713. Doi:10.1016/S0302-2838(03)00415-9.

33. *Hiatt R. A.* et al. Frequency of urolithiasis in a prepaid medical care programme. American journal of epidemiology. 1982. Т.115. №. 2. С. 255-265.

34. *Honeck P.* et al. Does open stone surgery still play a role in the treatment of urolithiasis? Data of a primary urolithiasis centre. Journal of Endourology. 2009. Т. 23. №. 7. С. 1209-1212.

35. *Jinga V., Iconaru V.* Penile Abscess and Urethrocutaneous Fistula Following Intracavernous Injection: A Case Report. J Sex Med. 2012. Vol. 9, № 12. P. 3270-3273.

36. *Kim D.S., Yoo K.H., Jeon S.H., Lee S.H.* Risk Factors of Febrile Urinary Tract Infections Following Retrograde Intrarenal Surgery for Renal Stones. Medicine (Baltimore). 2021 Apr 2;100(13):E25182. Doi: 10.1097/MD.0000000000025182. PMID: 33787599; PMCID: PMC8021282.

37. *Knoll T.* et al. Urolithiasis through the ages: data on more than 200,000 urinary stone analyses. The Journal of urology. 2011. Т. 185. №. 4. С. 1304-1311.

38. *Lopez M., Hoppe B.* (2010) History, Epidemiology and Regional Diversities of Urolithiasis. Pediatr Nephrol 25 (1):49-59. Doi:10.1007/S00467-008-0960-5.

39. *Lulich J.P., Osborne C. A.* Changing paradigms in the diagnosis of urolithiasis. Veterinary Clinics of North America: Small Animal Practice. 2009. Т. 39. №.1. С. 79-91.

40. *Moran M.E.* Urolithiasis. - Springer-Verlag New York, 2016.

41. *Morokuma F, Sadashima E, Chikamatsu S, Nakamura T, Hayakawa Y, Tokuda N.* The Risk Factors of Febrile Urinary Tract Infection After Ureterorenoscopic Lithotripsy. Kobe J Med Sci. 2020 Sep 10;66(2):E75-E81. PMID: 33024068; PMCID: PMC7837653.

42. *Naber K.G.* et al. Guidelines for the perioperative prophylaxis in urological interventions of the urinary and male genital tract. International journal of antimicrobial agents. 2001. Т. 17. №.4. С. 321-326.

43. *Nicoletta J.A., Lande M. B.* Medical evaluation and treatment of urolithiasis. Pediatric Clinics. 2006. Т. 53. №. 3. С. 479-491.

44. *Nicolle L.E.* Urinary Tract Infections in Special Populations: Diabetes, Renal Transplant, HIV Infection and Spinal Cord Injury. Infect Dis North Am. 2014. Vol. 28, № 1. P. 91-104.

45. *Peng C., Chen Z., Xu J.* Risk Factors for Urinary Infection after Retrograde Upper Urinary Lithotripsy: Implication for Nursing. Medicine (Baltimore). 2021 Aug 6;100(31):E26172. Doi: 10.1097/MD.0000000000026172. PMID: 34397789; PMCID: PMC8341329.

46. *Rivera M., Viers B., Cockerill P., Agarwal D., Mehta R., Krambeck A.* Pre- and Postoperative Predictors of Infection-Related Complications in Patients Undergoing Percutaneous Nephrolithotomy. J Endourol. 2016 Sep;30(9):982-6. Doi: 10.1089/End.2016.0191. Epub 2016 Aug 3. PMID: 27393153.

47. *Romero V., Akpinar H., Assimos DG (2010) Kidney Stones: A* Global Picture of Prevalence, Incidence, and Associated Risk Factors. Rev Urol 12 (2-3):E86-96.

48. *Sanchez-Martin F.M., Millan Rodriguez F., Esquena Fernandez S., Segarra Tomas J., Rousaud Baron F., Martinez-Rodriguez R., Villavicencio Mavrich H* (2007) [Incidence and Prevalence of Published Studies about Urolithiasis in Spain. A Review]. Actas Urol Esp 31 (5):511-520. Doi:10.1016/S0210-4806(07)73675-6.

49. *Schwaderer A.L., Wolfe A.J.* (2017) The Association between Bacteria and Urinary Stones. Ann Transl Med 5 (2):32. Doi:10.21037/Atm.2016.11.73.

50. *Sebastian N.* et al. Clinical presentation and management of urolithiasis in the obstetric patient: a matched cohort study. The Journal of Maternal-Fetal & Neonatal Medicine. 2022. Т. 35. №. 25. С. 6449-6454.

51. *Shen J., Sun F., Chen F.M., Wu Z.P., Li S.W..* Therapy and Prevention of Postoperative Urosepsis of Ureter Endoscopic Lithotripsy for Non-Infection. Chin Med Sci J. 2016 Mar 20;31(1):49-53. Doi: 10.1016/S1001-9294(16)30022-0. PMID: 28031088.

52. *Shokeir A.A, Al Ansari A.A.* Iatrogenic Infections in Urological Practice: Concepts of Pathogenesis, Prevention

and Management. Scand J Urol Nephrol. 2006;40(2):89-97. Doi: 10.1080/00365590510031093. PMID: 16608804.

53. *Skolarikos A.* et al. Urolithiasis. EAU guidelines. Edn. presented at the EAU Annual congress Amsterdam. - 2022.

54. *Smith L.H..* The medical aspects of urolithiasis: an overview. The Journal of urology. 1989. Т. 141. №. 3. С. 707-710.

55. *Stamatelou K.K, Francis M.E., Jones C.A., Nyberg L.M., Curhan G.C.* (2003) Time Trends in Reported Prevalence of Kidney Stones in the United States: 1976-1994. Kidney Int 63 (5):1817-1823. Doi:10.1046/j.1523-1755.2003.00917.x.

56. *Straub M., Gschwend J., Zorn C.* Pediatric urolithiasis: the current surgical management. Pediatric nephrology. 2010. VOL. 25. PP. 1239-1244.

57. *Strohmaier W.L.* (2000) [Socioeconomic Aspects of Urinary Calculi and Metaphylaxis of Urinary Calculi]. Urologe A 39 (2):166-170. Doi:10.1007/S001200050026.

58. *Sui W.* et al. Timing and predictors of early urologic and infectious complications after renal transplant: an analysis of a New York statewide database. Exp Clin Transplant. 2018. Т. 16. №. 6. С. 665-670.

59. *Tandogdu Z., Cek M., Wagenlehner F., Naber K., Tenke P., van Ostrum E., Johansen T.B.* Resistance Patterns of Nosocomial Urinary Tract Infections in Urology Departments: 8-Year Results of the Global Prevalence of Infections in Urology Study. World J Urol. 2014. 32 (3):791-801. Doi:10.1007/S00345-013-1154-8.

60. *Thomas B., Hall J.* Urolithiasis. Surgery (Oxford). - 2005. Т.23. №.4. С. 129-133.

61. *Tsaven* Badamsuren. Epidemiology and Prevention of urinary tract infections in urology hospitals. Dis. Candidate of Medical Sciences 14.00.30 / Tsaven Badamsuren. - Saint-Petersburg, 2005. - 111 p.

62. *Türk C.* et al. Guidelines on urolithiasis. European association of urology. - 2011.

63. *Unno R., Hosier G., Hamouche F., Bayne D.B., Stoller M.L., Chi T.* Single-Use Ureteroscopes Are Associated with Decreased Risk of Urinary Tract Infection After Ureteroscopy for Urolithiasis Compared to Reusable Ureteroscopes. J Endourol. 2022 Nov 9. Doi: 10.1089/End.2022.0480. Epub Ahead of Print. PMID: 36267020.

64. *Wagenlehner F., Tandogdu Z., Bartoletti R., Cai T., Cek M., Kulchavenya E, Koves B., Naber K., Perepanova T., Tenke P., Wullt B., Bogenhard F., Johansen T.E..* The Global Prevalence of Infections in Urology Study: A Long-Term, Worldwide Surveillance Study on Urological Infections. Pathogens 2016. 5 (1). Doi:10.3390/Pathogens5010010.

65. *Wang R.C.* Managing urolithiasis. Annals of emergency medicine. 2016. Т. 67. №. 4. С. 449-454.

66. *Wollin D.A.* et al. Antibiotic use and the prevention and management of infectious complications in stone disease. World journal of urology. 2017. Т. 35. С. 1369-1379.

67. *Yamamichi F., Shigemura K., Kitagawa K., Arakawa S., Tokimatsu I., Fujisawa M.* Should We Change the Initial Treatment of Renal or Retroperitoneal Abscesses in High Risk Patients. Urol Int. 2017. Vol. 98, № 2. P. 222-227.

*68. Zumstein V.* et al. Surgical management of urolithiasis-a systematic analysis of available guidelines. BMC. 2018. Т.18. №.1. С. 1-8.

**Information about the authors:**

**Ruslan B. Isakhanov –** PhD student, Non-profit Joint Stock Company “Semey Medical University”, Ust-Kamenogorsk, Republic of Kazakhstan; Postal address: 070003, Republic of Kazakhstan, East Kazakhstan region, Ust-Kamenogorsk, Voronina st., house 33. E-mail: Isakhanov_irb@mail.ru. Phone: +7 707 280 98 28

**Ulanbek Zhanbyrbekuly -** Candidate of Medical Sciences, Associate Professor of the Department of Urology, NAO "Astana Medical University"» Republic of Kazakhstan, Astana. https://orcid.org/0000-0003-1849-6924. Postal address: 010000. E-mail Ulanbek.amu@gmail.com. Phone number: +77071652019

**Merkhat N. Akkaliyev -** PhD, Acting Associate Professor of the Department of Surgical Disciplines, NAO "Semey Medical University", Republic of Kazakhstan; https://orcid.org/0000-0003-3122-7411, Postal address: 071400, Republic of Kazakhstan, Abai region, Semey, Abai Kunanbayev str., 103, e-mail: merhat.akkaliev@smu.edu.kz; Phone number: +7 777 153 9854

**Maral G. Nogayeva**– Candidate of Medical Sciences, Professor of the Department of Rheumatology, Kazakh National Medical University named after S.D. Asfendiyarov, e-mail: maral.nogaeva@xmail.ru, Almaty, +7 708 800 52 65; https://orcid.org/0000-0003-1182-5967

**Elena G. Novikova -** Candidate of Medical Sciences**,** Senior Researcher, Endocrinology Laboratory, Federal Research Center for Fundamental and Translational Medicine, Urologist-Andrologist, RMDC Clinic, Novosibirsk, Russia; e-mail: rmdc.nsk@gmail.com. ORCID ID https:// orcid.org/ 0000-0003-4723-0666 https:

**Corresponding author:**

**Isakhanov Ruslan B. –** PhD student, Non-profit Joint Stock Company “Semey Medical University”, Ust-Kamenogorsk, Republic of Kazakhstan;

**Postal address:** 070003, Republic of Kazakhstan, East Kazakhstan region, Ust-Kamenogorsk, Voronina st., house 33.

**E-mail:** Isakhanov_irb@mail.ru

**Phone:** +7 707 280 98 28

Received: 11 February 2025 / Accepted: 16 June 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2024.27.3.022***

***UDC 611.018.4:578.52-053.2-053.6***

This work is licensed under a Creative Commons Attribution 4.0 International License

# PREVALENCE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE AS A GLOBAL HEALTH PROBLEM

**Umytzhan S. Samarova[1], https:// https://orcid.org/0000-0002-8037-2677**
**Zhadra Ye. Kalbagaeva[1], https://orcid.org/0000-0003-4398-3927**
**Nurbike S. Zgotova[1], https://orcid.org/0000-0002-9498-9969**
**Gaukhar S. Yegizbayeva[1], https://orcid.org/0009-0000-4756-9294**
**Maral G. Nogayeva[2], https://orcid.org/0000-0003-1182-5967**
**Karlygash. N. Tazhibayeva [3], https://orcid.org/0000-0003-4947-3717**
**Torgyn B. Ibrayeva[4], https://orcid.org/0009-0007-4788-7410**
**Assel M. Iskakova[1], https://orcid.org/0009-0003-0144-6100**

**[1] NCJSC «Semey Medical University», Semey, Republic of Kazakhstan;**
**[2] NJSC «Kazakh National Medical University named after S.D. Asfendiyarov», Almaty, Republic of Kazakhstan;**
**[3] NCJSC «Al-Farabi Kazakh National University», Almaty, the Republic of Kazakhstan;**
**[4] NCJSC «Astana Medical University», Astana, Republic of Kazakhstan**

**Abstract**

**Introduction.** Chronic obstructive pulmonary disease (COPD) is one of the most important problems of modern health care by all over the world [55.67], cause of the prevalence, frequency of complications of this disease and mortality from it constantly increasing. The relevance of COPD is evidenced by the results of modern epidemiological studies, which indicates that over the past few decades, the incidence, mortality and disability rates have increased significantly. [70]. According to publishing journal Lancet in 2020 "Global burden of 369 diseases and injuries in 204 countries and territories in 1990-2019" COPD among all age groups by cause of mortality ranks 6th in the world and 4th in the age group from 50 to 74 years, about 2.8 million people die from COPD annually, which is 4.8% of all causes of death [22.49]. In 2021, it claimed the lives of 3.5 million people, it is approximately 5% of all deaths worldwide.[62] In 2021 it took the lives of 3.5 million people - this is approximately 5% of all deaths in the world.

Thus, due to the increasing of frequency rates, mortality and disability in COPD, this disease is a medical and social problem of modern healthcare.

**Objective:** to analyze the prevalence and risk factors for the development of chronic obstructive pulmonary disease (COPD).

**Search strategy.** A literature search was conducted in the following databases: PubMed, Medline, eLibrary, Google Scholar. Search depth was 10 years. 263 sources were found totally.70 publications were selected for analysis. Inclusion criteria: publications in Russian and English, since 2014 to 2024, the results of authentic research, meta-analyses, clinical cases, dissertations on the research topic and sources were found manually; Exclusion criteria: publications without clear formulation of results and conclusions; articles, abstracts with paid access. Several sources published earlier than the given period (1999, 1990) were also taken for analysis in 10 years, due to the content of the necessary data to make comparison.

**Results and conclusions.** The literature analysis showed that the high prevalence of COPD is becoming a heavy burden for society and is a socio-economic evil for most developed countries.

According to the forecasts of WHO experts, COPD will take the 3rd place among other causes of mortality by 2030 and will overtake mortality from injuries and accidents. Risk factors are the spreading epidemic of smoking,stable environmental pollution and recurring respiratory infectious diseases. According to scientists, COPD is the only disease, the mortality rate from which has increased by 25.5% over the past 10 years. Consequently, COPD is currently becoming a global international health problem**.**

***Key words:*** *epidemiology of COPD, chronic obstructive pulmonary disease, risk factors, smoking, harmful production**.***

***For citation:***

Samarova U.S., Kalbagaeva Zh.Ye., Zgotova N.S., Yegizbayeva G.S., Nogayeva M.G., Tazhibayeva K.N., Ibrayeva T.B., Iskakova A.M. The prevalence of chronic obstructive pulmonary disease as a global health problem // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 200-214 *doi 10.34689/SH.2025.27.3.022*

**Резюме**

# РАСПРОСТРАНЕННОСТЬ ХРОНИЧЕСКОЙ ОБСТРУКТИВНОЙ БОЛЕЗНИ ЛЕГКИХ КАК ГЛОБАЛЬНАЯ ПРОБЛЕМА ЗДРАВООХРАНЕНИЯ

**Умытжан С. Самарова[1], https://orcid.org/0000-0002-8037-2677**
**Жадра Е. Калбагаева[1], https://orcid.org/0000-0003-4398-3927**
**Нурбике С. Зготова[1], https://orcid.org/0000-0002-9498-9969**
**Гаухар С. Егизбаева[1], https://orcid.org/0009-0000-4756-9294**
**Марал Г. Ногаева[2], https://orcid.org/0000-0003-1182-5967**
**Карлыгаш Н. Тажибаева[3], https://orcid.org/0000-0003-4947-3717**
**Торгын Б. Ибраева[4], https://orcid.org/0009-0007-4788-7410**
**Асель М. Искакова[1], https://orcid.org/0009-0003-0144-6100**

**[1] НАО «Медицинский университет Семей», г. Семей, Республика Казахстан;**
**[2] НАО «Казахский национальный медицинский университет им. С.Д. Асфендиярова», г. Алматы, Республика Казахстан;**
**[3] НАО «Казахский Национальный университет им. аль-Фараби», г. Алматы, Республика Казахстан;**
**[4] НАО «Медицинский университет Астана», г. Астана, Республика Казахстан;**

**Актуальность:** Хроническая обструктивная болезнь легких (ХОБЛ) - одна из важнейших проблем современного здравоохранения во всем мире [55,67], т. к. распространенность, частота осложнений этой болезни и смертность от нее постоянно возрастает. Доказательством актуальности ХОБЛ, являются результаты современных эпидемиологических исследований, которые свидетельствуют о том, что за последние нескольких десятилетий значительно выросли показатели частоты, смертности и инвалидности. [70]. В журнале Lancet опубликованные данные в 2020 г. «Глобальное бремя 369 болезней и травм в 204 странах и территориях 1990-2019» ХОБЛ среди всех возрастных групп по причине смертности занимает 6 место в мире и 4 место в возрастной группе от 50 до 74 лет, ежегодно от ХОБЛ умирает около 2.8 млн человек, что составляет 4.8% всех причин смерти [22, 49]. В 2021 г. унесла жизни 3,5 млн человек – это примерно 5% всех случаев смерти в мире. [62]

Таким образом в связи с возрастанием показателей частоты, смертности и инвалидности при ХОБЛ, это заболевания является медико-социальной проблемой современного здравоохранения.

**Цель:** анализ распространенности и факторов риска развития хронической обструктивной болезни легких (ХОБЛ)

**Стратегия поиска.** Поиск литературы проведен в базах данных: PubMed, Medline, eLibrary, Google Scholar. Глубина поиска - 10 лет. Всего было найдено 263 источника. Для анализа были отобраны 70 публикаций. Критерии включения: публикации на русском и английском языках, с 2014 года по 2024 год, результаты оригинальных исследований, мета анализы, клин. случаи, диссертации по теме исследования и источники, найденные ручным способом. Критерии исключения: публикации без четкого формулирования результатов и выводов; статьи, тезисы, имеющие платный доступ. Также были взяты для анализа несколько источников, опубликованных ранее указанного периода (1999, 1990), в 10 лет, поскольку содержали необходимые данные для проведения сравнения.

**Результаты и выводы.** Анализ литературы показал, что высокая распространенность ХОБЛ становится тяжелым бременем для общества и несет социально-экономическое зло большинству развитых стран мира.

По прогнозам Экспертов ВОЗ ХОБЛ к 2030 году среди других причин летальности будет занимать 3-е место и опередит летальность от травм и несчастных случаев. Факторами риска являются распространяющаяся эпидемия курения, непрекращающиеся загрязнения окружающей среды и повторяющиеся респираторные инфекционные заболевания. По мнению ученых, ХОБЛ является единственной болезнью, летальность от которой, за последние 10 лет, выросла на 25,5%. Следовательно, ХОБЛ в настоящее время становиться глобальной международной проблемой здравоохранения.

***Ключевые слова:*** *эпидемиология ХОБЛ, хроническая обструктивная болезнь легких, факторы риска, курение, вредное производство.*

***Для цитирования:***

*Самарова У.С., Калбагаева Ж.Е., Зготова Н.С., Егизбаева Г.С., Ногаева М.Г., Тажибаева К.Н., Ибраева Т.Б., Искакова А.М.* Распространенность хронической обструктивной болезни легких как глобальная проблема здравоохранения // Наука и Здравоохранение. 2025. Vol.27 (3), С.200-214. *doi 10.34689/SH.2025.27.3.022*

**Түйіндеме**

# ЖАҺАНДЫҚ ДЕНСАУЛЫҚ ПРОБЛЕМАСЫ РЕТІНДЕ СОЗЫЛМАЛЫ ОБСТРУКТИВТІ ӨКПЕ АУРУЛАРЫНЫҢ ТАРАЛУЫ

**Умытжан С. Самарова[1],** https://orcid.org/0000-0002-8037-2677
**Жадра Е. Калбагаева[1],** https://orcid.org/0000-0003-4398-3927
**Нурбике С. Зготова[1],** https://orcid.org/0000-0002-9498-9969
**Гаухар С. Егизбаева[1],** https://orcid.org/0009-0000-4756-9294
**Марал Г. Ногаева[2],** https://orcid.org/0000-0003-1182-5967
**Карлыгаш Н. Тажибаева[3],** https://orcid.org/0000-0003-4947-3717
**Торгын Б. Ибраева[4],** https://orcid.org/0009-0007-4788-7410
**Асель М. Искакова[1],** https://orcid.org/0009-0003-0144-6100

**[1] «Семей медицина университеті» КеАҚ, Семей қ., Қазақстан Республикасы.**
**[2] ҚеАҚ «С. Ж. Асфендияров атындағы Қазақ ұлттық медицина университеті», Алматы қ., Қазақстан Республикасы;**
**[3] «Әл-Фараби атындағы Қазақ ұлттық университеті» КЕАҚ, Алматы қ., Қазақстан Республикасы;**
**[4] «Астана медицина университеті» КеАҚ, Астана қ., Қазақстан Республикасы.**

**Өзектілігі:** Өкпенің созылмалы обструктивті ауруы (ӨСОА) дүние жүзіндегі заманауи денсаулық сақтаудың маңызды мәселелерінің бірі болып табылады [55.67], өйткені бұл аурудың таралуы, асқыну жиілігі және одан болатын өлім-жітім үнемі өсіп келеді. ӨСОА өзектілігін қазіргі эпидемиологиялық зерттеулердің нәтижелері дәлелдейді, бұл соңғы бірнеше онжылдықта сырқаттанушылық, өлім-жітім және мүгедектік көрсеткіштері айтарлықтай өскенін көрсетеді. [70]. Lancet журналында 2020 жылы жарияланған «204 ел мен аумақтағы 369 ауру мен жарақаттың жаһандық ауыртпалығы 1990–2019» ӨСОА өлім себебі бойынша барлық жас топтары арасында әлемде 6-шы және 50-ден 74 жасқа дейінгі 4-ші орында, жыл сайын шамамен 2,8 миллион адам қайтыс болады. өлім [22.49]. 2021 жылы ол 3,5 миллион адамның өмірін қиды, бұл дүние жүзіндегі барлық өлімнің шамамен 5%-ын құрады. [62]

Осылайша, ӨСОА-дағы аурушаңдық, өлім және мүгедектік көрсеткіштерінің артуына байланысты бұл ауру заманауи денсаулық сақтаудың медициналық-әлеуметтік мәселесі болып табылады..

**Мақсаты:** Өкпенің созылмалы обструктивті ауруларының (ӨСОА) таралуы мен қауіп факторларын талдау.

**Іздеу стратегиясы.** Келесі дерекқорларда әдебиеттерді іздеу жүргізілді: PubMed, Medline, eLibrary, Google Scholar. Іздеу тереңдігі – 10 жыл. Барлығы 263 дереккөз табылды. Талдау үшін 70 басылым таңдалды. Қосылу критерийлері: 2014 жылдан 2024 жылға дейін орыс және ағылшын тілдеріндегі жарияланымдар, түпнұсқа зерттеулердің нәтижелері, мета-талдаулар, клиникалық жағдайлар, зерттеу тақырыбы бойынша диссертациялар және қолмен табылған дереккөздер; Алып тастау критерийлері: нәтижелер мен қорытындылар нақты тұжырымдалмаған жарияланымдар; ақылы қолжетімді мақалалар, тезистер. Көрсетілген мерзімнен бұрын (1999, 1990 ж.) жарияланған бірнеше дереккөздер де 10 жыл ішінде талдауға алынды, өйткені оларда салыстыру үшін қажетті деректер болды.

**Нәтижелер мен қорытындылар.** Нәтижелер мен қорытындылар. Әдебиеттерге шолу COPD-ның жоғары таралуы қоғамға ауыр жүк және әлемнің көптеген дамыған елдері үшін әлеуметтік-экономикалық ауыртпалық екенін көрсетті.

ДДҰ сарапшыларының пікірінше, ӨСОА 2030 жылға қарай жарақаттар мен жазатайым оқиғалардан болатын өлім-жітімнен асып түсетін өлімнің үшінші себебі болады. Тәуекел факторларына темекі шегу эпидемиясының таралуы, қоршаған ортаның тұрақты ластануы және қайталанатын респираторлық инфекциялар жатады. Ғалымдардың айтуынша, ӨСОА – соңғы 10 жылда өлім көрсеткіші 25,5%-ға өскен жалғыз ауру. Демек, COPD қазір жаһандық халықаралық денсаулық мәселесіне айналуда.

***Негізгі сөздер:*** *ӨСОА эпидемиологиясы, өкпенің созылмалы обструктивті ауруы, қауіп факторлары, темекі шегу, қауіпті өндіріс.*

***Дәйексөз үшін:***

*Самарова У.С., Калбагаева Ж.Е., Зготова Н.С., Егизбаева Г.С., Ногаева М.Г., Тажибаева К.Н., Ибраева Т.Б., Искакова А.М.* Жаһандық денсаулық проблемасы ретінде созылмалы обструктивті өкпе ауруларының таралуы // Ғылым және Денсаулық сақтау. 2025. Vol.27 (3), Б. 200-214. *doi 10.34689/SH.2025.27.3.022*

**Introduction**

Currently, chronic obstructive pulmonary disease (COPD) is the only one of the most common diseases, the mortality rate from which continues to increase, ranking 4th in the structure of mortality in the world. [19] Statistics predict that by 2030, about 4.5 million people could die from COPD and related diseases in the world. [1,26.] About 90% COPD mortality among people under 70 years of age occurs in low- and middle-income countries [55**].**

WHO data for 2019 shows that 212.3 million patients were diagnosed with COPD, 3.3 million patients died, and the DALYs rate was 74.4 million all over the world. WHO data, for 2019 shows that 212.3 million patients worldwide were diagnosed with COPD, 3.3 million patients died, and the DALYs rate was 74.4 million. The prevalence of COPD was 2638.2 per 100,000 people, mortality was 42.5 per 100,000 people [42].

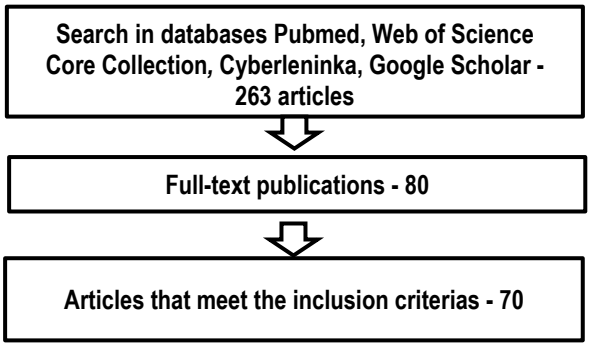
**Aim:** analysis of prevalence and risk factors for the development of chronic analysis of prevalence and risk factors for chronic obstructive pulmonary disease (COPD)

**Search strategy**. The study examined full-text publications in English and Russian, which are devoted to the prevalence and risk factors for the development of gestational diabetes mellitus. The following searching mechanisms were used in the literature searching process: Pubmed, Web of Science Core Collection, Cyberleninka, Google Scholar by key words.

*Inclusion criteria:* the search depth was 10 years: since 2013-2024 years, original full text scientific publications, literature reviews, systematic reviews, WHO guidelines, management of international organizations of health protection, State programs of the Ministry of Health, thematic studies in the field of health policy and economics in open access in English and Russian. Exclusion criteria: publications without a clear formulation of results and conclusions; articles, theses, which have paid access. Several sources published before the specified period were also taken for analysis (1999, 1990), in 10 years, because of they contained the necessary data to carry out the comparison

*Picture 1.*

**Article selection algorithm.**




**Results of discussion.**

**Modern characteristics of COPD**

According to the definition of A.Chuchalin, chronic obstructive pulmonary diseases (COPD) include a heterogeneous group of pulmonary diseases (bronchial asthma, emphysema, chronic obstructive bronchitis, etc.), which are united by a disorder of the external respiratory function of the lungs of the obstructive type. [36]

Chronic obstructive pulmonary disease (COPD) is the disease which is characterized, persistent airflow limitation that is usually progressive and results from a chronic inflammatory response of the airways and lung tissue to exposure to inhaled noxious particles or gases. Exacerbations and comorbid conditions are an integral part of the disease and make a significant contribution to the clinical picture and prognosis. [54].

COPD is a preventable and treatable disease characterized by persistent airflow limitation (usually progressive) and associated with an increased chronic inflammatory response in the airways and lungs to exposure to noxious particles or gases. [10.].

In the International document “Global Iniatiative on Chronic Obstructive Lung Disease” (Global Initiative for Chronic Obstructive Lung Disease – GOLD, 2023) The following definition of the disease is given: COPD is heterogeneous lung disease, characterized by chronic respiratory symptoms (dyspnea, cough, sputum production) and/or exacerbations due to respiratory pathology (bronchitis, bronchiolitis) and/or alveoli (emphysema), which causes persistent, often progressive airflow obstruction. [52]

Therefore, based on the above mentioned definitions of COPD, as well as the presence of frequent exacerbations and concomitant diseases we can talk about the global medical significance of this disease, both in the clinical aspect and in the organizational aspect of healthcare.

**Prevalence of COPD**

According to scientific data, there is an increase in the incidence of chronic obstructive pulmonary disease (COPD), which is why this disease is currently becoming one of the most pressing health problems worldwide and is acquiring increasing social significance. Comparing the prevalence of COPD since 1997, it turned out to be so great that it has become a real socio-economic evil for most developed countries of the world. [38,4,7.]. Most deaths (about 90%) from COPD occurs in developing countries, and complications cause about 3 million deaths [54,69].

The prevalence of COPD varies considerably both between countries and between different groups within a country. According to the WHO forecast, in 2020 COPD will take 2nd place among the overall incidence and 3rd place in the mortality structure among all morbidities. [54] 10 million patients with COPD were identified during medical examinations in the United States. At the same time, according to other data, 24 million adults in the United States had a disorder of external respiratory function, which indicates underdiagnosis. The reason for underdiagnosis of COPD is the late seeking of medical care by patients, which results in late detection of the disease. [63]

Statistics from the World Health Organization (WHO) showed that the average prevalence of COPD all over the world is 9.34/1000 and 7.33/1000 among men and women, respectively.

According to the statistics above, for every 30-45 cases of COPD, an average of 5-7 new cases are diagnosed annually. [31].

According to literary data from 2006-2007, there has been a steady increase in the prevalence of COPD [60,47]. The incidence of COPD is steadily increasing throughout almost the entire world. Literary data from authors of the 90s, 2015, 2022 note that the prevalence of COPD is high,

especially in the USA [3,63], in Europe [58, 3, 67], the prevalence rates lower in Korea and China [64,48,] In China, differences were found according to the geographic region, the highest prevalence reported in Southwest China (20.2%, 95% CI 14.7–25.8) and the lowest in central China (10,2%, CI 8,2 – 12,2). Among adults with COPD, 56, 4% (95% CI 53,7 – 59,2) was a mild degree of the disease (GOLD I), 36,3% (34,3 – 38,3) – moderate degree (GOLD II stages), 6,5% (5,5 – 7,4) had severe (GOLD III), and 0,9% (0,6 – 1,1) very severe degree of the disease (GOLD I) [48]. Data obtained from the analysis of the 5th Korea National Health and Nutrition Examination Survey showed that the prevalence of COPD from 2010 to 2012 was 13.7%, The prevalence of the disease has been steadily increasing: in 2010 it formed 12,2%, in 2011 - 13,2%, and in 2012 - 15,5%.[48] and the Russian Federation is no exception [3,].Among the population of the Russian Federation, in contrast to the general morbidity for the period 2002-2006, COPD shows a steady annual growth of at least 10%. [3] According to the official statistics of the Ministry of Health of the the Russian Federation, in Russia the number of COPD patients is approximately 3 million people. However, individual epidemiological studies show a wider prevalence of the disease and some authors claim that the actual number of patients is 16-20 million. [15]

In some literature data the frequency of COPD among adults is 4-15%. [35,52].

According to foreign authors *Davis Adeloye*, *Stephen Chua, Chinwei Lee and others*, who used epidemiologic model of metaregression and gave them an evaluation of about 227,3 million cases of COPD in 1990 among people aged 30 and over, and showed the global prevalence of 10,7% (95% confidence interval (CI) 7,3%-14,0%) in this age group.In 2010 currently, the number of COPD cases increased to 384 million, with global prevalence 11,7% (8,4%-15,0%).

Thus, the increase in COPD was 68.9%, the reason for this was the global demographic changes. [45]

Among WHO regions, the highest epidemiological incidence was in the America (13,3% in 1990 and 15,2% in 2010), and COPD was the leading cause of death from chronic lower respiratory disease, the fourth leading cause of death in the United States in 2016. In 2015 approximately 15.5 million adults aged ≥18 years (unadopted prevalence = 6,3% and age-adapted = 5,9%) announced about the diagnose of COPD. Estimates of the prevalence of COPD at the level of different states range from 3.8% in Utah to 12.0% in the Virginia economy. Corrected according to age the rate of death in a particular state (per 100 000 population) in 2015 hesitated from 15,8 in Hawaii till 64,3 in Oklahoma [44]. Between 1990 and 2010, the highest percentage of COPD was in the Eastern Mediterranean region (118,7%), the next was African region (102,1%), and the European region recorded the lowest growth (22,5%). [45].In 1990 the authors estimated that there was approximately 120.9 million cases of COPD among the urban population (prevalence 13,2%) and 106,3 million cases among rural population (prevalence 8,8%). In 2010 more than 230 million cases of COPD were registered among the urban population (prevalence 13,6%) and 153,7 million among rural population (prevalence 9,7%). [45]

In 2015 a meta-analysis of five spirometric studies showed that in Africa average prevalence of COPD compiled 13,4%, varying from 9,4 till 22,1% [55]. One of the nine researches of meta-analysis conducted in Sub Sahara showed prevalence the disease ranges from 4 to 25% [49,56]. In research of *G.Gashaw and others* where spirometry results showed prevalence of COPD equal to 17,8%.[70]. This observation will be compared with previous studies conducted in Uganda, where the prevalence of COPD was high and the lowest was in the South-East Asia/West Pacific region (8.80%). [61]

In the Cone of Southern countries of Latin America, the overall prevalence of COPD was 9.3%, according to the study. (95 CI 8,4, 10,2%). [47]

Ten countries with the highest number of COPD cases (China, India, Indonesia, the United States, Bangladesh, Japan, Pakistan, Russia, Vietnam and Germany) accounted for 255.4 million (65.2%) of the worldwide COPD cases in 2019. [37]

Global Burden of the Disease research showed that in 2019 who suffered from COPD is 212.3 million people in the world. The largest increase in COPD during the study period was observed in several countries such as Egypt (62%), Georgia (54.9%) and Nicaragua (51.6%) demonstrated the largest increase in COPD during the study period.[65]

From the first half of 2013 to the end of 2015, experts from Ukraine, Kazakhstan and Azerbaijan conducted research on the prevalence of COPD in megacities such as Kyiv, Almaty and Baku, involving 2842 adult participants (964 from Ukraine, 945 from Kazakhstan and 933 from Azerbaijan). [24]. The study used questionnaire and spirometry methods. The results of the survey for this study showed that the prevalence of COPD in Kazakhstan is 13.8 cases per 1000 people, in Ukraine - 10.4 cases per 1000 people, and in Azerbaijan - 4.3 cases per 1000 people. According to the results of the spirometry method, the prevalence of COPD was significantly higher in Ukraine: 31.9 cases per 1000 people, in Kazakhstan - 66.7 cases per 1000 people, and in Azerbaijan - 37.5 cases per 1000 people. [24,14]. According to the study data, a higher prevalence of COPD in Kazakhstan and Azerbaijan was noted in the age group ≥65 years, it means 73.5 and 38.5 per 1000, accordingly. However, in Ukraine, the highest prevalence was observed in the 40–64 age group: 14.8 per 1000.[24] Official statistics from Kazakhstan show that the incidence of COPD ranges from 360 to 500 cases per 100,000 adults. [14]. In 2013 the incidence of COPD was 64.4 per 100 thousand population, in 2014 – 73.5, (increased 9,1%). Among the regions of Kazakhstan, the highest rates were observed in the South Kazakhstan region – 145.5 per 100 thousand population, the lowest – in the Aktobe region – 19.4 per 100 thousand population [16].
While conducting a study using the GOLD questionnaire in the Pavlodar region, it was found that 13.8% of respondents were presumably diagnosed with COPD. Among them, those who is with possible COPD were city residents who made up 10.5%, while those who living in rural areas made up 18.6%. During the study, only survey data were taken into account, without the using of clinical diagnostic studies. [2]

According to the estimates of the Ministry of Health of the Republic of Kazakhstan, the number of patients with COPD in the country is at least 800,000 people, although this figure does not appropriate to the results of international studies - it is significantly underestimated. [14]**.** Official statistic of Kazakhstan shows that the prevalence of COPD remains between 360-500 per 100,000 adults, although according to WHO expert estimates, in real life the amount can be 7-9 times higher. In 2013 the incidence of COPD in Kazakhstan was 64.4 per 100 thousand. In 2014 - 73.5, which is 9.1 higher than the previous year. The highest incidence rate of COPD according to the regions among the population is noted in region of South Kazakhstan, it is 145.5 per 100 thousand people, the lowest incidence rate of COPD is noted in Aktobe region – 19.4 per 100 thousand people [13].

There is also no separate statistical record of mortality due to COPD in Kazakhstan. And it is only known that respiratory diseases take up to 10,000 lives per year [12]

Thus, analyzing the above data, we can say that chronic obstructive pulmonary disease remains a global, pressing problem in the world and also in Kazakhstan for both healthcare and practical medicine. Prevalence and mortality of COPD significantly varies depending on developing and developed countries, according to different social, economic, ecologic and other differences. Statistical data on COPD in the Republic of Kazakhstan record the highest incidence rate of COPD in the South Kazakhstan region - 145.5 per 100 thousand people, the lowest incidence rate of COPD in the Aktobe region - 19.4 per 100 thousand people.

**Risk factors**

**Prevalence according to the age.**

One of the risk factors for the prevalence of COPD among others is the age of the population.

According to all literature data, COPD occurs at an age of ≥40, and it should also be noted that, according to some data, up to 50% of patients with COPD are people of working age (40 to 67 years) (A. Chuchalin, 2014). The authors' of the research data, *Davis Adeloye, Catriona Basquill, Angelique Papana and others*, show that in Africans, the difference in COPD prevalence between spirometry and non-spirometry data showed that in individuals aged 40 years and older (13.4%; IQR: 9.4%-22.1%) and (4.0%; IQR: 2.1%-8.9%),with statistical significance (p = 0,001) [46]. According to statistics in 2010, in relation to the corresponding age group (40 years and older), it was 196.4 million people in Africa, the prevalence is approximately 26.3 million (18.5-43.4 million) cases of COPD, similar figures for 2000, based on the same prevalence rates, would be 20.0 million (14.1-33.1), which would imply an increase of 31.5% per decade that can be explained only by the aging of the African population [46].

According to the research data of *G.Gashaw and others* prevalence of determined spirometry of COPD among men 16,6% and women 19,5%) [70]. Research work devoted to the problem of COPD in countries of Latin America among men and women showed high prevalence, men [11,8% (95% CI 0,3, 13,3%)], women [7,3% (95% CI 6,2, 8,3%)] at a fixed ratio. [53]

In Kazakhstan, according to the results of the GOLD questionnaire and demographic data in the Pavlodar region, increase in frequency of COPD was noted in the older age group: 50-59 years – 8%, 60-69 years – 27.8%. [53]

In the Turkestan region, the research was conducted on the problem of the spread of chronic non-communicable diseases among the elderly population, where it was determined that the incidence of COPD among people over 65 was 25.8% of the total number of surveyed respondents.

There are works among scientific data which are devoted to the study of prevalence of COPD among young people. A total of 986 people aged 18 to 44 years (358 men and 628 women) were examined, average age – 28.95±8.2 years. The newly diagnosed COPD accounted for 1.8% of the total number of respondents examined, among which first stage of COPD was detected in 16.7% of patients, the second stage - in 83.3%. The proportion of men was 72.2% compared with women 27.8%. [5] Consequently, COPD also occurs among young people, especially men, which is associated with the spread of smoking and the physiological decrease in respiratory function.

Thus, analyzing the data of the studies included in the review, it can be concluded that the epidemiological prevalence of COPD varies both in different countries and in different age groups within countries. The increased frequency of COPD in older age can be explained by higher exposure to risk factors and a physiological decrease in respiratory function according to the age, which begins at about 30-40 years.

**Prevalence by gender.**

Comparison of statistical data from studies in developed countries since 1999 shows that gender should be considered as a risk factor for the development of COPD. [60,2] Based on the results of scientific research, we observe a high prevalence of COPD among men, however, there is some research data that show the same prevalence of COPD among men and women. [ 60,2]

Due to the increase in tobacco consumption among women, there is an increase in the prevalence of diseases among them. Thus, the Global Adult Tobacco Survey (GATS) revealed that 43.9 million people smoke in the Russian Federation: 21.7% women, 60.2% men.

In the most economically and demographically active age group from 19 to 44 years old, 4 out of 10 women and 7 out of 10 men smoke. [11] According to S. Ovcharenko and co-authors (2009), the rapid development of COPD in women is facilitated by the following features: a shorter medical history; development of pathology with a shorter smoking history; the course of the disease with more pronounced dyspnea; decreased tolerance to physical activity; fewer concomitant diseases; worse quality of life parameters than in men; higher survival. [25.]

Totally 60 articles were reviewed with the 127,598 topics of the total sample size. The pooled prevalence of COPD was 15.70% (13.80–18.59%) in men and 9.93% (8.73–11.13%) in women.[61] The pooled prevalence among men aged 30 years and older was 14.3% (95% CI 13.3%–15.3%) compared with 7.6% (95% CI 7.0%–8.2%) in women.[ 45]

By gender, men had a higher prevalence of COPD compared to women (15.47%; 95% CI 12.22%-19.02% for men 8.79%; 95% CI 6.94%-10.82% for women). Using the LLN criteria, the prevalence of COPD was almost equal in both sexes (8.67%; 95% CI 8.44%–8.90% for men and 8.00%; 95% CI 6.42%–9.73% for women). [32]

In the countries of Latin America and the Caribbean, the prevalence of COPD in the general over 35 years was 8.9%. Among men, the prevalence was 13.7% and among women, 6.7%. [58] In the Southern Cone Countries of Latin America, men had a higher prevalence of 11.8% (95% CI 10.3, 13.3%) than women 7.3% (95% CI 6.2, 8.3%) with a fixed ratio [47].

**Smoking as a risk factor**. In the context of the progression of the development of unfavorable ecology, the prevalence of tobacco smoking increases and, accordingly, the incidence of COPD and mortality increases. [31,30] The role of tobacco use is one of the main etiological factors of COPD, which has been proven as a result of more than 45 years of studying this problem. [ 31]

Tobacco smoking is one of the main causes of development and the most studied risk factor for COPD, however, the disease can also develop in non-smokers, the reason for this is still not entirely clear [31,30] Even after adjusting for other respiratory diseases (asthma and tuberculosis), male gender, older age, smoking was the reason of higher prevalence of COPD, obesity and higher education was the reason for the lower prevalence of COPD.[30]The risk of developing the disease while smoking tobacco is 80–90%. [22,30.] The prognostic features of COPD are the following: age at which smoking began, its duration and intensity, the social status of the smokers, which also influence the lethal outcome from this disease.

According to foreign studies, the prevalence among smokers and ex-smokers was 24.3%.[37] The main risk factors for COPD, beside the age are smoking. A cross-sectional observational study conducted from November 2016 to December 2019 by Jia-Xi Duan, Wei Cheng, Yu-Qin Zeng, Yan Chen Shan Cai and others were included 5183 patients with COPD. Interpretation of the results showed that tobacco exposure combined with other risk factors resulted in significantly higher CAT scores (16.0 ± 6.7 vs. 15.3 ± 6.3, P = 0.003) and more severe dyspnea (patients with mMRC ≥ 2, 71.5% vs. 61.6%, P < 0.001) than tobacco exposure only. Additionaly, patients with COPD who was exposed by the smoke of biomass had the highest rates of CAT, than patients who was exposed by the tobacco or occupational exposure only (17,5 ± 6,3 against 15,3 ± 6,3 и 15,2 ± 6,3 accordingly, *P* <0,05 f), and were more likely the women and older. [57].

According to the World Epidemiological Research on Tobacco Consumption among girls aged 13-15, 61.3% of them tried smoking for the first time, and 29.8% were regular users of the tobacco products. [49]. The frequency of active smoking among girls – students of lyceum are 19%, students of vocational schools - 31%, among asocial teenagers (homeless) - 100 [22]. It should be noted that the sifnificant factor of using the tobacco is the passive smoking or exposure of “sidestream smoke” in families. [31].

The most researched factor among others in developing illnesses among women is smoking [22,31]. One of the first sign of lung disease is a cough, therefore during the research the effect of tobacco smoke on the appearance of the sympthom of cough was demonstrated among 232 women cough on the background of smoking was recorded in 53.4% of cases (n = 124), without the smoking factor - in 46.6% (n = 108) [20].

At the *Samara City Polyclinic, the authors V.Lotkova, and A.Dzyubailo* studied a cohort of 107 smoking women of childbearing age with varying degrees of nicotine dependence, who was divided into 2 groups: 53 patients - active smokers who consume passive smoking at home (first group), 54 patients - active smokers without passive smoking (second group). The conducted studies showed that the probability of developing moderate COPD in the first group is in the range of 0.04<P<0.98. Moreover, the gradient of the probability that COPD formulates in different years of smoking increased from 4% in non-smokers 48% in 10 year smoking patients and 98% in 20 year smoking patients, and in the second group, the probability of developing COPD was in the range 0.00<P <1.00. Moreover, the gradient of the probability that COPD will develop with different smoking history increased from 0% in non-smokers to 40% in patients with the smoking history of 10 years and 100% with the smoking history over 20 years. [22]

Thus, based on the presented research data, it can be said that passive smoking, in addition to active smoking, increases the nicotine load with the formation of more pronounced prerequisites for the pathogenetic processes of the development of COPD. Despite the decrease of the probability gradient in developing COPD in the second group, it is possible that the number of cigarettes nicotine load from 10 to 16 cigarettes per day) is to a greater extent the main factor in the development of the disease than in passive smoking. Accordingly the passive smoking, in patients with the smoking history of 11 years, additionally active, accelerates formation of the nicotine addiction which is the prerequisite for the development of COPD. In patients who has 20 years of smoking and more the predominant factor of the developing of COPD becomes the length of smoking [22].

In Japan, the combined effect of 40-years-old air pollution and concomitant smoking on lung function has been studied officially among women because women are more susceptible to the adverse effects of both irritants than men. A total of 655 subjects who live in the 40-years-old air pollution area, and 572 women lived in the area without pollution. Lung function of respondents measured in 2000 so first group with the air pollution (130 smoking and 525 non-smokers; average age 68,4 years), according to the period since 2004 till 2013 the second group is without air pollution (113 smokers and 459 non-smokers; average age 69,0 years). Victims with a smoking history had significantly lower volume of forced exhalation in 1 second (OFV 1% of predicted) (average 74%) and significantly lower OFV 1/increased lung capacity (FEVL) (average 70%), observed in women smokers than non-smokers (P <0.001). Thus, smoking worsens lung function in officially recognized female smokers, despite improvements in air pollution and ongoing medical care. [67] Authors *Kenji Kotaki[1], Hisao Ikeda[2], Takeshi Fukuda* and others in their research work used results of spirometry and medical questionnaires for screening 433 men from the city Omuta, Japan, Interpretation of obtained data showed, that non-smokers had a high estimated prevalence of COPD – 16%. Among smokers groups from 50 till 74 years estimated prevalence of COPD was 29%, in the group >75 years 37%. [59]

Results of the statistics in Canada 2012 of Aboriginal Peoples Survey (APS) data were reported at the work of Yelena Bird and others. The research was conducted among the indigenous population 35 years of age. According to the results, the incidence of COPD was 6.80%. Higher rates were observed in regular smokers (odds ratio [OR] 2,28; 95% confidence interval [95% CI] 1,65–3,14), aged 55 years and over (OR 3,04; 95% CI 2,14–4,30), who had a low socio-economic status also participated at the research which conducted in the Samarkand region among geriatric age groups diagnosed with COPD, where patients were divided into three groups. First group consist of 36 patients with COPD (29 men, 7 women) at the age of 60 to 74 years (average age 66,49±6,09 years). Another group involved 16 patients (14 men, 2 women) at the age of 75 to 89 years (average age 79,2±2,7 years). The control group included 18 patients (15 men, 3 women) at the age from 35 to 55 years (average age 46,1±3,6 years).

The duration of the disease among patients in the first and second group was more than 15 years, and in the third group the duration of the disease was up to 5 years. Among elderly and senile patients, the “Smoking Index” was found in 42 (80.8%), 19 (36.5%) of them were “heavy smokers”. [32]

Authors *E.Alexandrova, G.Ignatova, I.Zakharova and others* during conducting research at the age of 18 to 44, average age – 28,95±8,2 years, the number of smokers with COPD was found significantly higher – 69,2% against 46,5% accordingly. [5]

The survey was conducted among Nizhny Novgorod State Medical Academy (NizhNovSMA) students. The study involved 280 students, including 92 boys and 188 girls (average age 19.8 ± 1.2 years).

The purpose of the survey of students was to determine the smoking status, calculate the smoking index (pack/years), study the reasons and age of starting smoking, and assess subjective manifestations [23]. An analysis of the survey showed that among the students of the Nizhny Novgorod State Medical Academy students, smokers accounted for 18.9% of the respondents. The frequency of smoking among young men (32.6%) was 2.7 times higher than among young women (12.2%).

The results of the scientific research among the students of Nizhny Novgorod State Medical Academy are mainly comparable with the data of different authors, where they characterize the all-Russian situation with the prevalence of tobacco smoking among students, varying from 23 to 32%.

The beginning of smoking among students of Nizh Nov SMA was among the boys 8-9 years, girls 13-16 years, permanent smoking (at least 1 cigarette a week) was noted on average with 14.3 2.7 years.

Thus, according to these data, it can be said that young people generally start smoking at school. The smoking experience ranged from 1 year to 8 years (on average 5.4 ± 2.5 years), the smoking index was 2.6 ± 1.9 packs/year. [5].

The results of the study of lung function as indicators of peak speed of lung (PLV), forced vital capacity (FVC) and cardiac output (CO25) in smokers were significantly lower than in non-smokers ($p = 0.027$; $p = 0.0038$ and $p = 0.002$, respectively). There was also a trend ($p = 0.103$) towards a decrease in FEV1 in smokers compared with non-smokers. In addition, 30.8% of smokers and 8% of non-smoking students ($p = 0.035$) showed a “dip” in the descending part of the flow-volume curve, which is an early sign of broncho-obstructive disorders that precedes quantitative changes in FVD. [31] Researcher *A.Chuchalin (*2008) noted that the beginning of smoking in adolescence leads to a decrease in the age-related increase in FEV1 and “underdevelopment” of this indicator.

From the above data, it can be said that when studying the external respiratory function in a group of smoking students, a decrease in the FVC, PSV, and MOS25 indicators was revealed compared to non-smokers, as well as the presence of subjective symptoms of respiratory tract damage (in 20% of smokers).These data indicate the development of early broncho-obstructive disorders in young smokers.

Thus, the provision of a scientific evidence base contributes to understanding the importance of the role of tobacco smoking in the genesis of COPD development and the fight against it is an important measure for the prevention and treatment of this disease.

**Occupational hazards.**

COPD is the polyetiological and heterogeneous disease and dust and gases from the industrial environment play a significant etiological role in its development, which have been proven in epidemiological and experimental studies. [8,9,18,]. The proportion of occupational COPD (PCOPD) is 10-15% of cases in the disease structure.[50] It is a steadily progressive, disabling condition with the high probability of an unfavorable prognosis. [8,9] Work in production with harmful occupational factors (dust of various types, chemicals) affecting the respiratory system contributes to the development of COPD in non-smokers and increases the risk in smokers.

According to the authors *G.Prozorov, O.Tudanova and others* (2004), in sheet of rolling production with harmful working conditions of the working group there were 441 workplaces, 39% of them smoking. COPD was detected in 140 surveyed workers, which composed (31,8%). Among the 98% of surveyed workers were smokers. COPD I stage identified in 122 and second stage isin 18. Among workers who had no contact with harmful production factors and did not smoke, COPD was diagnosed in 123 (8.3%), 9 of them were non-smokers. Scientific research was conducted in the main workshops of the Nizhny Tagil Metallurgical Plant (Nizhny Tagil) and the Pervouralsk New Pipe Plant (Pervouralsk), where workers were exposed to industrial dust containing iron oxide, graphite, divandium pentoxide, and mangene oxide. The concentration of these dusts was 2-6 times higher than the permissible limits. Out of 2,053 examined workers, 1,468 (71.5%) of them were selected for the research of external respiration function (EFD). According to the ERF data, COPD was diagnosed in 515 workers who are selected for ERF, which amounted to 35.1%. An average age is 45,9 ± 9,4 years. Among those who suffers from COPD, 480 people (93.2%) were smokers with a smoking index of 21.2 ± 1.2 pack years.[22]

Authors of the research *I.Leshenko, I.Baranova and others (*2004) revealed that COPD of mild severity (stage I according to GOLD) was found in 351 examined people (68.1%) and COPD of moderate severity was found in 123

(23.9%) and 41 people (8.0%) (stages II A and II B, accordingly).

In the research of COPD patients who suffers from an occupational exposure, more severe dyspnea developed who exposed to tobacco only (70.8% vs. 61.6%, P<0.05), than those who exposed to the smoke of biomass only (74.2% vs. 61.6%, P<0.05). This difference stayed significantly even after adjustment for potential factors that may interfere with the treatment. [57]

Not only tobacco smoke, but also occupational dust, chemicals (vapors, irritants and fumes) can themselves cause the development of COPD in women. Among the 49 (16.1%) surveyed women reported that working in conditions of dust pollution for more than 1 year and 21 (6.9%) of them smoked. Prevalence of smoking factor among women who exposed to dust pollution amounted to 42.9%.[21]

Among 49 (16,1%) women, 12 (24,5%) of them were diagnosed violation of bronchial patency, from 21 of smoking women —6 of them (28,6%) had a decrease in indicator FEV1<80% D; among 28 non-smoking women —6 (21,4%). [21]

In addition, COPD patients with occupational exposure developed more severe dyspnea than those who exposed to tobacco alone (70.8% vs 61.6%, P < 0.05), as those who exposed to biomass smoke only (74.2% vs 61.6%, P < 0.05).This difference stayed significant even after adjusting by taking account potential factors, which can interfere with treatment. [21].

The researches of *A.Kuzubova, E.Kiseleva, O.Titova, N.Egorova* studied the influence of risk factors, exactly occupational hazards, on the development of COPD in men of working age in St. Petersburg

The data of 314 men (average age 53.7 ± 3.8 years) was analyzed, 98 men (31.2%) worked in conditions of dust pollution for more than 1 year. In 70 respondents (71.4%), a combination of risk factors (occupational hazards and smoking history) was observed, and 1/3 of respondents had occupational hazards and did not smoke. The data obtained by the authors *A.Kuzubova, E.Kiseleva and others* are consistent with the results of international scientific works. There are 10,000 adults in the III NHANES large-scale research.

Authors *L.Aftanas and others* conducted research on determining the connection between COPD and profession, which was studied at the Department of Occupational Patology of the Novosibirsk Clinical Hospital №2.The data obtained in conditions of exposure to inorganic dust indicating that the professional COPD (PCOPD) differed from the tobacco COPD by high serum concentrations: serous concentration of monocyte-based chemotaxis protein 1 ( MCH1) (in patients with PCOPD - 3 times, in workers with normal lung function - 1.5 times), extracellular superoxide dismutase (SOD3) (in patients with PCOPD - 1.9 times, in healthy workers - 1.6 times), fibroblast growth factor 2 (FGF2) (in patients with PCOPD - 6.1 times, in healthy workers - 3.9 times) and 8-isoprostaglandin F2α (8-iso-PGF2α) PGF2α (in patients with PCOPD - 3.6 times). [6]

The development of occupational chronic obstructive pulmonary disease from the action of toxic gases was studied in the research work, where the high serum concentration (HMI) was determined at 3 times, and in workers with normal lung function - 1,5 times, the enzyme of the antioxidant system extracellular copper/zinc-dependent supero sidymo 3 (Cu/ZnSOD 3) in patients with PCOPD and healthy workers - 2 times. , interleukin 1 beta (IL-1β ) 11.2 0.39, and in non-sufferers 1.8 0.26, the factor of fibroblast growth 2 (FGF2) (in patients with PCOPD - 3.1 0.68, in healthy workers - 1.5 0.98). [34] Therefore, from both scientific studies we see that patients who exposed to toxic gases and inorganic dust there is an impact on the cellular and molecular mechanisms of COPD inflammation.

Thus occupational chronic obstructive pulmonary disease (COPD) is the severe illness caused by exposure to industrial aerosols, resulting in severe consequences for the body and increasing mortality.

**Discussion**

The analysis of the literature has shown that the relevance of chronic obstructive pulmonary disease is gaining worldwide global importance both in clinical medicine and in public health. Evidence of this situation is the increasing prevalence and mortality of FOBD. Since 2006-2007 there is the steady development of the prevalence of COPD almost all over the world [60,47] Authors noted that the prevalence of COPD is high, especially in the USA [3,63] in Europe [58, 3, 67], lower prevalence rates are in Korea and China. [64,48] Every year about 3 million people die from COPD worldwide. Researchers predict that by 2030 about 4,5 mln people could die from COPD related with the complications of this disease. [1, 26.]. According to the above mentioned data COPD could be the third cause of the death after cardiovascular and oncological diseases. [26]

The frequency of the prevalence of COPD is observed at the age of 40 and older also it is noted that according to some data up to 50 % of patients with COPD are people of working age (from 40 to 67 years) (*A.Chuchalin*, 2014). The prevalence of COPD among elderly age can be explained by expose of risk factors and the decline of physiological respiratory functions related to the age which starts at about 30-40 years.

Comparing the literature data for 1999,2017 and 2020 the prevalence of COPD among men is higher than among women, as is the risk of gender. [64,58,75.] However, it was noted that the rapid development of COPD in women according to *S.Ovcharenko and co-author* (2009) contribute to the following features of the flow: shorter anamnesis; development of pathology with less smoking age; course of disease with more pronounced shortness of breath; reduced tolerance to physical exertion; fewer associated diseases; parameters of quality of life are worse than in men; higher survival rate [25].

Smoking tobacco is the most researched risk factor of COPD and it should be noted that the disease could be developed in non-smokers. The reason of the prevalence of COPD in non-smokers is not clear still. The risk of the developing of the disease during smoking is 80–90%. [5,31] The prognostic characteristics of COPD are the following: beginning age of smoking, duration and intensity of smoking, social status of smokers, which also affects the death rate from this disease. [3, 23]

The next important risk of developing of COPD is the occupational harmfulness (dust, gas etc.), which affects the

respiratory organs promote the developing of COPD in non-smokers and raise the risk in smokers. The case proportion of occupational COPD(PCOPD) is 10–15 % [50] in the structure of the disease.

**Conclusion.**

Thus, chronic obstructive pulmonary disease is the polyethiological heterogeneous disease, which characterized by increased frequency and mortality. Important risk factors such as age, gender, smoking and occupational harmfulness play important role in the development of this disease. Therefore, COPD is characterized by the pronounced comorbidity, which determines its relevance.

***Conflict of interests.*** *Authors claim about the absence of interests of conflict.*

***Transparency of research.*** *The research was not sponsored. Researchers are fully responsible for providing the final version of the manuscript to the press.*

***Declaration of financial and other interactions.*** *All authors participated in the development of the concept and in designing the research and in writing manuscripts. The final version of the manuscript has been approved by all authors. The authors did not receive a research fee.*

***Литература:***

*1. Авдеев С.Н., Лещенко И.В., Айсанов З.Р., Архипов В.В., Белевский А.С., Овчаренко С.И., Емельянов А.В., Синопальников А.И., Шмелев Е.И., Чучалин А.Г.,* от имени рабочей группы по разработке и пересмотру Федеральных клинических рекомендацийпо ХОБЛ. Новые клинические рекомендации по ХОБЛ – смена парадигмы. Терапевтический архив. 2024. 96(3):292–297.DOI: 10.26442/00403660.2024.03.202646

*2. Альмуханова А.Б., Пивцова А.М., Исмаилова У.У.* Эпидемиологические тенденции хронической обструктивной болезни легких (обзор литературы). Вестник КазНМУ 2020. №2. С.268-272

*3. Антонов Н.С.* Хронические обструктивные болезни легких. М., 1998. С.71.

*4. Архипов В. А., Мендыбаев Е. С., Арингазина А. М.* Эпидемиология хронических неинфекционных заболеваний среди пожилого населения Туркестанской области Республики Казахстан. Наука и здравоохранение. 2019. №6. С. 22-29.

*5. Александрова Е.А., Игнатова Г.Л., Захарова И.А., Гребнева И.В., Королева А.А* Частота выявления хронической обструктивной болезни легких у лиц молодого возраста. Вестник Совета молодых учёных и специалистов Челябинской области 2013. №1 С. 45-49.

*6. Афтанас Л.И., Шпагина2 Л.А., Котов О.С., Шпагин И. С., Кузнецова Г. В., Паначева Л. А., Камнева Н.В., Ерихова С.М.* Клеточно-молекулярные особенности воспаления и выживаемость больных профессиональной хронической обструктивной болезнью легких в условиях воздействия неорганической пыли. Сибирский научный медицинский журнал, 2018. Том 38, № 6, С. 35-42.

*7. Белевский А.С., Визель А.А., Зырянов С.К., Игнатова Г.А., Колбин А.С., Лещенко И.В., Титова О.Н., Фролов М.Ю.* Хроническая обструктивная болезнь легких: проблемы сегодняшнего дня. Практическая пульмонология. 2015. 3: 18-23

8.*Васильева О.С., Кравченко Н.Ю*. Хроническая обструктивная болезнь легких как профессиональное заболевание: факторы риска и проблема медико-социальной реабилитации больных. Рос.мед. журн. 2015. 21. (5). 22–26.

*9. Васильева О.С., Кузьмина Л.П, Кравченко Н.Ю.* Роль молекулярно-генетических исследований в диагностике и профилактике развития профессиональных заболеваний органов дыхания. Пульмонология. 2017. Т. 27, № 2. С.198–205.

*10. Ватутин Н.Т., Смирнова А.С. Тарадин, Г.Г.* Хроническая обструктивная болезнь легких: определение, эпидемиология, патофизиология, клиника и лечение (пересмотр рекомендаций gold 2013 г.). Архив внутренней медицины. 2015. № 6(26). С.5-13.

11. Глобальный опрос взрослого населения о потреблении табака (GATS) в России. URL: http://www.minzdravsoc.ru/health/habits/12 (дата обращения: 06.02.2011).

*12. Джубанова Г.И., Ниязбакиева Г.М., Нускабаева Д.Н., Рауанова Т.Б., Тургумбаева Ф.Д.* Анамнестические данные больных хронической обструктивной болезни легких. Вестник КАЗНМУ. №3-2015. С.147-149

*13. Есетова Г.У., Джунусбекова Г.А., Беркинбаев С.Ф.* Распространенность хронической обструктивной болезни легких среди жителей города Павлодар и Павлодарской области. Медицина. Алматы: 2017. №8. С. 182-186.

*14. Жамакурова А.Н., Смаилова Д.С., Ауезова А.М., Кауышева[1] А. А., Жолдасбекова А. С. Глушкова Н. Е., Кульжанов М. К.* Распространенность и факторы риска хронических респираторных заболеваний: обзор литературы. Наука и Здравоохранение, 2022, 5 (Т.24) Обзор литературы, С.203-211.

*15. Зайцев. А.А., Крюков Е.В.* Обострение хронической обструктивной болезни легких:эпидемиология, основы диагностики,режимы антибактериальной терапии. Практическая пульмонология. 2017. № 4. С.58-61

*16. Зейтказиева С.М.* и др. Эпидемиология хронической обструктивной болезни легких. Вестник Казахского Национального медицинского университета. 2018. №3. С. 130–131.

*17. Измеров Н.Ф., Бухтияров И.В., Прокопенко Л.В., Шиган Е.Е.* Реализация глобального плана действий ВОЗ по охране здоровья работающих в Российской Федерации. Мед. труда и пром. экология. 2015. (9). 4–10.

*18. Измеров Н.Ф, Чучалин. А.Г.* Профессиональные заболевания органов дыхания: национальное руководство / ред. М.: ГЭОТАР-Медиа, 2015. 792 с

*19. Кудрявцева Э.З.* Особенности обострений хронической обструктивной болезни легких у пациентов с различными фенотипами заболевания. Автореферат диссертации на соискание ученой степени кандидата медицинских наук. Москва. 2021. С.23

*20. Кузубова А.Н., Киселева Е.А., Титова О.Н., Егорова Н.В.* Анализ респираторной симптоматики и факторов риска развития хронической обструктивной болезни легких у мужчин трудоспособного возраста Санкт-Петербурга. Коллектив авторов, Санкт-Петербург, 2013, С.15-21.

*21. Кузубова Н.А., Киселева Е.А., Титова О.Н., Ковалева Л.Ф* 1 Вероятные факторы риска развития ХОБЛ у женщин/Вестник УДК 616.24-004 СПбГУ. Сер. 11. 2013. Вып. 2. С.47-57/

*22. Котков В.С., Дзюбайло А. В.* Прогнозирование вероятности развития ХОБЛ в зависимости от стажа курения женщин фертильного возраста. DOI:10.20969/VSKM.2023.16(2).34-38.

*23. Макарова Е.В., Шония М.Л., Любавина Н.А., Меньков Н.В., Сальцев,Варварина Г.Н., Новиков В.В.* Курение у лиц молодого возраста: частота, влияние на функцию лёгких и сывороточный уровень растворимых молекул адгезии. Архив внутренней медицины. 2014. № 2(16), С.60-63

*24. Нугманова Д., Фещенко Ю., Яшина Л.* и др. Распространенность, бремя и факторы риска, связанные с хронической обструктивной болезнью легких в Содружестве Независимых Государств (Украина, Казахстан и Азербайджан): результаты исследования CORE. BMC Pulm. Med. 2018. №18(1). С. 26-34.

25.*Овчаренко С.И., Капустина В.А*. Хроническая обструктивная болезнь легких: особенностиу женщин. Пульмонология. 2009. Т.2. С. 102–112.

*26. Окороков А.Н., Бураков И.И.* Хроническая обструктивная болезнь легкого. Практическое пособие. Минск. «Вышая школа». 2024. С. 21

27. Проект Global Burden of Disease 2019 объединил данные о различных заболеваниях из 204 стран с 1990 по 2019 год

*28. Ризаханова О.А., Авдеев С.Н., Авдеева М.В., Никитина Л.Ю.* Проблемы оказания медицинской помощи больным с хронической обструктивной болезнью легких на административных территориях Российской Федерации. Журнал: Профилактическая медицина. 2023. 26(6): 76-82 DOI: 10.17116/profmed20232606176

*29. Сахарова Г.М., Антонов Н.С. Табакокурение* и репродуктивная функция женщин. РМЖ. Мать и дитя. 2013. №1. С. 12-20.

*30. Серебряков, П.В., Карташев О.И., Федина И.Н.* Клинико-гигиеническая оценка состояния здоровья работников производства меди в условиях Крайнего Севера. Медицина труда и промышленная экология. 2016. № 1. С.25–28.

*31. Чучалин А.Г.* Российское респираторное общество. Федеральные клинические рекомендации по диагностике и лечению хронической обструктивной болезни легких. Пульмонология. 2014. № 3. С.15—54.

32. *Шеранов А.М., Таджиев Ф.С., Джаббарова Н.М.* Особенности клинического течения хронической обструктивной болезни легких у больных гериатрического возраста в Самаркандском регионе Тюменский медицинский журнал. 2013. Том 15, № 2, 32.С.32

*33. Шляфер С.И.* Заболеваемость населения старше трудоспособного возраста Российской Федерации. Современные проблемы здравоохранения и медицинской статистики. 2014. №1. С.16-27.

*34. Шпагина Л.А., Котова О.С., Шпагин И.С., Кузнецова Г.В.* Оптимизация диагностики профессиональной хронической обструктивной болезни легких у работающих в условиях воздействия токсичных газов на основе изучения эндотипов. Вестник современной клинической медицины 2019 Том 12, вып. 1. С.69-78. DOI: 10.20969/VSKM.2019.12(1).69-78

35. Федеральные клинические рекомендации по диагностике и лечению хронической обструктивной болезни легких (проект). М.: Российское респираторное общество; 2017. 68 с.

*36. Adeloye D, Basquill C, Papana A, Chan KY, Rudan I, Campbell H.* An estimate of the prevalence of COPD in Africa: a systematic analysis. COPD. 2015. №12(1). P. 71–81.

*37. Adeloye D.* [и др.]. Global, regional, and national prevalence of, and risk factors for, chronic obstructive pulmonary disease (COPD) in 2019: a systematic review and modelling analysis. The Lancet Respiratory Medicine. 2022. № 5 (10). С. 447–458.

*38. Antonelli Incalzi R., Fuso L., De Rosa M.* et al. Comorbiditycontrybutes to predict mortality of patients with chr onic obstructive pulmonary disease. Eur. Respir. J. 1997. № 10. P. 2794-2800.

39 Barnes P.J. Infl ammatory mechanisms in patients withchronic obstructive pulmoMnary disease. J. Allergy Clin. Immunol. 2016. Vol. 138, № 1. P.16–27

*40. Bird Y., Moraros J., Mahmood R., Esmaeelzadeh S., Soe N.M.* Prevalence and associated factors of COPD among aboriginal peoples in Canada: a cross-sectional study. Int J COPD. 2017. №12. P. 1915–1922.

41. Chen J.C., Mannino M.D. // Curr. Opinionin Pulmonary Medicine. 1999. V. 5. P. 93.

*42. Chuchalin A.G., Khaltaev N., Antonov N.S.* et al. Chronic respiratory diseases and risk factors in 12 regions of the Russian Federation. Int J COPD 2014; 12:963-74.

*43. Chuchalin A.G.* Chronic respiratory diseases and risk factors in 12 regions of the Russian Federation. / A.G. Chuchalin, N.G. Khaltaev, N.S. Antonov [et al.]. Int J Chron Obstruct Pulmon Dis. 2014. Vol.12, №9. P.963-974.

*44. Croft J.B.* et al. Urban-rural county and state differences in chronic obstructive pulmonary disease—United States, 2015. Morbidity and Mortality Weekly Report. 2018. Vol. 67., №7. P. 205-212.

*45. Davis Adeloye, Stephen Chua, Chinwei Lee, Catriona Basquill, Angeliki Papana,* Europa Theodoratou, Harish Nair, Daniela Gasevich, Devi Sridhar, Harry Campbell, Keith Yee Chan, Aziz Sheikh, Igor Rudan Global and regional estimates of the prevalence of COPD: a systematic review and meta-analysis. 2015 Dec;5(2):020415. doi: 10.7189/jogh.05.020415.

*46. Davis Adeloye I, Catriona Baskwill , Angeliki Papana , Keith Yee Chan , Igor Rudan , Harry Campbell.* Estimating the prevalence of COPD in Africa: a systematic review. 2015 Feb. 12(1):71–81. doi: 10.3109/15412555.2014.908834. Epub 2014 Jun 19.1.(38) . ERS. The Europen Respiratory Society Task Force // Eur. Respir.J. 1995. № 8. P. 1398-1420.

47. Edgardo Sobrino, Vilma E. Irazola, Laura Gutierrez, Chun-Shuang Chen, Fernando Lanas, Matias Calandrelli, Jacqueline Ponzo, Nora Mores, Pamela Ceron, Allison Lee, Jiang He, Adolfo L. Rubinstein. Estimating the prevalence of chronic obstructive pulmonary disease in the Southern Cone of Latin America: how different spirometric criteria

may influence disease burden and health policy 82017 Dec 11;17(1):187. doi: 10.1186/s12890-017-0537-9

*48. Fang L.* et al. Chronic obstructive pulmonary disease in China: a nationwide prevalence study. The Lancet Respiratory Medicine. 2018. Vol. 6., №6. P. 421-430.

*49. Finney L.J, Feary J.R, Leonardi-Bee J., Gordon S.B., Mortimer K.* Chronic obstructive pulmonary disease in sub-Saharan Africa: a systematic review. Int J Tuber Lung Dis. 2013. №17. P. 583–589.

50. Fishwick D., Sen D., Barber C., Bradshaw L.,Robinson E., Sumner J. Occupational chronic obstructive pulmonary disease: a standard of care. Occup.Med. (Lond.). 2015. 65. (4). 270–282.

51.GBD 2019 Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease 96 Study 2019. Risk Factors Collaborators*. Lancet. 2020. Vol.396. P.1204– 1222

52. Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease. 2018. Availableьfrom: http://goldcopd.org/gold-reports/ Accessed 2018 Mar 22.

53**.** Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2024. Available at: http://www.goldcopd.org/ Accessed: 29.12.2023.

54. GOLD. Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2018. URL: https://goldcoped.org/. Accessed May 7, 2020.

55. Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease. 2020 https://goldcopd.org

*56. Halpin DMG, Celli BR, Criner GJ,* et al. The GOLD Summit on chronic obstructive pulmonary disease in low- and middle-income countries.*Int* J Tuberc Lung Dis. 2019;23(11):1131-41. DOI:10.5588/ijtld.19.0397

*57. Jia-Xi Duan, Wei Cheng, Yu-Qin Zeng, Yan Chen, Shan Cai, Xin Li, Ying-Qun Zhu, Ming Chen, Mei-Ling Zhou, Li-Bing Ma, Qi-Mi Liu, Ping Chen* Characteristics of Patients with Chronic Obstructive Pulmonary Disease Exposed to Different Environmental Risk Factors: A Large Cross-Sectional Study. 2020 Nov 6:15:2857-2867. doi: 10.2147/COPD.S267114. Collection 2020.

*58. Juan J. Olortegui-Rodriguez, David R. Soriano-Moreno, Alejandro Benitez-Bullón, Pilar P. Pelayo-Luis, Jorge Waringa-Marcelo* Prevalence and incidence of chronic obstructive pulmonary disease in Latin America and the Caribbean: a systematic review and meta-analysis 2022 Jul 6;22(1):273. doi: 10.1186/s12890-022-02067-y. перевести

*59. Kenji Kotaki, Hisao Ikeda, Takeshi Fukuda, Kawano Yuhei, Fumiko Yuki, Masayuki Kawasaki, Kentaro Wakamatsu, Kenzo Sugahara* Trends in the prevalence of COPD in older adults in a Japanese city with air pollution: a cross-sectional study. 2019 Apr 3:14:791–798. doi: 10.2147/COPD.S189372. Electronic Collection 2019.

*60. Landbo C., Prescott E., Lange P.* et al. Prognostis value of nutritional status in chronic obstructive pulmonary disease. Am. J. Respir. Crit. Care Med. 1999. Vol. 160. P. 1856-1861

*61. Mehdi Varmaghani, Mina Dehghani, Elham Heydari, Farshad Sharifi, Sahar Saidi Moghaddam, Farshad Farzadfar.* Global prevalence of chronic obstructive pulmonary disease: a systematic review and meta-analysis. 2019 Mar 19;25(1):47-57. doi: 10.26719/emhj.18.014.

*62. Nadia Al Wahamy, Morad Ghennouni, Younes Iderdar, Karima Boumendil, Maryem Arraji, Yassmin Mouradjid, Fatima Zahra Bouchachi, Mohamed Barkaoui, Mohamed Lahbib Louerdi, Abderraouf Hilali, Mohamed Chahboun.* Estimating the global prevalence of chronic obstructive pulmonary disease (COPD): a systematic review and meta-analysis. BMC Public Health 2024 Jan 25;24(1):297. doi: 10.1186/s12889-024-17686-9.

63. National Health and Nutrition Examination Survey III (NHANES III, 1998.94), Centers for Disease Control and Prevention/National Center for Health Statistics

*64. Park H.* et al. Prevalence of chronic obstructive lung disease in Korea using data from the fifth Korea national health and nutrition examination survey. Korean journal of family medicine. 2015. Vol. 36, №3. P. 128-136

*65. Saeid Safiri, Kristin Carson-Chahhoud, Maryam Noori,* et al, Burden of chronic obstructive pulmonary disease and its attributable risk factors in 204 countries and territories, 1990-2019: results from the Global Burden of Disease Study 2019. BMJ 2022;378:e069679

*66. Sobrino E.* et al. Estimating prevalence of chronic obstructive pulmonary disease in the Southern Cone of Latin America: how different spirometric criteria may affect disease burden and health policies. BMC pulmonary medicine. 2017. Vol. 17, №1. P. 1-10

*67. Tsuyoshi Nishinakagawa, Hideaki Senju, Takako Tanaka, Masaharu Asai, Kenji Kotaki, Yudai Yano, Naomi Miyamoto, Yorihide Yanagita, Ryo Kozu, Mitsuru Tabusadani, Sumihisa Honda.* Smoking worsens lung function in women officially exposed to air pollution 40 years ago. 2014 Oct. 234(2):151-60.doi: 10.1620/tjem.234.151

*68. Van Gemert F, Kirenga B., Chavannes N., Kamya M., Luzige S., Musinguzi P.,* et al. Prevalence of chronic obstructive pulmonary disease and associated risk factors in Uganda (FRESH AIR Uganda): a prospective cross-sectional observational study. Lancet Glob Health. 2015. №3. P. 44–56

69. World Health Organization. Chronic obstructive pulmonary disease (COPD). 2017. URL: https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd). Accessed 7 May 2020.

*70. Woldeamanuel G.G., Mingude A.B., Geta T.G.* Prevalence of chronic obstructive pulmonary disease (COPD) and its associated factors among adults in Abeshge District, Ethiopia: a cross sectional study. BMC Pulmonary Medicine. 2019. Vol. 19, №1. P. 181-188.

***References: [1-35]***

1. Avdeev S.N., Leshchenko I.V., Aisanov Z.R., Arkhipov V.V., Belevskii A.S., Ovcharenko S.I., Emel'yanov A.V., Sinopal'nikov A.I., Shmelev E.I., Chuchalin A.G. Ot imeni rabochei gruppy po razrabotke i peresmotru Federal'nykh klinicheskikh rekomendatsiipo KhOBL. Novye klinicheskie rekomendatsii po KhOBL – smena paradigm

[On behalf of the working group for the development and revision of Federal Clinical Guidelines for COPD. New clinical guidelines for COPD: a paradigm shift.]. *Terapevticheskii arkhiv* [Therapeutic archive]. 2024. 96(3):292–297. DOI:10.26442/00403660.2024.03.202646 [in Russian]

2. Al'mukhanova A.B., Pivtsova A.M., Ismailova U.U. Epidemiologicheskie tendentsii khronicheskoi obstruktivnoi bolezni legkikh (obzor literatury) [Epidemiological trends in chronic obstructive pulmonary disease (literature review)]. *Vestnik KazNMU* [Bulletin of KazNMU]. 2020. №2. pp.268-272 [in Russian]

3. Antonov N.S. Khronicheskie obstruktivnye bolezni legkikh [Chronic obstructive pulmonary diseases]. M., 1998. p.71. [in Russian]

4. Arkhipov V. A., Mendybaev E. S., Aringazina A. M. Epidemiologiya khronicheskikh neinfektsionnykh zabolevanii sredi pozhilogo naseleniya Turkestanskoi oblasti Respubliki Kazakhstan [Epidemiology of chronic non-communicable diseases among the elderly population of the Turkestan region of the Republic of Kazakhstan]. *Nauka i zdravookhranenie* [Science and Healthcare]. 2019. №6. pp. 22-29. [in Russian]

5. Aleksandrova E.A., Ignatova G.L., Zakharova I.A., Grebneva I.V., Koroleva A.A Chastota vyyavleniya khronicheskoi obstruktivnoi bolezni legkikh u lits molodogo vozrasta [Frequency of detection of chronic obstructive pulmonary disease in young people]. *Vestnik Soveta molodykh uchenykh i spetsialistov Chelyabinskoi oblasti* [Bulletin of the Council of Young Scientists and Specialists of the Chelyabinsk Region] 2013. №1. pp. 45-49. [in Russian]

6. Aftanas L.I., Shpagina2 L.A., Kotov O.S., Shpagin I. S., Kuznetsova G. V., Panacheva L. A., Kamneva N.V., Erikhova S.M. Kletochno-molekulyarnye osobennosti vospaleniya i vyzhivaemost' bol'nykh professional'noi khronicheskoi obstruktivnoi bolezn'yu legkikh v usloviyakh vozdeistviya neorganicheskoi pyli [Cellular and molecular features of inflammation and survival of patients with occupational chronic obstructive pulmonary disease exposed to inorganic dust]. *Sibirskii nauchnyi meditsinskii zhurnal* [Siberian Scientific Medical Journal], 2018. Tom 38, № 6, pp. 35-42. [in Russian]

7. Belevskii A.S., Vizel' A.A., Zyryanov S.K., Ignatova G.A., Kolbin A.S., Leshchenko I.V., Titova O.N., Frolov M.Yu. Khronicheskaya obstruktivnaya bolezn' legkikh: problemy segodnyashnego dnya [Chronic obstructive pulmonary disease: problems of today]. *Prakticheskaya pul'monologiya* [Practical pulmonology]. 2015. 3: 18-23. [in Russian]

8. Vasil'eva O.S., Kravchenko N.Yu. Khronicheskaya obstruktivnaya bolezn' legkikh kak professional'noe zabolevanie: faktory riska i problema mediko-sotsial'noi reabilitatsii bol'nykh [Chronic obstructive pulmonary disease as an occupational disease: risk factors and the problem of medical and social rehabilitation of patients.]. *Ros.med. zhurn.* [Ros.med. zhurn.]. 2015. 21. (5). 22–26. [in Russian]

9. Vasil'eva O.S., Kuz'mina L.P., Kravchenko N.Yu. Rol' molekulyarno-geneticheskikh issledovanii v diagnostike i profilaktike razvitiya professional'nykh zabolevanii organov dykhaniya [The role of molecular genetic studies in the diagnosis and prevention of occupational respiratory diseases]. *Pul'monologiya* [Pulmonology]. 2017. T. 27, № 2. pp.198–205. [in Russian]

10. Vatutin N.T., Smirnova A.S. Taradin, G.G. Khronicheskaya obstruktivnaya bolezn' legkikh: opredelenie, epidemiologiya, patofiziologiya, klinika i lechenie (peresmotr rekomendatsii gold 2013 g.) [Chronic obstructive pulmonary disease: definition, epidemiology, pathophysiology, clinical picture and treatment (revision of the 2013 gold recommendations)]. *Arkhiv vnutrennei meditsiny* [Archives of Internal Medicine]. 2015. № 6(26). pp. 5-13. [in Russian]

11. *Global'nyi opros vzroslogo naseleniya o potreblenii tabaka (GATS) v Rossii* [Global Adult Tobacco Survey (GATS) in Russia.]. URL: http://www.minzdravsoc.ru/health/habits/12 (accessed: 06.02.2011). [in Russian]

12. Dzhubanova G.I., Niyazbakieva G.M., Nuskabaeva D.N., Rauanova T.B., Turgumbaeva F.D. Anamnesticheskie dannye bol'nykh khronicheskoi obstruktivnoi bolezni legkikh [Anamnestic data of patients with chronic obstructive pulmonary disease]. *Vestnik KAZNMU* [Bulletin of KAZNMU]. №3-2015. pp.147-149. [in Russian]

13. Esetova G.U., Dzhunusbekova G.A., Berkinbaev S.F. Rasprostranennost' khronicheskoi obstruktivnoi bolezni legkikh sredi zhitelei goroda Pavlodar i Pavlodarskoi oblasti [Prevalence of chronic obstructive pulmonary disease among residents of Pavlodar and Pavlodar region]. Meditsina [Medicine]. Almaty: 2017. №8. pp. 182-186. [in Russian]

14. Zhamakurova A.N., Smailova D.S., Auezova A.M., Kauysheva¹ A. A., Zholdasbekova A. S. Glushkova N. E., Kul'zhanov M. K. Rasprostranennost' i faktory riska khronicheskikh respiratornykh zabolevanii: obzor literatury [Prevalence and risk factors of chronic respiratory diseases: a literature review]. *Nauka i Zdravookhranenie* [Science and Healthcare], 2022, 5 (T.24) Obzor literatury, pp.203-211. [in Russian]

15. Zaitsev. A.A., Kryukov E.V. Obostrenie khronicheskoi obstruktivnoi bolezni legkikh:epidemiologiya, osnovy diagnostiki,rezhimy antibakterial'noi terapii [Exacerbation of chronic obstructive pulmonary disease: epidemiology, diagnostic principles, antibacterial therapy regimens]. *Prakticheskaya pul'monologiya* [Practical pulmonology]. 2017. № 4. pp.58-61. [in Russian]

16. Zeitkazieva S.M. i dr. Epidemiologiya khronicheskoi obstruktivnoi bolezni legkikh [Epidemiology of chronic obstructive pulmonary disease]. *Vestnik Kazakhskogo Natsional'nogo meditsinskogo universiteta* [Bulletin of the Kazakh National Medical University]. 2018. №3. pp. 130–131. [in Russian]

17. Izmerov N.F., Bukhtiyarov I.V., Prokopenko L.V., Shigan E.E. Realizatsiya global'nogo plana deistvii VOZ po okhrane zdorov'ya rabotayushchikh v Rossiiskoi Federatsii [Implementation of the WHO global action plan for workers' health in the Russian Federation]. *Med. truda i prom. Ekologiya* [Med. labor and industrial ecology]. 2015. (9). 4–10. [in Russian]

18. Izmerov N.F, Chuchalin. A.G. Professional'nye zabolevaniya organov dykhaniya: natsional'noe rukovodstvo [Occupational respiratory diseases: national guidelines]. red. M.: GEOTAR-Media, 2015. 792 p. [in Russian]

19. Kudryavtseva E.Z. *Osobennosti obostrenii khronicheskoi obstruktivnoi bolezni legkikh u patsientov s razlichnymi fenotipami zabolevaniya*. Avtoreferat dissertatsii na soiskanie uchenoi stepeni kandidata meditsinskikh nauk [Features of exacerbations of chronic obstructive pulmonary disease in patients with different phenotypes of the disease. Abstract of a dissertation for the degree of candidate of medical sciences]. Moskva. 2021. p.23. [in Russian]

20. Kuzubova A.N., Kiseleva E.A., Titova O.N., Egorova N.V. *Analiz respiratornoi simptomatiki i faktorov riska razvitiya khronicheskoi obstruktivnoi bolezni legkikh u muzhchin trudosposobnogo vozrasta Sankt-Peterburga* [Analysis of respiratory symptoms and risk factors for the development of chronic obstructive pulmonary disease in men of working age in St. Petersburg], Sankt-Peterburg, 2013, pp.15-21. [in Russian]

21. Kuzubova N.A., Kiseleva E.A., Titova O.N., Kovaleva L.F. Veroyatnye faktory riska razvitiya KhOBL u zhenshchin [Probable risk factors for the development of COPD in women]. *Vestnik UDK* [Bulletin of UDC] 616.24-004 SPbGU. Ser. 11. 2013. Vyp. 2. pp.47-57. [in Russian]

22. Kotkov V.S., Dzyubailo A. V. *Prognozirovanie veroyatnosti razvitiya KhOBL v zavisimosti ot stazha kureniya zhenshchin fertil'nogo vozrasta* [Predicting the likelihood of developing COPD depending on the smoking experience of women of childbearing age]. DOI:10.20969/VSKM.2023.16(2).34-38. [in Russian]

23. Makarova E.V., Shoniya M.L., Lyubavina N.A., Men'kov N.V., Sal'tsev,Varvarina G.N., Novikov V.V. Kurenie u lits molodogo vozrasta: chastota, vliyanie na funktsiyu legkikh i syvorotochnyi uroven' rastvorimykh molekul adgezii [Smoking in young people: frequency, impact on lung function and serum levels of soluble adhesion molecules]. *Arkhiv vnutrennei meditsiny* [Archives of Internal Medicine]. 2014. № 2(16), pp.60-63. [in Russian]

24. Nugmanova D., Feshchenko Yu., Yashina L. i dr. Rasprostranennost', bremya i faktory riska, svyazannye s khronicheskoi obstruktivnoi bolezn'yu legkikh v Sodruzhestve Nezavisimykh Gosudarstv: (Ukraina, Kazakhstan i Azerbaidzhan): rezul'taty issledovaniya CORE. [Prevalence, burden and risk factors associated with chronic obstructive pulmonary disease in the Commonwealth of Independent States: (Ukraine, Kazakhstan and Azerbaijan): results of the CORE study]. *BMC Pulm. Med.* 2018. №18(1). pp. 26-34. [in Russian]

25. Ovcharenko S.I., Kapustina V.A. Khronicheskaya obstruktivnaya bolezn' legkikh: osobennostiu zhenshchin [Chronic obstructive pulmonary disease: features in women]. Pul'monologiya [Pulmonology] [in Russian]. 2009. T.2. pp. 102–112. [in Russian]

26. Okorokov A.N., Burakov I.I. *Khronicheskaya obstruktivnaya bolezn' legkogo. Prakticheskoe posobie* [Chronic obstructive pulmonary disease. Practical manual]. Minsk. «Vyshaya shkola». 2024. 21 p. [in Russian]

27. Proekt Global Burden of Disease 2019 ob"edinil dannye o razlichnykh zabolevaniyakh iz 204 stran s 1990 po 2019 god [The Global Burden of Disease 2019 project combined data on various diseases from 204 countries from 1990 to 2019]. [in Russian].

28. Rizakhanova O.A., Avdeev S.N., Avdeeva M.V., Nikitina L.Yu. Problemy okazaniya meditsinskoi pomoshchi bol'nym s khronicheskoi obstruktivnoi bolezn'yu legkikh na administrativnykh territoriyakh Rossiiskoi Federatsii [Problems of providing medical care to patients with chronic obstructive pulmonary disease in the administrative territories of the Russian Federation]. *Zhurnal: Profilakticheskaya meditsina* [Journal: Preventive Medicine]. 2023. 26(6): 76 82 DOI: 10.17116/profmed20232606176 [in Russian]

29. Sakharova G.M., Antonov N.S. Tabakokurenie i reproduktivnaya funktsiya zhenshchin [Tobacco smoking and reproductive function of women]. *RMZh. Mat' i ditya* [RMJ. Mother and Child]. 2013. №1. pp. 12-20. [in Russian]

30. Serebryakov, P.V., Kartashev O.I., Fedina I.N. Kliniko-gigienicheskaya otsenka sostoyaniya zdorov'ya rabotnikov proizvodstva medi v usloviyakh Krainego Severa [Clinical and hygienic assessment of the health status of copper production workers in the Far North. Occupational]. *Meditsina truda i promyshlennaya ekologiya* [Medicine and Industrial Ecology]. 2016. № 1. pp.25–28. [in Russian]

31. Chuchalin A.G. Rossiiskoe respiratornoe obshchestvo. Federal'nye klinicheskie rekomendatsii po diagnostike i lecheniyu khronicheskoi obstruktivnoi bolezni legkikh [Russian Respiratory Society. Federal clinical guidelines for the diagnosis and treatment of chronic obstructive pulmonary disease]. *Pul'monologiya* [Pulmonology.]. 2014. № 3. pp.15—54. [in Russian]

32. Sheranov A.M., Tadzhiev F.S., Dzhabbarova N.M. Osobennosti klinicheskogo techeniya khronicheskoi obstruktivnoi bolezni legkikh u bol'nykh geriatricheskogo vozrasta v Samarkandskom regione [Features of the clinical course of chronic obstructive pulmonary disease in geriatric patients]. *Tyumenskii meditsinskii zhurnal* [Samarkand region Tyumen Medical Journal]. 2013. Tom 15, № 2, 32. pp.32[in Russian]

33. Shlyafer S.I. Zabolevaemost' naseleniya starshe trudosposobnogo vozrasta Rossiiskoi Federatsii [Morbidity of the population over working age in the Russian Federation]. *Sovremennye problemy zdravookhraneniya i meditsinskoi statistiki* [Modern problems of health care and medical statistics]. 2014. №1. pp.16-27. [in Russian]

34. Shpagina L.A., Kotova O.S., Shpagin I.S., Kuznetsova G.V. Optimizatsiya diagnostiki professional'noi khronicheskoi obstruktivnoi bolezni legkikh u rabotayushchikh v usloviyakh vozdeistviya toksichnykh gazov na osnove izucheniya endotipov [Optimization of diagnostics of occupational chronic obstructive pulmonary disease in workers exposed to toxic gases based on the study of endotypes]. *Vestnik sovremennoi klinicheskoi meditsiny* [Bulletin of Modern Clinical Medicine]. 2019 Tom 12, vyp. 1. pp.69-78. DOI: 10.20969/VSKM.2019.12(1).69-78 [in Russian]

35. *Federal'nye klinicheskie rekomendatsii po diagnostike i lecheniyu khronicheskoi obstruktivnoi bolezni legkikh (proekt). M.: Rossiiskoe respiratornoe obshchestvo* [Federal clinical guidelines for the diagnosis and treatment of chronic obstructive pulmonary disease (draft). Moscow: Russian Respiratory Society]. 2017. 68 p. [in Russian]

**Контактная инфмация:**
**Самарова Умытжан Сапаргалиевна -** к.м.н., доцент кафедры «Общественное здоровье», НАО "Медицинский университет Семей". г. Семей, Республика Казахстан. Почтовый адрес: Республика Казахстан, 071400, г. Семей, ул. Абая, д.103. E-mail: samarova58@mail.ru; Телефон: +77779845030
**Калбагаева Жадра Ерболовна -** докторант 1-го года обучения по специальности «Общественное здравоохранение», НАО "Медицинский университет Семей". г. Семей, Республика Казахстан. Почтовый индекс: Республика Казахстан, 071400, г. Семей, ул. Абая, д.103. E-mail: zhadra.kalbagayeva@edu.med.kz Телефон: +77771315558
**Зготова Нурбике Сагимуратовна -** кафедра пропедевтики внутренних болезней НАО "Медицинский университет Семей". г. Семей, Республика Казахстан. Почтовый адрес: Республика Казахстан, 071400, г. Семей, ул. Абая, д.103; E-mail: znurbike16@mail.ru; Телефон: +77771344530
**Егизбаева Гаухар Сериковна -** Начальник отдела медико-статистического анализа и экспертизы .ВКО филиал РГП на ПХВ «Национальный научный центр развития здравоохранения им. Салидат Каирбековой" МЗ РК. Г.Усть-Каменогорск, Республика Казахстан. Почтовый адрес: Республика Казахстан, 070003, ВКО, г. Усть-Каменогорск, ул. Серикбаева,1 E-mail: eqqay1986@mail.ru Телефон: +77714355043
**Ногаева Марал Газизовна** – кандидат медицинских наук, профессор кафедры ревматологии Казахского национального медицинского университета имени С.Д. Асфендиярова, Алматы, Республика Казахстан; https://orcid.org/0000-0003-1182-5967; Почтовый адрес: Республика Казахстан, 050012, г. Алматы, ул. Толе Би 94; e-mail: maral.nogaeva@xmail.ru; Тел.: +7 708 800 52 65.
**Тажибаева Карлыгаш Нартбаевна** — заведующая кафедрой хирургии факультета медицины и здравоохранения Казахского национального университета им. аль-Фараби, г. Алматы, Казахстан. «Алматинская региональная многопрофильная клиника» Министерства здравоохранения Республики Казахстан, доктор медицинских наук, профессор Тел.: +7(778)5704616. Email: karlygashtazhibay@gmail.com, karla_ag@mail.ru; ORCID: https://orcid.org/0000-0003-4947-3717 Scopus ID: 57914882300
**Ибраева Торгын Берикжановна** - магистр, ассистент кафедры дерматовенерологии и дерматокосметологии, НАО «Медицинский университет Астана», г. Астана, Республика Казахстан, ibraeva.t@amu.kz; https://orcid.org/0009-0007-4788-7410
**Искакова Асель Маратбековна** - доктор философии, кафедра общественного здравоохранения, НАО «Медицинский университет Семей», г. Семей, iskassel@yandex.ru, https://orcid.org/0009-0003-0144-6100

**Автор-корреспондент:**
**Самарова Умытжан Сапаргалиевна -** к.м.н., доцент кафедры «Общественное здоровье», НАО "Медицинский университет Семей". г. Семей, Республика Казахстан.
**Почтовый адрес:** Республика Казахстан, 071400, г. Семей, ул. Абая, д.103.
**E-mail:** samarova58@mail.ru;
**Телефон:** +77779845030

Received: 11 February 2025 / Accepted: 20 June 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2025.27.3.023***

***UDC 616.24-002.5-036.22:613.95***

This work is licensed under a Creative Commons Attribution 4.0 International License

# THE QUALITY OF LIFE OF PATIENTS WITH COPD. LITERATURE REVIEW

**Zhadra Ye. Kalbagayeva[1],** **http://orcid.org/0000-0003-3310-4490**
**Zaituna A. Khismetova[1],** **https://orcid.org/0000-0001-5937-3045**
**Nazym S. Iskakova[1],** **https://orcid.org/0000-0001-5631-5499**
**Aliya K. Atabayeva[1],** **http://orcid.org/0000-0001-7725-2255**
**Dinara S. Serikova-Esengeldina[1],** **https://orcid.org/0000-0002-9470-9488**
**Nurgul G. Razakova[1],** **https://orcid.org/0000-0003-2031-8692**
**Aizhan B. Zheksebergenova[1],** **https://orcid.org/0009-0001-4633-1222**

**[1] NCJSC «Semey Medical University», Semey, Republic of Kazakhstan.**

**Abstract**

**Background:** Chronic obstructive pulmonary disease (COPD) is a progressive respiratory condition that substantially impairs patients' health-related quality of life (HRQoL). Beyond lung function deficits, a variety of clinical, psychological, and social factors influence how COPD patients experience their daily lives. Over the past decade, research has increasingly focused on identifying key determinants of QoL in COPD, recognizing that improving QoL is a primary goal of COPD management. This narrative review summarizes evidence (2015–2025) on major factors affecting QoL in COPD patients, including disease severity, comorbid conditions, psychological status, physical activity, exacerbation frequency, social support, access to care, and treatment adherence. Consistent themes and gaps in the literature are highlighted, and we conclude by discussing how these factors interact to shape patient outcomes and where future research is needed.

**Objective.** The primary objective of this review was to summarize and analyze modern approaches aimed at improving the quality of life in patients with chronic obstructive pulmonary disease (COPD). Specific focus was placed on pharmacological therapies, pulmonary rehabilitation, psychosocial interventions, telehealth, self-management education, lifestyle modifications, and integrated care models.

**Search strategy.** A narrative literature review was conducted using electronic databases including PubMed, Scopus, and Cochrane Library. The search included studies published from 2015 to 2025 using keywords such as: "COPD", "quality of life", "pulmonary rehabilitation", "self-management", "psychological interventions", "digital health", "triple therapy", and "integrated care". Preference was given to systematic reviews, randomized controlled trials, and high-quality cohort studies published in peer-reviewed journals in English.

**Results and conclusions.** Recent studies confirm that various modern interventions can significantly improve the quality of life in COPD patients. Optimized pharmacological treatments, particularly triple inhaler therapy, help reduce symptoms and exacerbations. Pulmonary rehabilitation consistently enhances physical function and well-being. Psychological support, including cognitive-behavioral therapy, reduces anxiety and depression, positively affecting emotional health. Telehealth and mobile tools improve patient engagement and self-management, while structured education programs lead to better disease control and reduced hospital visits. Nutritional support and regular physical activity improve strength, endurance, and daily functioning. Integrated, multidisciplinary care models have shown the strongest overall impact, improving both quality of life and healthcare outcomes when delivered in a coordinated and patient-centered manner.

***Keywords:*** *COPD, quality of life, pulmonary rehabilitation, self-management, psychological interventions, digital health, triple therapy, integrated care.*

***For citation:***

*Kalbagayeva Zh.Ye., Khismetova Z.A., Iskakova N.S., Atabayeva A.K., Serikova-Esengeldina D.S. Razakova N.G., Zheksebergenova A.B.* The quality of life of patients with COPD. Literature review // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 215-226. *doi 10.34689/SH.2025.27.3.023*

**Резюме**

# КАЧЕСТВО ЖИЗНИ ПАЦИЕНТОВ С ХОБЛ. ОБЗОР ЛИТЕРАТУРЫ

**Жадра Е. Калбагаева[1],** http://orcid.org/0000-0003-3310-4490
**Зайтуна А. Хисметова[1],** https://orcid.org/0000-0001-5937-3045
**Назым С. Искакова[1],** https://orcid.org/0000-0001-5631-5499
**Алия К. Атабаева[1],** http://orcid.org/0000-0001-7725-2255
**Динара С. Серикова-Есенгелдина[1],** https://orcid.org/0000-0002-9470-9488
**Нургуль Г. Разакова[1],** https://orcid.org/0000-0003-2031-8692
**Айжан Б. Жаксебергенова[1],** https://orcid.org/0009-0001-4633-1222

**[1] НАО «Медицинский университет Семей», г. Семей, Республика Казахстан.**

**Введение:** Хроническая обструктивная болезнь легких (ХОБЛ) - это прогрессирующее респираторное заболевание, которое существенно ухудшает качество жизни пациентов, связанное со здоровьем. Помимо нарушения функции легких, на повседневную жизнь пациентов с ХОБЛ влияют различные клинические, психологические и социальные факторы. В течение последнего десятилетия исследования все больше фокусировались на выявлении ключевых факторов, определяющих качество жизни при ХОБЛ, признавая, что улучшение качества жизни является основной целью лечения ХОБЛ. В этом обзоре обобщены фактические данные (2015-2025 гг.) об основных факторах, влияющих на качество жизни пациентов с ХОБЛ, включая тяжесть заболевания, сопутствующие состояния, психологический статус, физическую активность, частоту обострений, социальную поддержку, доступ к медицинской помощи и приверженность лечению. Выделяются общие темы и пробелы в литературе, и в заключение мы обсуждаем, как эти факторы влияют на результаты лечения пациентов и где необходимы будущие исследования.

**Цель.** Основной целью данного обзора было обобщение и анализ современных подходов, направленных на улучшение качества жизни пациентов с хронической обструктивной болезнью легких (ХОБЛ). Особое внимание было уделено фармакологической терапии, легочной реабилитации, психосоциальным вмешательствам, телемедицине, обучению самоуправлению, изменению образа жизни и моделям комплексного ухода.

**Стратегия поиска.** Обзор научной литературы был проведен с использованием электронных баз данных, включая PubMed, Scopus и Кокрановскую библиотеку. Поиск включал исследования, опубликованные с 2015 по 2025 годы, с использованием таких ключевых слов, как “ХОБЛ”, “качество жизни”, “легочная реабилитация”, “самоуправление”, “психологические вмешательства”, “цифровое здравоохранение”, “тройная терапия” и “комплексная помощь”. Предпочтение отдавалось систематическим обзорам, рандомизированным контролируемым исследованиям и высококачественным когортным исследованиям, опубликованным в рецензируемых журналах на английском языке.

**Результаты и выводы.** Недавние исследования подтверждают, что различные современные вмешательства могут значительно улучшить качество жизни пациентов с ХОБЛ. Оптимизированные фармакологические методы лечения, в частности терапия тройными ингаляторами, помогают уменьшить симптомы и обострения. Легочная реабилитация неизменно улучшает физические функции и самочувствие. Психологическая поддержка, включая когнитивно-поведенческую терапию, снижает тревожность и депрессию, положительно влияя на эмоциональное здоровье.

Телемедицина и мобильные инструменты улучшают взаимодействие с пациентами и их самоуправление, в то время как структурированные образовательные программы улучшают контроль заболеваний и сокращают количество посещений больниц. Поддержка в питании и регулярная физическая активность повышают силу, выносливость и улучшают повседневную жизнедеятельность. Интегрированные, мультидисциплинарные модели оказания медицинской помощи показали наибольший общий эффект, улучшая как качество жизни, так и результаты медицинского обслуживания, если они предоставляются скоординированно и с учетом интересов пациента.

***Ключевые слова:*** *ХОБЛ, качество жизни, легочная реабилитация, самоуправление, психологические вмешательства, цифровое здравоохранение, тройная терапия, комплексная помощь.*

***Для цитирования:***

*Калбагаева Ж.Е., Хисметова З.А., Искакова Н.С., Атабаева А.К., Серикова-Есенгелдина Д.С., Разакова Н.Г., Жаксебергенова А.Б.* Качество жизни пациентов с ХОБЛ (обзор литературы) // Наука и Здравоохранение. 2025. Т.27 (3), С. 215-226. doi: 10.34689/SH.2025.27.3.023

**Түйіндеме**

# СОӨА БАР НАУҚАСТАРДЫҢ ӨМІР САПАСЫ. ӘДЕБИЕТТІК ШОЛУ

**Жадра Е. Калбагаева[1], http://orcid.org/0000-0003-3310-4490**
**Зайтуна А. Хисметова[1], https://orcid.org/0000-0001-5937-3045**
**Назым С. Искакова[1], https://orcid.org/0000-0001-5631-5499**
**Алия К. Атабаева[1], http://orcid.org/0000-0001-7725-2255**
**Динара С. Серикова-Есенгелдина[1], https://orcid.org/0000-0002-9470-9488**
**Нургуль Г. Разакова[1], https://orcid.org/0000-0003-2031-8692**
**Айжан Б. Жаксебергенова[1], https://orcid.org/0009-0001-4633-1222**

**[1] «Семей медицина университеті» КеАҚ,**
**Семей қ., Қазақстан Республикасы.**

**Кіріспе:** Созылмалы обструктивті өкпе ауруы (СОӨА) – науқастың денсаулыққа байланысты өмір сапасын айтарлықтай төмендететін үдемелі респираторлық ауру. Өкпе қызметінің бұзылуымен қатар, СОӨА-мен ауыратын науқастардың күнделікті өміріне түрлі клиникалық, психологиялық және әлеуметтік факторлар әсер етеді. Соңғы онжылдықта зерттеулер СОӨА жағдайында өмір сапасына әсер ететін негізгі факторларды анықтауға көбірек көңіл бөлуде, өйткені өмір сапасын жақсарту осы ауруды емдеудің басты мақсаты ретінде қарастырылады. Бұл шолуда 2015–2025 жылдар аралығындағы дәлелді деректер негізінде СОӨА-мен ауыратын науқастардың өмір сапасына әсер ететін негізгі факторлар қарастырылады: аурудың ауырлығы, қатар жүретін аурулар, психологиялық жағдай, физикалық белсенділік, өршулердің жиілігі, әлеуметтік қолдау, медициналық көмекке қолжетімділік және емдеуге бейілділік. Әдебиеттегі ортақ тақырыптар мен олқылықтар айқындалып, соңында осы факторлардың ем нәтижелеріне қалай әсер ететіні және болашақ зерттеулердің бағыттары талқыланады.

**Мақсаты:** Бұл шолудың негізгі мақсаты – созылмалы обструктивті өкпе ауруымен (СОӨА) ауыратын науқастардың өмір сапасын жақсартуға бағытталған заманауи тәсілдерді жинақтап, талдау. Ерекше назар фармакологиялық терапияға, өкпелік оңалтуға, психоәлеуметтік араласуларға, телемедициналық шешімдерге, өзін-өзі басқаруды оқытуға, өмір салтын өзгертуге және кешенді күтім үлгілеріне аударылды.

**Іздеу стратегиясы:** Ғылыми әдебиеттерге шолу PubMed, Scopus және Кокрейн кітапханасы секілді электронды мәліметтер базасы арқылы жүргізілді. Іздеу 2015–2025 жылдар аралығында жарияланған зерттеулерді қамтыды және келесі негізгі сөздер пайдаланылды: "СОӨА", "өмір сапасы", "өкпелік оңалту", "өзін-өзі басқару", "психологиялық араласулар", "цифрлық денсаулық сақтау", "үштік терапия" және "кешенді көмек". Артықшылық жүйелі шолуларға, рандомизацияланған бақыланатын зерттеулерге және жоғары сапалы когорттық зерттеулерге берілді, олар ағылшын тіліндегі рецензияланған журналдарда жарияланған.

**Нәтижелер мен қорытындылар:** Соңғы зерттеулер көрсеткендей, түрлі заманауи араласулар СОӨА-мен ауыратын науқастардың өмір сапасын едәуір жақсарта алады. Фармакологиялық емдеу әдістерін оңтайландыру, әсіресе үштік ингаляциялық терапия, симптомдар мен өршулерді азайтады. Өкпелік оңалту физикалық функция мен әл-ауқатты тұрақты жақсартады. Когнитивті-бихевиоральдық терапияны қамтитын психологиялық қолдау мазасыздық пен депрессияны төмендетіп, эмоционалдық денсаулықты жақсартады.

Телемедицина мен мобильді құралдар пациенттердің өз-өзін басқаруын және медицина қызметкерлерімен өзара іс-әрекетін жақсартады, ал құрылымдалған білім беру бағдарламалары ауруды бақылауды жақсартып, ауруханаға жатқызу жиілігін төмендетеді. Тамақтануды қолдау және тұрақты физикалық белсенділік бұлшықет күшін, төзімділікті арттырып, күнделікті өмір сапасын жақсартады. Интеграцияланған, мультидисциплинарлық медициналық көмек үлгілері жалпы тиімділікке қол жеткізіп, өмір сапасы мен медициналық қызмет нәтижелерін жақсартады, егер олар үйлестіріліп және пациенттің мүддесін ескере отырып ұсынылса.

***Кілт сөздер:*** *СОӨА, өмір сапасы, өкпелік оңалту, өзін-өзі басқару, психологиялық араласулар, цифрлық денсаулық сақтау, үштік терапия, кешенді көмек.*

***Дәйексөз үшін:***

*Калбагаева Ж.Е., Хисметова З.А., Искакова Н.С., Атабаева А.К., Серикова-Есенгелдина Д.С., Разакова Н.Г., Жаксебергенова А.Б.* СОӨА бар науқастардың өмір сапасы. Әдебиеттік шолу // Ғылым және Денсаулық. 2025. Т.27 (3), Б. 215-226. doi: 10.34689/SH.2025.27.3.023

**Introduction**

The quality of life (QoL) in patients with Chronic Obstructive Pulmonary Disease (COPD) is significantly impacted by various factors, including disease severity, comorbidities, and lifestyle habits. COPD is known to cause both physical and mental health challenges, leading to a compromised health-related quality of life (HRQOL) for patients. The presence of comorbid conditions such as hypertension, diabetes, and cardiovascular diseases further exacerbates the decline in QoL. This overview will delve into the specific factors affecting QoL in COPD patients.

Comorbidities like hypertension, diabetes, and hyperlipidemia are associated with a lower QoL in COPD patients. For instance, hypertension affects the "Activity" and "Impact on life" domains, while hyperlipidemia impacts the "Symptoms" and "Impact on life" subscales.

Comorbid conditions such as cardiovascular diseases and diabetes mellitus are significant contributors to the reduced QoL in COPD patients.

The severity of COPD, as classified by the Global Initiative for Obstructive Lung Disease (GOLD) staging, correlates with a decline in HRQOL. More severe stages of COPD result in higher symptom, activity, and impact scores, indicating a poorer QoL[21].

Age is another factor, with older patients experiencing a more significant decline in QoL, particularly in the functional and psychological domains.

Smoking, obesity, and exposure to air pollutants are lifestyle factors that negatively affect the QoL in COPD patients. These factors contribute to both physical and mental health deterioration.

Poor quality of sleep and the presence of comorbidities increase the risk of a poor QoL, with comorbidities posing a 2.716 times higher risk.

While the primary focus is on the negative impacts of COPD on QoL, it is essential to consider the potential for improvement through early diagnosis, lifestyle changes, and comprehensive management plans. Integrating pulmonary rehabilitation and addressing comorbid conditions can help mitigate the decline in QoL for COPD patients.

**Objective.** The primary objective of this review was to summarize and analyze modern approaches aimed at improving the quality of life in patients with chronic obstructive pulmonary disease (COPD). Specific focus was placed on pharmacological therapies, pulmonary rehabilitation, psychosocial interventions, telehealth, self-management education, lifestyle modifications, and integrated care models.

**Search strategy.** A narrative literature review was conducted using electronic databases including PubMed, Scopus, and Cochrane Library. The search included studies published from 2015 to 2025 using keywords such as: “COPD”, “quality of life”, “pulmonary rehabilitation”, “self-management”, “psychological interventions”, “digital health”, “triple therapy”, and “integrated care”. Preference was given to systematic reviews, randomized controlled trials, and high-quality cohort studies published in peer-reviewed journals in English.

**Search results and their discussion.**

***Factors Affecting Quality of Life in COPD Patients***

Objective markers of disease severity correlate with COPD patients’ quality of life. Patients with more severe airflow obstruction (lower $FEV_1$% predicted) generally report worse HRQoL [9]. Similarly, severe dyspnea is a key driver of poor QoL. *Rosińczuk J. et al.* (2018) found that greater dyspnea intensity was associated with significant deterioration in QoL scores [37]. In a cohort of severe COPD patients, dyspnea level (e.g. higher mMRC grade) emerged as an independent predictor of worse St. George’s Respiratory Questionnaire (SGRQ) scores [36]. These findings confirm that difficulty in breathing—central to COPD—strongly compromises daily functioning and well-being. Measures of functional exercise tolerance also relate closely to QoL. A reduced six-minute walk distance (6MWD) or other exercise capacity indices correspond to lower HRQoL [11]. For instance, *Esteban C. et al.* (2020) reported about a 5% QoL improvement per 25-meter increase in 6MWD over time [9], underscoring that patients who maintain better exercise capacity tend to have higher quality of life. Conversely, severe fatigue and exercise intolerance limit patients’ activities and social engagement, contributing to worse mental and physical health status. Longer duration of COPD has been linked to gradually declining QoL [38]. Patients in advanced stages who require long-term oxygen therapy experience particularly poor QoL. Dependence on supplemental oxygen is associated with markedly lower scores across QoL domains [38] reflecting the burden of advanced disease and mobility limitations.

Acute exacerbations of COPD (periods of worsened respiratory symptoms often requiring additional treatment or hospitalization) have a profound negative impact on quality of life. Frequent exacerbations accelerate lung function decline and introduce physical and emotional stressors that degrade patients’ health status. *Fazekas-Pongor V. et al.* (2021) identified frequent exacerbations as one of the most important factors adversely affecting HRQoL in COPD [11]. Patients with a history of repeated exacerbations report significantly worse QoL than those with infrequent or no exacerbations. Each hospitalization for a COPD exacerbation can lead to enduring declines in physical functioning and independence. In a 5-year longitudinal study, Esteban et al. (2020) found that the cumulative number of hospitalizations was among the strongest predictors of poorer HRQoL over time [9]. Exacerbations not only cause acute deterioration but also often have lasting effects – patients may develop heightened anxiety about breathing or activity, reduced confidence, and social withdrawal after a severe episode. Preventing exacerbations (through optimal therapy and self-management) is therefore critical not just for survival but for maintaining better QoL. Consistently, studies demonstrate that exacerbation frequency has a dose-dependent relationship with QoL impairment: fewer exacerbations equate to better preserved quality of life [9].

Most COPD patients, especially older adults, have one or more comorbid conditions – such as cardiovascular disease, metabolic syndrome, osteoporosis, diabetes, or others – which can compound the disease burden and impair quality of life. Multimorbidity in COPD is common and is linked to worse health status. *Rosińczuk J. et al.* (2018) observed that the presence of additional chronic illnesses was associated with significant QoL deterioration in COPD patients [38]. Similarly, a large cross-sectional study found that the number of comorbidities correlated negatively with

QoL: patients with several comorbid conditions had much poorer HRQoL than those with none or few [9]. Comorbid illnesses impose extra symptoms, disability, and treatment complexity that can aggravate the limitations imposed by COPD itself. Certain comorbidities appear especially impactful. Cardiovascular disease (e.g. chronic heart failure or ischemic heart disease) in a COPD patient is associated with more severe dyspnea and worse overall QoL [28]. For example, concurrent heart disease can worsen exercise capacity and fatigue, directly lowering physical health scores, and can also heighten anxiety about health. Musculoskeletal conditions like arthritis or osteoporosis may further limit mobility and physical activity, compounding COPD-related activity limitations. Depression and anxiety – discussed in the next section – are also frequent comorbidities that markedly worsen QoL. In some cases, clusters of comorbidities (for example, the coexistence of cardiovascular, metabolic, and musculoskeletal disorders) have an additive detrimental effect on quality of life beyond the impact of each condition alone. Notably, recent research emphasizes assessing and managing the overall comorbidity burden. Comprehensive indices (e.g. Charlson Comorbidity Index) or simple counts of comorbid diseases predict QoL and prognosis in COPD better than any single diagnosis [11].

Psychological comorbidities are highly prevalent in COPD and have a well-documented negative influence on patients' quality of life. In particular, depression and anxiety affect a substantial subset of COPD patients (with prevalence estimates ranging from about 20% up to 50% in many studies) [45]. The presence of a depressive or anxiety disorder significantly amplifies the subjective burden of COPD – patients experience worse symptom distress, lower motivation, and poorer social well-being, all of which are reflected in lower HRQoL scores [44]. A recent meta-analysis confirmed that comorbid depression in COPD is associated with markedly worse quality of life (pooled correlation coefficient ~0.48 between depression scores and poorer HRQoL) [35]. Comorbid anxiety also shows a significant association with worse HRQoL (pooled r ~0.36), although the impact of depression tends to be even stronger [35]. In fact, depression can be one of the single strongest predictors of poor QoL in COPD. Jang et al. (2019) conducted a multicenter study of patients with severe COPD and found that, among various factors evaluated, the presence of clinical depression was the major determinant of both disease-specific and generic QoL measures [17]. In that study, depression status explained more variance in SGRQ scores than airflow limitation, dyspnea level, or even exacerbation frequency. This suggests that the emotional and psychological toll of COPD (helplessness, hopelessness, loss of interest, etc.) can overshadow even some physical aspects of the disease in terms of impact on daily life. Anxiety, likewise, contributes to worse patient-reported outcomes – for example, anxiety about breathing or fear of breathlessness may limit activity and social engagement, leading to a downward spiral in QoL.These psychological factors and COPD severity can also interact bidirectionally. Depression and anxiety not only worsen QoL directly, but they are linked to worse disease outcomes (higher exacerbation risk, hospitalizations, and even mortality), which in turn further impairs QoL. Patients with untreated depression may be less motivated to adhere to treatments or stay physically active, fueling clinical deterioration [4].

Physical activity level is a potent modulator of quality of life in COPD. Patients who maintain regular physical activity and avoid a sedentary lifestyle experience better functional status, fewer symptoms, and higher QoL, while physical inactivity has the opposite effect [15]. In a longitudinal study*, Esteban C. et al.* (2020) found that physical activity (PA) was among the variables with the strongest influence on HRQoL over a 5-year period, with higher activity levels associated with significantly better QoL scores [9]. Conversely, physical inactivity and prolonged sedentary time are well-known to worsen health outcomes in COPD, including HRQoL [15]. Patients who are chair-bound or rarely active tend to report more dyspnea and fatigue during daily tasks, lower mood, and a sense of social isolation, all contributing to poorer quality of life. Cross-sectional studies reinforce this link. For example, a recent analysis of a COPD cohort in Austria (the CLARA II study) reported that low self-reported physical activity was associated with worse respiratory symptoms, more depressive symptoms, and poorer QoL scores. The authors noted that physical activity could be a relevant predictor of exacerbation risk, QoL, and even depressive symptom burden in COPD patients. This aligns with earlier findings that patients with very limited activity have higher risk of hospitalizations and mortality. On the positive side, interventions that increase physical activity capacity – notably pulmonary rehabilitation programs involving exercise training – consistently improve QoL in COPD [16]. Even low-intensity daily activities like walking or gardening, if done regularly, can yield improvements in exercise tolerance and self-efficacy, translating into better HRQoL. It is important to note that physical inactivity may be both a cause and consequence of worse COPD. Patients with severe disease often reduce activity due to breathlessness, leading to deconditioning that further worsens symptoms. This vicious cycle underscores why breaking the sedentary pattern (through rehabilitation, support for home exercise, etc.) is crucial [50].

Psychosocial factors, particularly the presence or absence of social support, significantly affect how COPD patients cope with their illness and thus influence QoL. Support can come from family members, friends, caregivers, or patient support groups. A recent scoping review by Aravantinou-Karlatou A. et al. (2023) concluded that social support has a strong positive influence on patient-reported outcomes in COPD, including quality of life and emotional well-being [2]. Patients who report having adequate emotional and practical support tend to experience less stress and better mental health, buffering some of the negative impacts of COPD. In contrast, those with inadequate social/emotional support are at higher risk of depression and also show a decline in HRQoL over time. Simply put, patients who feel isolated or unsupported in dealing with their disease often have worse health status and lower life satisfaction. Specific aspects of social support have been studied. For instance, living with a spouse/partner or with family is generally associated with higher QoL than living alone for COPD patients. Caregivers can assist with daily activities, treatment management, and

provide encouragement to stay active. One study found that COPD patients who had a dedicated caregiver (often a spouse) were far more likely to participate in pulmonary rehabilitation and other beneficial activities than those without a caregiver. This implies that the presence of someone to help and motivate the patient can directly translate into better engagement with care and thus better outcomes. Social support also extends to peer support groups and pulmonary rehabilitation programs where patients support each other – these have shown psychosocial benefits like reduced loneliness and anxiety [34]. Notably, a 2020 mixed-methods study in Thailand highlighted social support as the strongest predictor of HRQoL among COPD patients in that region. In their analysis, social support exceeded even clinical factors in explaining variance in QoL scores, underscoring how critical support networks are in chronic disease management. Adequate social support can help patients adhere to treatments, maintain physical activity, and manage stress. On the other hand, social isolation can create a vicious cycle of worsening mood, inactivity, and poor self-care. It is also linked with increased healthcare utilization; patients lacking support may delay seeking care or have difficulty navigating health services, leading to worse health episodes. In summary, consistent evidence indicates that strong social support correlates with better quality of life in COPD, whereas social isolation or low support correlates with worse outcomes [24].

Broader social determinants – such as socioeconomic status (SES), education level, and access to healthcare – also play a role in COPD patients' quality of life. Lower SES often correlates with worse COPD outcomes and by extension poorer HRQoL. Patients of lower socioeconomic means may have more exposure to risk factors (e.g. continued occupational smoke exposure), higher stress, and less access to optimal care, contributing to a heavier symptom burden and limitations. For example, Fazekas-Pongor V. et al. (2021) reported that current smoking and physical inactivity were significant negative predictors of HRQoL in COPD [11]; these lifestyle factors are often intertwined with socioeconomic context (smoking prevalence is higher in lower SES groups, and opportunities for exercise may be fewer). Educational attainment is another important factor: higher education was associated with better QoL in a Polish COPD cohort, whereas patients with less education had worse QoL. Education likely improves health literacy and self-management skills, enabling patients to better understand and adhere to treatments and maintain healthier behaviors. Limited access to healthcare resources can substantially impact quality of life. COPD patients who face barriers to care – such as long distances to clinics, lack of transportation, or financial constraints – may have uncontrolled symptoms and more frequent exacerbations. A rapid review by Shatto et al. (2024) found significant geographic and socioeconomic disparities in COPD outcomes: for instance, patients from more deprived areas had higher hospitalization rates and worse mortality [42].

Lower education level was associated with a higher risk of acute exacerbations in some studies [42], which, as noted, leads to QoL decline. These findings suggest that inequities in care access (like availability of primary care, pulmonary rehabilitation programs, or specialists) can translate into differences in patient quality of life. Indeed, roughly half of the studies in that review reported significant geographical variation in access to COPD care and related health outcomes. While direct research on "access to care vs. QoL" is somewhat limited, it stands to reason that patients who receive guideline-concordant care (pharmacotherapy, immunizations, rehab, follow-up) experience better symptom control and QoL than those who do not. Socioeconomic challenges can also influence treatment adherence and psychosocial stress. Financial difficulties may lead patients to skip medications or appointments, worsening disease control. Additionally, those in lower SES brackets might have poor housing (exacerbating respiratory symptoms) or lack social support [3].

Adherence to prescribed treatments (such as inhaled bronchodilators, inhaled corticosteroids, oxygen therapy, and other medications) is a crucial determinant of symptom control and quality of life in COPD. Poor medication adherence is unfortunately common in COPD and has been consistently linked to worse outcomes and lower QoL. Studies in the last decade show that roughly 40–50% of COPD patients do not take their medications as directed, due to factors ranging from forgetfulness and incorrect inhaler technique to side-effect concerns and cost [31]. Mohsen et al. (2019) reported that about 45% of patients in their sample were nonadherent to treatment, and these patients had significantly worse HRQoL than those who were adherent [31]. In that study, nonadherence was associated with higher symptom burden and more frequent hospital visits, which translated into poorer QoL scores. The relationship between adherence and QoL can be cyclical: patients who feel better and have higher QoL may be more motivated to adhere, whereas those who are depressed or experiencing side effects may be less adherent, leading to uncontrolled symptoms that further erode QoL [40]. Several patient-, disease-, and therapy-related factors affect both adherence and QoL. For example, complex regimens or inhalers that are difficult to use can lower adherence and thus worsen symptom control. Conversely, simplifying therapy and educating patients on proper inhaler technique can improve adherence and often yields improved HRQoL as a result of better disease management. There is evidence that interventions like adherence counseling, reminders, or personalized education can modestly improve medication adherence in COPD. When adherence improves, studies note reductions in exacerbation rates and hospitalizations, likely leading to better perceived health and QoL. Beyond medications, adherence extends to other aspects of self-management – such as following exercise recommendations, using supplemental oxygen as prescribed, avoiding risk factors, and attending pulmonary rehabilitation. Adherence to these non-pharmacologic therapies also influences QoL. For instance, patients who adhere to an at-home exercise regimen after rehab are more likely to sustain the fitness and QoL gains from rehabilitation, whereas those who do not may lose those benefits over time. Treatment adherence is thus an area of high importance: while strong evidence exists that nonadherence is linked to worse clinical outcomes and

QoL, achieving high adherence in real-world patients remains a challenge [54].

Quality of life in COPD is a multifactorial outcome shaped by the complex interaction of the factors described above. Importantly, these factors do not act in isolation; they often influence one another in positive or negative feedback loops. For example, a patient with severe airflow limitation and frequent exacerbations may develop depression due to loss of function, and that depression can in turn reduce the patient's motivation to stay active or adhere to therapy – leading to further clinical deterioration and even worse QoL. Similarly, low social support might worsen a patient's anxiety and self-management, resulting in more hospitalizations that then further diminish QoL [51]. By contrast, improving one domain can have spillover benefits: successful pulmonary rehabilitation can increase physical activity and exercise capacity, improve mood, and enhance self-efficacy in disease management, jointly lifting QoL. The evidence base over the last decade is strong for certain factors. Disease severity (lung function, dyspnea) and exacerbation frequency are consistently shown to be major determinants of HRQoL, supported by numerous longitudinal and cross-sectional studies. The impact of psychological comorbidities, particularly depression, is also well-established as a critical factor reducing QoL in COPD [25]. Physical inactivity and poor exercise tolerance are universally recognized as contributors to worse outcomes and QoL, lending support to interventions that target fitness. These areas represent strong evidence where clinicians can be confident that addressing the issue (e.g. treating depression or encouraging activity) is likely to improve patient quality of life. On the other hand, some domains have comparatively limited evidence or mixed findings. For instance, the role of socioeconomic status and health care access in QoL, while intuitively important, has been less directly studied – existing data suggest an influence, but more research is needed to quantify how improving access to care translates into QoL gains [8]. Social support, too, is clearly important, but interventions to enhance support (such as peer support programs or caregiver training) have not been extensively evaluated for QoL outcomes in COPD. Additionally, factors like cognitive impairment or frailty are emerging considerations that may affect QoL but remain under-researched in COPD populations. Inconsistent findings exist for demographic factors such as age and sex – some studies indicate older age is associated with worse QoL, while others find that older patients may report stable or even better mental QoL (perhaps due to adjusted expectations or better acceptance of illness). These variations highlight the need for more nuanced research into subgroup differences and the longitudinal trajectories of QoL as patients age with COPD [53].

***Modern Approaches to Improving Quality of Life in COPD Patients***

Optimized pharmacotherapy remains a cornerstone of improving COPD symptoms and quality of life. In the past ten years, combination inhalers have become standard for moderate-to-severe disease. Dual long-acting bronchodilator therapy (LABA/LAMA) provides greater bronchodilation, symptom relief, and modestly better health status compared to single bronchodilators. For patients with frequent exacerbations or severe symptoms, single-inhaler triple therapy (inhaled corticosteroid + LABA + LAMA) has emerged as an important advance. Clinical trials such as the IMPACT study showed that triple therapy significantly reduced exacerbation rates and led to small but significant improvements in St. George's Respiratory Questionnaire (SGRQ) scores [26]. A systematic review in 2021 confirmed that adding an ICS to LABA/LAMA (triple therapy) yields a greater improvement in SGRQ (mean ~1.7-point improvement versus dual therapy) along with improved lung function [22]. Although the average QoL gain from triple therapy is below the 4-point threshold for a clinically important difference, many patients experience better symptom control and fewer exacerbations, which cumulatively enhance daily well-being [22]. It is notable that triple therapy's benefits must be balanced against risks (e.g. pneumonia in ICS users), so current guidelines recommend it for patients with persistent symptoms or exacerbations despite dual therapy. Beyond inhalers, other pharmacologic approaches contribute to quality of life improvements in select cases. Phosphodiesterase-4 inhibitors (e.g. roflumilast) and long-term macrolide antibiotics have been used in patients with chronic bronchitic phenotypes or frequent exacerbations; these interventions primarily reduce exacerbation frequency, which can secondarily improve HRQoL by preventing illness episodes [12]. While their direct impact on QoL scores is modest, they address factors (exacerbations, bronchitis symptoms) that otherwise degrade quality of life. More recently, there is exploration of biologic therapies (e.g. anti-IL5 or anti-IL33 antibodies) in COPD, but to date trials have not shown clear improvements in exacerbation rates or QoL for most patients. Overall, the optimization of inhaled therapy (with newer devices and combinations) has been the most impactful pharmacologic development in the past decade for QoL – improving daily symptom burden, exercise tolerance, and reducing flare-ups that disrupt patients' lives [26].

Pulmonary rehabilitation (PR) is a comprehensive intervention (typically exercise training plus education and counseling) that has longstanding evidence for improving COPD outcomes. In the last ten years, further evidence has solidified PR's role in enhancing quality of life. A 2015 Cochrane review of 65 trials found that rehabilitation leads to clinically significant gains in disease-specific QoL measures and exercise capacity compared to usual care [29]. Patients in PR achieved greater improvements than the minimum clinically important difference on instruments like the Chronic Respiratory Questionnaire, across domains of dyspnea, fatigue, emotional function and mastery [29]. These benefits translate into patients feeling less breathless in daily activities, more energetic, and more confident in managing their disease – all key components of improved life quality. Notably, the Cochrane analysis concluded that further trials versus true usual care were unnecessary, given the unequivocal benefit of PR on HRQoL and functional exercise tolerance [29]. Recent work has focused on expanding access and sustaining PR benefits over time. Home-based and community-based pulmonary rehabilitation programs have been developed as alternatives to traditional center-based classes. Studies suggest that properly structured home-based PR can yield comparable short-term improvements in exercise

endurance and QoL as outpatient programs, which is promising for patients facing travel or mobility barriers [30]. However, maintaining the gains of PR long-term remains challenging. Follow-up studies show that without ongoing maintenance, improvements in 6-minute walk distance and symptom scores can diminish after 6–12 months. Efforts such as low-frequency maintenance exercise sessions or tele-rehabilitation are being tested to prolong PR's positive impact. Nonetheless, pulmonary rehabilitation is established as one of the most effective non-pharmacologic therapies to improve quality of life in COPD, yielding better exercise capacity, reduced dyspnea, and enhanced daily functioning [29].

Addressing the psychological burden of COPD has become increasingly recognized as essential for quality of life improvement. Many COPD patients suffer from depression, anxiety, panic related to breathlessness, and social isolation, which can all worsen perceived health status. In the past decade, studies of psychosocial and behavioral interventions have shown meaningful benefits. A comprehensive meta-analysis by *Farver-Vestergaard I. et al.* (2015) found that psychologically-based interventions (such as cognitive-behavioral therapy, anxiety management training, or supportive counseling) significantly reduced symptoms of anxiety and depression and led to improvements in COPD patients' quality of life [10]. The interventions in these studies ranged from brief education plus relaxation training to multi-session CBT programs, delivered individually or in groups. Overall, patients receiving structured psychological support had better HRQoL and emotional well-being than control groups, with effects beyond those achieved by standard pulmonary rehab alone [10]. This underscores that treating the mind-body interaction in COPD – alleviating fear, stress, and mood disturbance – translates into better daily functioning and coping. Specific behavioral strategies have been tested with positive results. Cognitive-behavioral therapy (CBT) tailored for COPD-related anxiety can reduce catastrophic thinking about breathing and improve self-management of panic symptoms. For instance, a randomized trial reported that a brief CBT program delivered by respiratory therapists not only lessened anxiety levels but also reduced urgent healthcare use, suggesting patients felt more in control. Patients who learn coping skills for breathlessness and anxiety tend to regain confidence in exerting themselves, thereby becoming more active and improving their life quality. Additionally, novel approaches such as group singing therapy have shown psychological and QoL benefits. In a community trial, COPD patients who participated in weekly group singing for 3–6 months had significantly reduced depression scores and better disease-specific quality of life (measured by the COPD Clinical Questionnaire) compared to controls [27]. Participating in singing (a form of musical therapy) likely provided both respiratory exercise and social interaction, highlighting the value of creative, enjoyable activities to improve mood and social well-being in COPD. Behavioral interventions like smoking cessation support, breathing techniques (e.g. pursed-lip breathing training), and energy conservation strategies also play a role. Smoking cessation is fundamental to slowing disease progression; quitting smoking can lead to improved cough and sputum symptoms over time and prevents further decline in exercise capacity, thereby contributing to better HRQoL long-term [7]. Meanwhile, training in breathing and pacing techniques helps patients manage dyspnea during activities, reducing fear of breathlessness and fostering independence. In summary, interventions targeting the psychological and behavioral dimensions of COPD – from formal therapy to support groups and relaxation techniques – have proven to enhance quality of life by improving mental health, self-efficacy, and coping. Incorporating psychological care into routine COPD management is a modern paradigm for holistic improvement of patient well-being [10].

Digital health innovations and telemedicine have expanded rapidly, especially in recent years, offering new ways to support COPD patients and potentially improve their quality of life. Telehealth interventions range from remote monitoring of symptoms and telecoaching, to videoconference pulmonary rehabilitation and smartphone applications for self-management. Evidence from the past decade indicates that these technologies can yield meaningful benefits [20]. For example, a 2024 network meta-analysis by Chang et al. compared various eHealth interventions and found that web-based programs and mobile apps significantly improved health-related quality of life in COPD patients (measured by validated questionnaires), relative to usual care [5]. Among different modalities, web-based interventions were identified as the most effective in enhancing QoL, while telemonitoring was most effective for improving exercise endurance. These findings suggest that giving patients interactive online tools – such as web portals with educational content, symptom tracking, and feedback – empowers them to better manage their condition, leading to improved daily health status. Several studies have shown specific outcomes from telehealth programs. Remote patient monitoring systems, where patients regularly upload spirometry readings or report symptoms via phone/app, can enable early intervention for exacerbations and personalized coaching [1]. Meta-analyses of telemonitoring report modest improvements in QoL scores and reductions in hospital admissions. Telehealth interventions often incorporate tele-consultations or telecoaching: nurses or respiratory therapists providing scheduled phone or video support. This ongoing support improves patients' confidence in self-care and adherence to treatments, translating into better HRQo. During the COVID-19 pandemic, telehealth pulmonary rehabilitation (home exercise training supervised by video call) became more common; studies found that tele-rehab can produce similar improvements in exercise capacity and QoL as center-based PR, broadening access to this vital service. Digital tools also include smartphone applications that guide inhaler use, remind patients to exercise or take medications, and educate patients with interactive content [19]. Many COPD apps now incorporate symptom diaries and action plan prompts. A common observation is that patients using such digital self-management tools report feeling more in control and less anxious about their disease, which in turn improves their perceived quality of life. Of course, the success of telehealth depends on patient engagement and the usability of technology, but when implemented well, telehealth programs can reduce isolation,

improve disease monitoring, and enhance access to care – all contributing to improved QoL [5].

Encouraging effective self-management through education and coaching has been a major focus of modern COPD care. Structured self-management programs aim to teach patients skills to manage symptoms, adhere to therapy, recognize early signs of exacerbation, and adopt healthy behaviors. In the last decade, strong evidence has accumulated that well-designed self-management interventions can improve health status and reduce hospitalizations [48]. A 2022 Cochrane review (updating prior analyses) included over 6000 COPD patients and found that self-management interventions likely improve health-related quality of life as measured by the SGRQ, with an average improvement of about 2.9 points versus usual care. Although this mean improvement did not quite reach the 4-point MCID, some trials did achieve clinically meaningful benefits, and importantly, the interventions significantly reduced the risk of respiratory-related hospital admissions (by about 25%) [41]. Fewer exacerbation hospitalizations directly correlates with better QoL, as patients avoid the physical and psychological stress of acute illness episodes. Key components of successful self-management programs include: individualized action plans for exacerbations (with instructions on medication adjustment and when to seek care), inhaler technique training, education about the disease and treatments, coping strategies for dyspnea, and regular follow-up to reinforce skills. Programs often involve multi-disciplinary input (nurses, respiratory therapists, pharmacists) and behavioral techniques to enhance adherence. Patients who are actively engaged in self-management gain a sense of autonomy and mastery over their condition, which improves their confidence and mental well-being. They also tend to have better medication adherence and make appropriate use of health resources, preventing crises [47]. The evidence supports that COPD self-management education improves multiple domains of quality of life – from physical aspects (exercise tolerance, symptom control) to emotional aspects (reducing anxiety about exacerbations). For example, patients frequently report that knowing how to respond early to symptom worsening reduces their fear and improves their day-to-day security. One notable finding is that self-management interventions are generally safe and not associated with increased mortality or adverse outcomes [41].

Given the systemic effects of COPD, attention to nutrition and lifestyle factors has become an important part of improving patient well-being. Many COPD patients, especially those with advanced disease, experience weight loss and skeletal muscle dysfunction (cachexia) which worsen exercise tolerance and HRQoL. Conversely, others may be overweight or have poor dietary quality, contributing to cardiovascular risk and dyspnea. Nutritional interventions in COPD focus on correcting malnutrition, optimizing body composition, and ensuring adequate energy for daily activity [32]. Recent studies have demonstrated that targeted nutritional support can yield benefits in functional status and quality of life. For example, a 2025 clinical study by Zhang et al. evaluated individualized nutrition management in COPD patients and found significant improvements in nutritional status, exercise capacity (6-minute walk test distance), and quality of life scores (CAT questionnaire) compared to standard diet advice. The group receiving personalized nutrition plans (with dietitian counseling and oral nutritional supplements when needed) had greater gains in weight and muscle strength, which translated into higher QoL scores and better pulmonary function than controls [52]. This aligns with earlier evidence that oral nutritional supplementation in underweight COPD patients can improve body weight, respiratory muscle strength, exercise tolerance, and HRQoL [6]. Gaining even a few kilograms of lean mass can help patients breathe and move more easily, directly enhancing daily life. Beyond addressing undernutrition, dietary quality and specific nutrients have been investigated for COPD benefits. Trials of high-protein diets, omega-3 fatty acid supplements, and vitamin D repletion have suggested improvements in muscle function and reductions in inflammation, which may positively affect QoL, though results are mixed [39]. One consistent finding is that malnutrition is associated with worse quality of life and higher mortality in COPD, so proactive nutritional support is recommended for patients with low BMI or unintentional weight loss. Equally, obese COPD patients may benefit from weight reduction combined with exercise, as excessive weight can worsen dyspnea and activity tolerance. Nutritional counseling therefore must be individualized. Lifestyle modifications also encompass exercise and physical activity outside of formal rehab. Regular physical activity is strongly correlated with better health status in COPD [14]. Patients who remain active (e.g. walking daily) tend to have less dyspnea and higher QoL, whereas a sedentary lifestyle leads to deconditioning and poorer outcomes. Programs that encourage daily walking or provide activity coaching (sometimes with step counters or fitness trackers) have shown increases in exercise endurance and modest QoL improvements. Even low-intensity activities, if done consistently, can interrupt the cycle of inactivity and breathlessness. Smoking cessation is another critical lifestyle change – while quitting smoking may not immediately improve lung function, it slows further decline and often improves coughing and sputum production within months, which patients perceive as a better quality of life [49]. Additionally, avoiding airborne irritants, using energy conservation techniques at home, and practicing breathing exercises are lifestyle adjustments that help patients carry out daily tasks more comfortably. In sum, paying attention to nutrition and lifestyle factors addresses the extrapulmonary contributors to poor QoL in COPD. By optimizing body composition, encouraging physical activity, and eliminating harmful habits, patients can achieve improvements in strength, endurance, and overall vitality [52].

Modern COPD management recognizes that a multidisciplinary, integrated care approach is necessary to tackle the diverse needs of patients and improve their quality of life. Integrated care models typically involve coordinated input from pulmonologists, primary care providers, nurses, respiratory therapists, physiotherapists, pharmacists, and sometimes palliative care or social services, all working together to implement a comprehensive care plan. Over the last decade, clinical trials and meta-analyses have shown that integrated disease management (IDM) programs can lead to better outcomes than fragmented care [18]. A Cochrane review

updated in 2021 (52 trials,>20,000 patients) concluded that integrated care programs probably improve health-related QoL (measured by SGRQ) in COPD, with a medium-term improvement of about 3.9 points versus usual care. Although this average improvement was just shy of the MCID, some programs achieved >4-point gains, and importantly IDM also produced significant reductions in hospital admissions and days in hospital [33]. These findings reinforce that when care is structured and proactive – rather than reactive – patients stay more stable and feel better in their daily lives [23]. Key elements of effective integrated care include: regular follow-up (often with case-manager nurses), personalized care plans, patient education and self-management support (as discussed earlier), optimization of pharmacotherapy, routine monitoring of symptoms and complications, and facilitation of access to pulmonary rehab, smoking cessation, or specialist referrals as needed [46]. For example, one primary care-based IDM program provided COPD patients with ongoing self-management coaching and scheduled telephonic check-ins; over 12 months it resulted in substantially improved COPD knowledge, fewer severe exacerbations, and better CAT quality-of-life scores compared to usual care. Patients in the integrated program were more likely to receive guideline-based interventions (vaccinations, rehab, etc.), which translated into improved QoL and functional status [13]. Another study targeting high-risk COPD patients in primary care found that an IDM intervention with case management led to a ~1.3 point improvement in CAT score and nearly 50% fewer severe exacerbations than controls – indicating a large impact on patients' well-being and stability. Crucially, integrated care often extends beyond medical management to address social and emotional needs – for instance, coordinating pulmonary rehabilitation, depression screening and treatment, nutritional advice, and even home care services. This holistic approach can reduce stress on patients and caregivers, thereby improving quality of life. Many severe COPD patients also benefit from early palliative care integration, focusing on symptom relief (breathlessness, anxiety, insomnia) and advance care planning, which has been shown to enhance QoL and satisfaction in advanced disease [43]. While more research continues on the optimal design of integrated care (e.g. which combination of components yields the greatest benefit), current evidence supports that multidisciplinary management improves patient-centered outcomes [33].

**Conclusion**

In the past decade, a multitude of strategies have evolved to improve the quality of life of patients living with COPD. Modern pharmacological treatments – especially the use of dual and triple inhaled therapy – have enhanced symptom control and reduced exacerbations, contributing to better daily functioning. Non-pharmacologic interventions are equally vital: pulmonary rehabilitation remains a gold-standard therapy for boosting exercise capacity and HRQoL, and it is now complemented by home-based and tele-rehab options. Addressing psychological and behavioral health needs has moved to the forefront, with evidence-based interventions like cognitive-behavioral therapy, support groups, and relaxation techniques mitigating the anxiety and depression that often accompany COPD and thereby improving overall well-being.

***Conflict of interests.*** *Authors claim about the absence of interests of conflict.*

***Transparency of research.*** *The research was not sponsored. Researchers are fully responsible for providing the final version of the manuscript to the press.*

***Declaration of financial and other interactions.*** *All authors participated in the development of the concept and in designing the research and in writing manuscripts. The final version of the manuscript has been approved by all authors. The authors did not receive a research fee.*

***Literature:***

*1. Akor A.A., Bamidele A., Erhabor G.E.* Predictors of Health-Related Quality of Life (HRQOL) in Patients With Chronic Obstructive Pulmonary Disease using the COPD Assessment Test (CAT). West African Journal of Medicine. 2020. № 3 (37). p. 275–280.

*2. Aravantinou-Karlatou A.* et al. The Influence of Social Support in PROMs of Patients with COPD in Primary Care: A Scoping Review. Healthcare. 2023. № 24 (11). p. 3141.

*3. Breen A.* et al. What is the impact of home non-invasive ventilation on the health-related quality of life of patients with chronic obstructive pulmonary disease? A systematic review. Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation. 2023. № 7 (32). p. 1843–1857.

*4. Ceyhan Y., Tekinsoy Kartin P.* The effects of breathing exercises and inhaler training in patients with COPD on the severity of dyspnea and life quality: a randomized controlled trial. Trials. 2022. № 1 (23). p. 707.

*5. Chang H.* et al. Comparative effectiveness of eHealth interventions on the exercise endurance and quality of life of patients with COPD: A systematic review and network meta-analysis. Journal of Clinical Nursing. 2024. № 9 (33). p. 3711–3720.

*6. Collins P. F., Elia M., Stratton R. J.* Nutritional support and functional capacity in chronic obstructive pulmonary disease: a systematic review and meta-analysis. Respirology (Carlton, Vic.). 2013. № 4 (18). p. 616–629.

*7. Criner G.J.* et al. COPD Advanced Patient Management. Chest. 2018. № 6 (153). p. 1497–1498.

*8. Dong J.* et al. Efficacy of pulmonary rehabilitation in improving the quality of life for patients with chronic obstructive pulmonary disease: Evidence based on nineteen randomized controlled trials. International Journal of Surgery (London, England). 2020. (73). p. 78–86.

*9. Esteban C.* et al. Predictive factors over time of health-related quality of life in COPD patients. Respiratory Research. 2020. № 1 (21). p. 138.

*10. Farver-Vestergaard I., Jacobsen D., Zachariae R.* Efficacy of psychosocial interventions on psychological and physical health outcomes in chronic obstructive pulmonary disease: a systematic review and meta-analysis. Psychotherapy and Psychosomatics. 2015. № 1 (84). p.37–50.

*11. Fazekas-Pongor V.* et al. Health-related quality of life of COPD patients aged over 40 years // Physiology International. 2021,p.1-10.

*12. Fei F.* et al. Synergistic Impact of the Symptom Cluster on Health-Related Quality of Life in Patients With Chronic Obstructive Pulmonary Disease: A Secondary Data Analysis. Clinical Nursing Research. 2022. № 6 (31). p. 991–999.

*13. Ferrone M.* et al. The impact of integrated disease management in high-risk COPD patients in primary care. NPJ primary care respiratory medicine. 2019. № 1 (29). p. 8.

*14. Halpin D.M.G.* et al. Global Initiative for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease. The 2020 GOLD Science Committee Report on COVID-19 and Chronic Obstructive Pulmonary Disease. American Journal of Respiratory and Critical Care Medicine. 2021. № 1 (203). p. 24–36.

*15. Horner A.* et al. Physical Activity, Depression and Quality of Life in COPD - Results from the CLARA II Study. International Journal of Chronic Obstructive Pulmonary Disease. 2023. (18). p. 2755–2767.

*16. Hurst J.R.* et al. Understanding the impact of chronic obstructive pulmonary disease exacerbations on patient health and quality of life. European Journal of Internal Medicine. 2020. (73). p. 1–6.

*17. Jang S.M.* et al. Depression is a major determinant of both disease-specific and generic health-related quality of life in people with severe COPD. Chronic Respiratory Disease. 2019. (16). p. 1479972318775422.

*18. Janjua S.* et al. Digital interventions for the management of chronic obstructive pulmonary disease. The Cochrane Database of Systematic Reviews. 2021. № 4 (4). p. CD013246.

*19. Jarab A.* et al. Patients' perspective of the impact of COPD on quality of life: a focus group study for patients with COPD. International Journal of Clinical Pharmacy. 2018. № 3 (40). p. 573–579.

*20. Jones G.L.* Quality of life changes over time in patients with chronic obstructive pulmonary disease. Current Opinion in Pulmonary Medicine. 2016. № 2 (22). C. 125–129.

*21. Kharbanda S., Anand R.* Health-related quality of life in patients with chronic obstructive pulmonary disease: A hospital-based study. The Indian Journal of Medical Research. 2021. № 4 (153). p. 459–464.

*22. Koarai A.* et al. Triple versus LAMA/LABA combination therapy for patients with COPD: a systematic review and meta-analysis. Respiratory Research. 2021. № 1 (22). p. 183.

*23. Levy A.R.* et al. An intervention for pulmonary rehabilitators to develop a social identity for patients attending exercise rehabilitation: a feasibility and pilot randomised control trial protocol. Pilot and Feasibility Studies. 2018. (4). p. 40.

*24. Li Y.* et al. Breathing Exercises in the Treatment of COPD: An Overview of Systematic Reviews. International Journal of Chronic Obstructive Pulmonary Disease. 2022. (17). p. 3075–3085.

*25. Liang Z.* et al. What conservative interventions can improve the long-term quality of life, depression, and anxiety of individuals with stable COPD? A systematic review and meta-analysis. Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation. 2022. № 4 (31). p. 977–989.

*26. Lipson D.A.* et al. Once-Daily Single-Inhaler Triple versus Dual Therapy in Patients with COPD. The New England Journal of Medicine. 2018. № 18 (378). p. 1671–1680.

*27. Liu H.* et al. Group singing improves depression and life quality in patients with stable COPD: a randomized community-based trial in China. Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation. 2019. № 3 (28). p. 725–735.

*28. Matsunaga K.* et al. Comorbid Conditions in Chronic Obstructive Pulmonary Disease: Potential Therapeutic Targets for Unmet Needs. Journal of Clinical Medicine. 2020. № 10 (9). p. 3078.

*29. McCarthy B.* et al. Pulmonary rehabilitation for chronic obstructive pulmonary disease. The Cochrane Database of Systematic Reviews. 2015. № 2 (2015). p. CD003793.

*30. Meijer E.* et al. Exploring characteristics of COPD patients with clinical improvement after integrated disease management or usual care: post-hoc analysis of the RECODE study. BMC pulmonary medicine. 2020. № 1 (20). p. 176.

*31. Mohsen S.* et al. Nonadherence to treatment and quality of life among patients with chronic obstructive pulmonary disease. Lung India: Official Organ of Indian Chest Society. 2019. № 3 (36). p. 193–198.

*32. Nagase F.I.* et al. Effectiveness of remote home monitoring for patients with Chronic Obstructive Pulmonary Disease (COPD): systematic review. BMC health services research. 2022. № 1 (22). p. 646.

*33. Poot C. C.* et al. Integrated disease management interventions for patients with chronic obstructive pulmonary disease. The Cochrane Database of Systematic Reviews. 2021. № 9 (9). p. CD009437.

*34. Qian Y.* et al. Analyses of Factors Associated with Acute Exacerbations of Chronic Obstructive Pulmonary Disease: A Review. International Journal of Chronic Obstructive Pulmonary Disease. 2023. (18). p. 2707–2723.

*35. Qiu C.-J., Wu S.* Depression and anxiety disorders in chronic obstructive pulmonary disease patients: Prevalence, disease impact, treatment. World Journal of Psychiatry. 2024. № 12 (14). p. 1797–1803.

*36. Rahi M.S.* et al. The Impact of Anxiety and Depression in Chronic Obstructive Pulmonary Disease. Advances in Respiratory Medicine. 2023. № 2 (91). p. 123–134.

*37. Rosińczuk J., Przyszlak M., Uchmanowicz I.* Sociodemographic and clinical factors affecting the quality of life of patients with chronic obstructive pulmonary disease. International Journal of Chronic Obstructive Pulmonary Disease. 2018. (13). p. 2869–2882.

*38. Rosińczuk J., Przyszlak M., Uchmanowicz I.* Sociodemographic and clinical factors affecting the quality of life of patients with chronic obstructive pulmonary disease. International Journal of Chronic Obstructive Pulmonary Disease. 2018. (13). p. 2869–2882.

*39. Rzadkiewicz M., Nasiłowski J.* Psychosocial Interventions for Patients with Severe COPD-An Up-to-Date Literature Review. Medicina (Kaunas, Lithuania). 2019. № 9 (55). p. 597.

*40. Saja M.F.* et al. The Association Between Medication Adherence and Health-Related Quality of Life in Patients with COPD: A Cross-Sectional Study. International Journal of Chronic Obstructive Pulmonary Disease. 2025. (20). p. 1567–1583.

*41. Schrijver J.* et al. Self-management interventions for people with chronic obstructive pulmonary disease. The Cochrane Database of Systematic Reviews. 2022. № 1 (1). p. CD002990.

*42. Shatto J.A., Stickland M.K., Soril L.J.J.* Variations in COPD Health Care Access and Outcomes: A Rapid Review. Chronic Obstructive Pulmonary Diseases (Miami, Fla.). 2024. № 2 (11). p. 229–246.

*43. Shioya T.* et al. Improvement of physical activity in chronic obstructive pulmonary disease by pulmonary rehabilitation and pharmacological treatment. Respiratory Investigation. 2018. № 4 (56). p. 292–306.

*44. Wang J.* et al. The complexity of mental health care for people with COPD: a qualitative study of clinicians' perspectives. NPJ primary care respiratory medicine. 2021. № 1 (31). p. 40.

*45. Wang J.G.* et al. Clinical Characteristics of Patients With COPD and Comorbid Depression and Anxiety: Data From a National Multicenter Cohort Study. Chronic Obstructive Pulmonary Diseases (Miami, Fla.). 2025. № 1 (12). p. 33–42.

*46. Wedzicha J.A.* et al. Management of COPD exacerbations: a European Respiratory Society/American Thoracic Society guideline. The European Respiratory Journal. 2017. № 3 (49). p. 1600791.

*47. Weina J.* et al. Therapeutic effects of statins drugs use and continuous nursing on patients with chronic obstructive pulmonary disease and the influence of life quality. Pakistan Journal of Pharmaceutical Sciences. 2018. № 3(Special) (31). p. 11794–11184.

*48. Yi M.* et al. Impact of Caregiving Burden on Quality of Life of Caregivers of COPD Patients: The Chain Mediating Role of Social Support and Negative Coping Styles. International Journal of Chronic Obstructive Pulmonary Disease. 2021. (16). p. 2245–2255.

*49. Yu C.-H.* et al. Dynamic changes in quality of life in older patients with chronic obstructive pulmonary disease: a 7-year follow up. Health and Quality of Life Outcomes. 2024. № 1 (22). p. 76.

*50. Yun R.* et al. How Breathing Exercises Influence on Respiratory Muscles and Quality of Life among Patients with COPD? A Systematic Review and Meta-Analysis. Canadian Respiratory Journal. 2021. (2021). p. 1904231.

*51. Zakrisson A.-B.* et al. Improved quality of care by using the PRISMS form to support self-management in patients with COPD: A Randomised Controlled Trial. Journal of Clinical Nursing. 2020. № 13–14 (29). p. 2410–2419.

*52. Zhang J.-H.* Effect of Nutritional Management on the Nutritional Status and Quality of Life of Patients with Chronic Obstructive Pulmonary Disease. International Journal of Chronic Obstructive Pulmonary Disease. 2025. (20). p. 487–496.

*53. Zhang S.* et al. Evaluation of the quality of life in patients with LC-COPD and the impact of inhalation therapy on the quality of life. Panminerva Medica. 2022. № 3 (64). p. 411–412.

*54. Zhang Z.-Y., Li Y.-H.* Effects of different exercise regimens on prognosis of patients with chronic obstructive pulmonary disease: a systematic reviews and meta-analysis. Annals of Medicine. 2024. № 1 (56). p. 2392022.

**Контактная информация:**

**Kalbagayeva Zhadra Erbolovna -** 1st year PhD student in Public Health, NJSC "Semey Medical University". Semey, Republic of Kazakhstan. Postal code: Republic of Kazakhstan, 071400, Semey, st. Abaya, 103. E-mail: zhadra.kalbagayeva@edu.med.kz Phone: +77771315558

**Khismetova Zaytuna Abdulkasimovna -** Professor, Head of the Department of Public Health, NJSC "Semey Medical University". Semey, Republic of Kazakhstan. Postal code: Republic of Kazakhstan, 071400, Semey, st. Abaya, 103. E-mail: zaituna.khismetova@smu.edu.kz Phone: +77772582681

**Iskakova Nazym Serikanovna –** PhD, teacher of the Department of Public Health, NJSC "Semey Medical University". Semey, Republic of Kazakhstan. Postal code: Republic of Kazakhstan, 071400, Semey, st. Abaya, 103. E-mail: nazym.iskakova@smu.edu.kz Phone: +77751030454

**Atabaeva Aliya Kalmetovna** - PhD, teacher of the Department of Public Health, NJSC "Semey Medical University". Semey, Republic of Kazakhstan. Postal code: Republic of Kazakhstan, 071400, Semey, st. Abaya, 103. E-mail: aliya.atabayeva@smu.edu.kz Phone: +77753900269

**Serikova-Esengeldina Dinara Serikovna-** - PhD, teacher of the Department of Public Health, NJSC "Semey Medical University". Semey, Republic of Kazakhstan. Postal code: Republic of Kazakhstan, 071400, Semey, st. Abaya, 103. E-mail: dinara.esengeldina@smu.edu.kz Phone: +77785886986

**Razakova Nurgul Gabdulbarovna -** Master of Pedagogical Sciences in the specialty "Biology", teacher of the Department of Microbiology named after Professor M.M. Urazalin, Semey Medical University, NCJSC. Semey, Republic of Kazakhstan. Postal code: Republic of Kazakhstan, 071400, Semey, Abay street, 103. E-mail: nurgul.razakova@smu.edu.kz Phone: +77772213211

**Zhaxebergenova Aizhan Bolatovna-** Semey, Republic of Kazakhstan. Postal code: Republic of Kazakhstan, 071400, Semey, st. Abaya, 103. E-mail: zh_a_b@mail.ru Phone: +77776686915

**Автор-корреспондент:**

**Калбагаева Жадра Ерболовна -** докторант 1-го года обучения по специальности «Общественное здравоохранение», НАО "Медицинский университет Семей". г. Семей, Республика Казахстан.

**Почтовый индекс:** Республика Казахстан, 071400, г. Семей, ул. Абая, д.103.

**E-mail:** zhadra.kalbagayeva@edu.med.kz

**Телефон:** +77771315558

Received: 24 January 2025 / Accepted: 19 May 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2025.27.3.024***

***UDC 616.12-008.46-036.12-02-07***

This work is licensed under a Creative Commons Attribution 4.0 International License

# THE SST2 BIOMARKER AS A PREDICTOR OF ADVERSE CLINICAL OUTCOMES IN HEART FAILURE. LITERATURE REVIEW

**Anar D. Kozhabayeva[1], https://orcid.org/0000-0003-4132-6755**
**Jamilya A. Mansurova[1], https://orcid.org/0000-0003-2439-2056**
**Aisulu S. Zhunuspekova[1], https://orcid.org/0000-0002-2413-317X**
**Andrey Yu. Orekhov[1], https://orcid.org/0000-0001-7201-1399**
**Assel A. Kassymova[1], https://orcid.org/0000-0001-9333-4146**
**Bolat A. Ashirov[2], https://orcid.org/0000-0003-0242-9700**
**Zhanargul K. Smailova[1], https://orcid.org/0000-0002-4513-4614**
**Mirgul A. Kapakova[1], https://orcid.org/0000-0003-4186-8933**
**Nailya M. Urazalina[1], https://orcid.org/0000-0003-0200-1763**
**Lyudmila K. Karazhanova[1], https://orcid.org/0000-0002-4719-6034**

**[1] NCJSC «Semey Medical University», Semey, Republic of Kazakhstan;**
**[2] South Kazakhstan Medical Academy, Shymkent, Republic of Kazakhstan.**

**Abstract**

**Introduction.** In recent years, there has been a growing number of studies aimed at identifying and evaluating novel biomarkers of cardiovascular diseases, particularly heart failure. This trend is driven by the need to enhance diagnostic accuracy, risk stratification, and personalized treatment approaches. Among these biomarkers, special attention is given to the soluble form of the ST2 receptor (sST2), which has demonstrated significant prognostic value across various forms of heart failure. This review focuses on the analysis of current data regarding the clinical relevance of sST2 and the prospects for its implementation in routine medical practice.

**Aim.** Analysis of literature data on the biomarker sST2 as a predictor of adverse clinical outcomes in patients with heart failure.

**Search Strategy.** A literature search was conducted using the scientific databases PubMed, Web of Science, and Google Scholar, as well as electronic scientific libraries eLibrary and CyberLeninka. The search covered a five-year period (2019–2024) and focused on cardiorenal biomarkers as predictors of adverse outcomes in cardiovascular diseases.

**Results.** This literature review analyzes studies on the prognostic significance of the sST2 biomarker in patients with heart failure. The findings indicate that sST2 reflects key pathophysiological processes, including myocardial fibrosis and systemic inflammation. Evidence from the literature suggests that the integration of sST2 into clinical assessment improves early identification of patients at risk, refines prognostic accuracy, and facilitates ongoing patient monitoring. The integration of this biomarker into clinical practice offers opportunities for more precise risk stratification and a personalized approach to treatment.

**Conclusions.** A review of contemporary literature on clinical and laboratory predictors of heart failure demonstrates that the biomarker sST2 has high diagnostic and prognostic significance. It reflects myocardial fibrosis and systemic inflammation—processes closely associated with the progression of heart failure. Further research is needed to determine optimal threshold values, validate assessment methodologies, and integrate sST2 into standardized clinical algorithms.

***Keywords:*** *cardiovascular diseases; clinical and laboratory predictors; sST2; prognosis; diagnosis.*

***For citation:***

*Kozhabayeva A.D., Mansurova J.A., Zhunuspekova A.S., Orekhov A.Yu., Kassymova A.A., Ashirov B.A., Smailova Zh.K., Kapakova M.A., Urazalina N.M., Karazhanova L.K.* The SST2 biomarker as a predictor of adverse clinical outcomes in heart failure. Literature review // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 227-235. *doi 10.34689/SH.2025.27.3.024*

**Резюме**

# БИОМАРКЕР SST2 КАК ПРЕДИКТОР НЕБЛАГОПРИЯТНЫХ КЛИНИЧЕСКИХ ИСХОДОВ ПРИ СЕРДЕЧНОЙ НЕДОСТАТОЧНОСТИ. ОБЗОР ЛИТЕРАТУРЫ

**Анар Д. Қожабаева[1], https://orcid.org/0000-0003-4132-6755**
**Джамиля А. Мансурова[1], https://orcid.org/0000-0003-2439-2056**
**Айсулу С. Жунуспекова[1], https://orcid.org/0000-0002-2413-317X**

**Андрей Ю. Орехов[1], https://orcid.org/0000-0001-7201-1399**
**Асель А. Касымова[1], https://orcid.org/0000-0001-9333-4146**
**Аширов Болат А.[2], https://orcid.org/0000-0003-0242-9700**
**Жанаргуль К. Смаилова[1], https://orcid.org/0000-0002-4513-4614**
**Миргуль А. Капакова[1], https://orcid.org/0000-0003-4186-8933**
**Найля М. Уразалина[1], https://orcid.org/0000-0003-0200-1763**
**Людмила К. Каражанова[1], https://orcid.org/0000-0002-4719-6034**

**[1] НАО «Медицинский университет Семей», г. Семей, Республика Казахстан;**
**[2] Южно-Казахстанская медицинская академия, Шымкент, Республика Казахстан.**

**Введение.** В последние годы наблюдается рост числа исследований, направленных на выявление и оценку новых биомаркеров сердечно-сосудистых заболеваний, в частности сердечной недостаточности. Такая тенденция обусловлена необходимостью повышения точности диагностики, стратификации риска и персонализации терапии. Среди биомаркеров особый интерес вызывает растворимая форма рецептора ST2 (sST2), демонстрирующая высокую прогностическую ценность при различных формах сердечной недостаточности. Настоящий обзор посвящён анализу актуальных данных о клинической роли sST2 и перспективам его применения в рутинной практике.

**Цель.** Анализ литературных данных о биомаркере sST2 как предикторе неблагоприятных клинических исходов у пациентов с сердечной недостаточностью.

**Стратегия поиска.** Проведен поиск научных публикаций в поисковых системах PubMed, Web of Science, Google Scholar, в электронных научных библиотеках eLibrary, CyberLeninka. Глубина поиска 5 лет (2019-2024). Поиск информации о кардиоренальных маркерах как предикторах неблагоприятных исходов при сердечно-сосудистых заболеваниях.

**Результаты.** В настоящем литературном обзоре проанализированы исследования, посвящённые прогностической значимости биомаркера sST2 у пациентов с сердечной недостаточностью. Показано, что sST2 отражает ключевые патофизиологические процессы, включая фиброз миокарда и системное воспаление. Данные литературы подтверждают, что применение sST2 в диагностике и прогнозировании неблагоприятных клинических исходов способствует более раннему выявлению риска, уточнению прогноза и динамическому наблюдению за пациентами. Внедрение этого биомаркера в клиническую практику открывает возможности для более точной стратификации риска и персонализированного подхода к лечению.

**Выводы.** Обзор современной литературы по клинико-лабораторным предикторам сердечной недостаточности показывает, что биомаркер sST2 обладает высокой диагностической и прогностической значимостью. Он отражает процессы миокардиального фиброза и системного воспаления, ассоциированные с прогрессированием сердечной недостаточности. Дальнейшие исследования необходимы для уточнения пороговых значений, валидации методов оценки и интеграции sST2 в стандартизированные алгоритмы клинической практики.

***Ключевые слова:*** *сердечно-сосудистые заболевания; клинико-лабораторные предикторы; sST2; прогноз; диагностика.*

***Для цитирования:***

*Қожабаева А.Д., Мансурова Ж.А., Жунуспекова А.С., Орехов А.Ю., Касымова А.А., Аширов Б.А., Смаилова Ж.К., Капакова М.А., Уразалина Н.М., Каражанова Л.К.* Биомаркер SST2 как предиктор неблагоприятных клинических исходов при сердечной недостаточности. Обзор литературы // Наука и Здравоохранение. 2025. Т.27 (3), С. 227-235. doi: 10.34689/SH.2025.27.3.024

**Түйіндеме**

# SST2 БИОМАРКЕРІ ЖҮРЕК ЖЕТКІЛІКСІЗДІГІ КЕЗІНДЕГІ ЖАҒЫМСЫЗ КЛИНИКАЛЫҚ НӘТИЖЕЛЕРДІ БОЛЖАУШЫ КӨРСЕТКІШ РЕТІНДЕ. ӘДЕБИ ШОЛУ

**Анар Д. Қожабаева[1], https://orcid.org/0000-0003-4132-6755**
**Джамиля А. Мансурова[1], https://orcid.org/0000-0003-2439-2056**
**Айсулу С. Жунуспекова[1], https://orcid.org/0000-0002-2413-317X**
**Андрей Ю. Орехов[1], https://orcid.org/0000-0001-7201-1399**
**Асель А. Касымова[1], https://orcid.org/0000-0001-9333-4146**
**Аширов Болат А.[2], https://orcid.org/0000-0003-0242-9700**
**Жанаргуль К. Смаилова[1], https://orcid.org/0000-0002-4513-4614**
**Миргуль А. Капакова[1], https://orcid.org/0000-0003-4186-8933**
**Найля М. Уразалина[1], https://orcid.org/0000-0003-0200-1763**
**Людмила К. Каражанова[1], https://orcid.org/0000-0002-4719-6034**

**[1] «Семей медицина университеті» КеАҚ, Семей қ., Қазақстан Республикасы;**
**[2] Оңтүстік Қазақстан медицина академиясы, Шымкент қ., Қазақстан Республикасы.**

**Кіріспе.** Соңғы жылдары жүрек-қан тамыр ауруларының, әсіресе жүрек жеткіліксіздігінің жаңа биомаркерлерін анықтау және бағалауға бағытталған зерттеулердің саны артып келеді. Мұндай үрдіс диагноз қоюдың дәлдігін, қауіп-қатерді стратификациялауды және емдеудің дербестендірілген тәсілдерін жетілдіру қажеттілігімен байланысты. Осы биомаркерлердің ішінде ST2 рецепторының ерігіш формасы (sST2) ерекше қызығушылық тудырып отыр, себебі ол жүрек жеткіліксіздігінің түрлі түрлерінде жоғары прогностикалық құндылық көрсетті. Бұл шолу sST2-нің клиникалық маңыздылығына және оны күнделікті медициналық тәжірибеге енгізу перспективаларына арналған

**Мақсат.** Жүрек жеткіліксіздігі бар науқастарда жағымсыз клиникалық нәтижелердің предикторы ретінде sST2 биомаркері туралы әдеби деректерді талдау.

**Іздеу стратегиясы.** Ғылыми мақалалар PubMed, Web of Science, Google Scholar іздеу жүйелерінде, eLibrary және CyberLeninka электрондық ғылыми кітапханаларында ізделді. Іздеу тереңдігі – 5 жыл (2019-2024). Іздеу жүрек-қантамыр аурулары кезіндегі жағымсыз клиникалық нәтижелердің предикторлары ретінде кардиоренальді маркерлерге қатысты ақпаратты қамтыды.

**Нәтижелер.** Осы әдеби шолуда жүрек жеткіліксіздігі бар науқастарда sST2 биомаркерінің прогностикалық маңыздылығына арналған зерттеулер талданды. Зерттеу нәтижелері бойынша sST2 миокард фиброзы мен жүйелік қабыну сияқты негізгі патофизиологиялық үдерістерді бейнелейді. Әдеби деректер sST2-ні жағымсыз клиникалық нәтижелерді диагностикалау және болжау үшін қолдану тәуекелді ерте анықтауға, болжамды нақтылауға және науқастарды динамикалық бақылауға мүмкіндік беретінін растайды. Бұл биомаркерді клиникалық практикаға енгізу тәуекелді дәлірек стратификациялауға және емдеудің дербестендірілген тәсілдерін жүзеге асыруға жол ашады.

**Қорытынды.** Жүрек жеткіліксіздігінің клиникалық және зертханалық предикторлары бойынша қазіргі әдебиеттерді шолу sST2 биомаркерінің жоғары диагностикалық және прогностикалық маңызға ие екенін көрсетеді. Бұл биомаркер жүрек жеткіліксіздігінің үдеуіне тікелей байланысты миокард фиброзы мен жүйелік қабыну үдерістерін бейнелейді. sST2 үшін шекті мәндерді нақтылау, бағалау әдістерін валидациялау және оны клиникалық тәжірибеге енгізу мақсатында қосымша зерттеулер қажет.

***Түйін сөздер:*** *жүрек-қантамыр аурулары; клиникалық және зертханалық предикторлар; sST2; болжам; диагностика.*

***Дәйексөз үшін:***

*Қожабаева А.Д., Мансурова Ж.А., Жунуспекова А.С., Орехов А.Ю., Касымова А.А., Аширов Б.А., Смаилова Ж.К., Капакова М.А., Уразалина Н.М., Каражанова Л.К.* SST2 биомаркері жүрек жеткіліксіздігі кезіндегі жағымсыз клиникалық нәтижелерді болжаушы көрсеткіш ретінде. Әдебиеттік шолу // Ғылым және Денсаулық. 2025. Т.27 (3), Б.227–235. doi: 10.34689/SH.2025.27.3.024

**Introduction**

Heart failure is a rapidly escalating public health concern associated with reduced quality of life and increased mortality, affecting approximately 64.3 million individuals worldwide (1). A meta-analysis reported that the 1-year, 2-year, 5-year, and 10-year survival rates for heart failure were 86.5%, 72.6%, 56.7%, and 34.9%, respectively (2). Since 2002, there has been an estimated 25% increase in the prevalence of heart failure, a rise primarily driven by population aging, improved post-coronary event survival, and the escalating prevalence of major risk factors, including hypertension and atrial fibrillation (3). In addition, the rates of both heart failure and obesity are escalating rapidly, representing a growing public health concern. Obesity is present in nearly one out of every three individuals with heart failure and is especially prevalent in cases of heart failure with preserved ejection fraction (HFpEF) (4) (5). In asymptomatic individuals, obesity has been linked to reduced concentrations of brain natriuretic peptide (BNP), while the degradation of natriuretic peptides by adipose tissue has been linked to increased aldosterone activity, plasma volume expansion, and reduced ventricular compliance —key factors in the pathophysiology of HfpEF (6). Currently, the most robust evidence supports the use of natriuretic peptides and cardiac troponins as key biomarkers for prognostic assessment in patients with heart failure (7) (8). Nevertheless, natriuretic peptide has limited informativeness in patients with obesity, as its levels are reduced due to degradation by adipose tissue. This reduction diminishes its diagnostic and prognostic value, particularly in HFpEF, where key pathophysiological factors include increased aldosterone activity, plasma volume expansion, and reduced ventricular compliance (6). The simultaneous evaluation of several biomarkers may offer superior prognostic accuracy for both risk stratification and outcome prediction in individuals with heart failure, compared to the use of a single biomarker (9) (10) (11). sST2 serves as a biomarker of inflammatory and hemodynamic stress and, to some extent, reflects the degree of myocardial strain. Moreover, soluble ST2 (sST2) is critically involved in the process of ventricular remodeling and has been linked to higher mortality rates among patients with established heart failure (15).

**Aim.** Analysis of literature data on the biomarker sST2 as a predictor of adverse clinical outcomes in patients with heart failure.

**Search Strategy.** A search for scientific publications was conducted using the databases PubMed, Web of Science, and Google Scholar, as well as the electronic scientific libraries eLibrary and CyberLeninka. The search

covered a five-year period (2019–2024). The focus was placed on biomarkers of adverse outcomes in cardiovascular diseases, with particular emphasis on sST2.

*Inclusion criteria:* Original studies focusing on the diagnostic and prognostic significance of the specified biomarkers, as well as peer-reviewed full-text publications.

*Exclusion criteria:* Abstracts, reviews, publication summaries, informational letters, and letters to the editor.

*Search queries: English:* «cardiovascular diseases», «heart failure», «biomarkers», «sST2», «cardiovascular prognosis», «risk stratification».

*Russian language: "cardiovascular diseases", "heart failure", "biomarkers", "sST2", "cardiovascular prognosis," "risk stratification".*

In the initial search phase, 3,395 articles were identified. After applying the inclusion criteria, 198 full-text publications were analyzed, of which 59 were included in the review. The distribution of sources was as follows: PubMed (30), Web of Science (15), Google Scholar (7), CyberLeninka (7). Additionally, data from international clinical guidelines and statistical reports were considered.

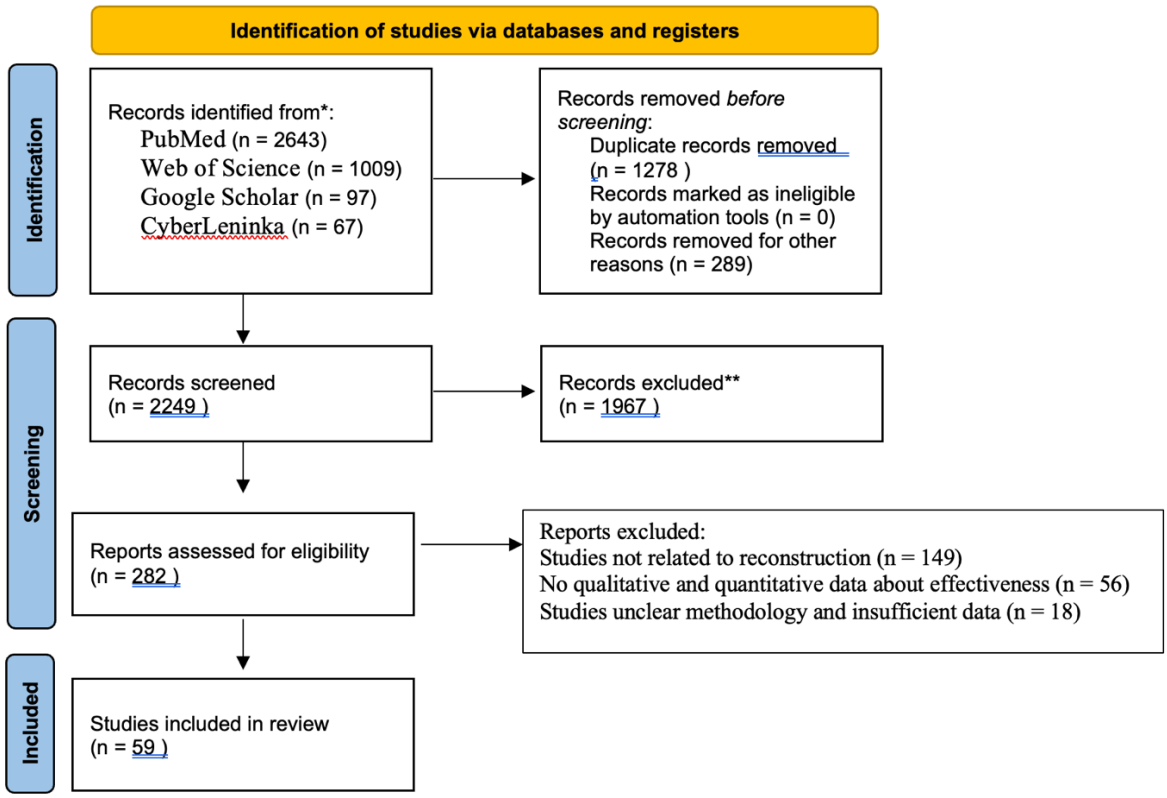



**Figure 1. PRISMA flowchart: literature search and study selection.**

**Results and Discussion**

In 1989, the ST2 receptor was first identified by two independent research groups studying fibroblasts activated by growth factors. The name "suppression of tumorigenicity" originated from the hypothesis that ST2 could restrict uncontrolled cell proliferation. Additionally, researcher *Shin-ichi Tominaga* had previously described another protein, later designated as ST1 (19). However, the functional significance of this protein remained undefined for several years. In 2002, *Weinberg et al.* conducted a gene expression analysis involving 7,000 genes in cardiomyocytes subjected to mechanical stress and observed a significant upregulation of ST2 in response to the stimulus (20). ST2 is classified within the interleukin-1 receptor superfamily and is encoded by a gene found at chromosome 2q12, within the interleukin-1 (IL1) gene locus (21). The IL-1 receptor comprises two main isoforms—soluble ST2 (sST2) and transmembrane ST2 (ST2L)—which are largely expressed in cardiomyocytes. In addition to indicating ventricular wall stress, these isoforms contribute to the regulation of immune and inflammatory pathways (22). Cardiac fibroblasts synthesize interleukin-33 (IL-33), an endogenous ligand of the ST2 receptor, while stromal cells release it in both cardiac and extracardiac tissues. The immunological role of IL-33 varies depending on the cellular environment, exhibiting either pro- or anti-inflammatory effects. In the heart, IL-33 interacts with the membrane-bound ST2L isoform, triggering a protective signaling cascade that counteracts cardiomyocyte hypertrophy, limits programmed cell death, and suppresses the development of myocardial fibrosis, thereby contributing to the preservation of cardiac structure and function (23). The binding of IL-33 to the transmembrane ST2L receptor mediates cardioprotective effects by limiting myocardial hypertrophy and preventing fibrotic remodeling. In contrast, the soluble form of ST2 (sST2) acts as a decoy receptor, capturing circulating IL-33 and blocking its beneficial signaling pathways, which contributes to the advancement of cardiac hypertrophy, fibrosis, and impaired ventricular function (24). The cardioprotective effect is mediated exclusively through the ST2L receptor and is not associated with the action of the soluble receptor form (25). Several hypotheses have been proposed to explain the functional role of sST2 in the pathogenesis of various diseases. In line

with the inflammatory hypothesis of atherosclerosis, sST2 binds to IL-33, amplifying inflammatory responses that contribute to plaque instability and elevate the risk of adverse cardiovascular events. Circulating levels of sST2 are regarded as a prognostic indicator of plaque instability, especially in individuals presenting with acute coronary syndrome (26). In oncology, sST2 is considered a key regulator of tumor growth, counteracting the tumorigenic effects of the IL-33/ST2 pathway. It may serve as a diagnostic and prognostic marker, as well as a tool for treatment monitoring. The membrane-bound receptor ST2L is linked to Th2-driven immune responses and serves a pivotal role in modulating immune regulation. The IL-33/ST2L signaling pathway is involved in the development of numerous inflammatory, autoimmune, and fibrotic diseases, including asthma, rheumatoid arthritis, pulmonary fibrosis, and ulcerative colitis (27). n liver diseases, the IL-33/ST2L signaling pathway has been shown to promote fibrotic processes, whereas elevated levels of sST2 have been observed in conditions such as cirrhosis, hepatocellular carcinoma, and hepatitis B infection—potentially reflecting a compensatory response aimed at resolving inflammation or limiting disease progression (28). Thus, sST2 plays a pivotal role in the pathogenesis of various diseases, including cardiovascular and inflammatory conditions, serving as a valuable prognostic and diagnostic marker. In cardiology, BNP and NT-proBNP are the principal biomarkers of heart failure (HF), as they reflect transmural myocardial wall stress and provide critical prognostic information. However, the clinical applicability of these biomarkers is limited by confounding factors, including comorbidities such as atrial fibrillation, renal impairment, and obesity, along with variations related to age and sex. Furthermore, BNP and NT-proBNP capture only specific aspects of the complex pathophysiology of HF (29). This underscores the necessity of expanding the biomarker panel to include sST2 to enhance diagnosis, risk stratification, and treatment monitoring. The prognostic relevance of sST2 was initially established in 2003. A subgroup analysis of the PRAISE-2 trial (Prospective Randomized Amlodipine Survival Evaluation-2), involving 161 patients with advanced heart failure (NYHA class III or IV), demonstrated a positive correlation between baseline sST2 levels and concentrations of natriuretic peptides. Moreover, changes in sST2 levels over two weeks emerged as an independent predictor of all-cause mortality and the need for heart transplantation, irrespective of natriuretic peptide concentrations (30). The strong prognostic significance of sST2, independent of NT-proBNP, was identified in a cohort of 593 patients presenting to the emergency department with acute dyspnea. This association was further validated in a cohort of 209 patients with a confirmed diagnosis of heart failure (31). Similar results were reported by *Müller et al.,* who found that higher sST2 concentrations at the time of admission in patients with acute heart failure were associated with a greater risk of mortality over the follow-up period (32). According to *Pascual-Figal et al.,* an sST2 level of 65 ng/mL serves as a critical cutoff point for identifying patients with acute heart failure who are at increased risk for adverse clinical events (33). Additionally, studies have shown that sST2 levels above 22 ng/mL are associated with a significantly increased risk of reaching the primary endpoint, which may be attributed to the inclusion of a wider array of predictive factors in the analysis (34). The prognostic utility of serial sST2 measurements in the context of acute heart failure has been explored in multiple studies. *Aimo et al.* showed that sST2 levels have significant prognostic value for all-cause mortality, cardiovascular death, and a combined endpoint including both death and heart failure-related hospitalizations in patients with acute decompensated heart failure. Importantly, sST2 concentrations measured at both admission and discharge were found to be predictive of the risk of rehospitalization due to heart failure (35). In a cohort of 150 patients who provided daily blood samples for sST2 measurement, the percentage change in this biomarker was found to be a strong predictor of 90-day mortality. Among patients who exhibited a reduction in sST2 levels of 15.5% or greater during the observation period, the observed mortality rate was 7%. In contrast, for patients with an sST2 reduction of less than 15.5%, the mortality risk reached 33%. The prognostic relevance of dynamic fluctuations in sST2 levels remained independent of concurrent changes in NT-proBNP concentrations (36). A multicenter study from the Netherlands involving 496 patients with acute heart failure reported that elevated baseline sST2 levels were significantly correlated with an increased risk of all-cause mortality and heart failure-related rehospitalization (hazard ratio [HR] per one standard deviation increase in $\log_2$-sST2: 1.30; 95% confidence interval [CI]: 1.08–1.56; p = 0.005). When evaluating repeated sST2 measurements over time, the HR increased to 1.85 (95% CI: 1.02–3.33; p = 0.044). A sub-analysis of the PIONEER-HF trial revealed that baseline sST2 concentrations held prognostic value for predicting both cardiovascular mortality and rehospitalization due to heart failure. Patients receiving sacubitril/valsartan exhibited a more pronounced reduction in sST2 levels as early as one week compared to those receiving enalapril, which correlated with improved clinical outcomes. The reduction in sST2 (6.4%) was less pronounced than that observed for hs-TnT (15.8%) and NT-proBNP (29.4%), likely reflecting the lower dependence of sST2 on decongestion (37). Januzzi et al. proposed an algorithm incorporating sST2 measurements to aid in the differential diagnosis of dyspnea. An sST2 threshold of ≥35 ng/mL was identified as a marker for both the presence of acute heart failure (AHF) and a heightened risk of adverse outcomes. Among patients presenting with dyspnea and elevated natriuretic peptide concentrations, sST2 levels allow for stratification into three distinct prognostic categories:

- sST2 concentrations below 35 ng/mL are observed in less than 10% of patients presenting to the emergency department with suspected AHF, strongly indicating the absence of the condition and aiding in its exclusion as a potential diagnosis.
- sST2 values in the range of 35–70 ng/mL require an assessment of the effectiveness of diuretic therapy in the emergency department; if clinical improvement is observed, the decision regarding the need for hospitalization is made accordingly.
- sST2 values >70 ng/mL are indicative of a high likelihood of AHF and provide strong justification for hospital admission and further clinical management (38).

sST2 levels above approximately 70 ng/mL have been linked to a heightened risk of mortality, both in the early phase (within 30 days) and during extended follow-up periods of up to one year (39). Recent findings indicate that implementing an sST2-guided strategy in patients arriving at the emergency department with dyspnea and elevated natriuretic peptides may improve diagnostic clarity, refine risk assessment, and assist in optimizing treatment decisions (40). Alongside established biomarkers like BNP and NT-proBNP, sST2 offers distinct prognostic value for predicting clinical outcomes. In a study by *Gaggin et al.,* sST2 demonstrated strong predictive power for mortality in both acute and chronic heart failure, underscoring its utility in assessing risk over both short-term and long-term follow-up (41). Research carried out at the Poznan University of Medical Sciences during 2016–2017 identified sST2 as an independent marker associated with all-cause mortality in patients diagnosed with heart failure with reduced ejection fraction (HFrEF). Deceased patients had significantly higher baseline sST2 levels (60.5 ± 53.3 pg/mL vs. 38.8 ± 32.0 pg/mL; $p$ = 0.0029). An sST2 level > 45.8 pg/mL was associated with an increased risk of mortality (50% vs. 21.6%; $p$ = 0.0025) (42). A meta-analysis involving over 4,000 patients confirmed that sST2 levels independently predict both all-cause and cardiovascular mortality, and also serve as a standalone risk factor for heart failure-related hospitalizations. Moreover, elevated sST2 levels were associated with increased concentrations of inflammatory markers, highlighting a potential relationship between inflammation and a heightened risk of adverse clinical outcomes (43). *Dupuy et al.* showed that simultaneous elevations in C-reactive protein (CRP) above 6.4 mg/L and sST2 levels above 47.6 ng/mL were strongly linked to increased mortality risk in patients with chronic heart failure. Importantly, incorporating NT-proBNP into the assessment did not provide additional prognostic benefit in this context (44). A heart failure study carried out in Pennsylvania with 1,141 patients suffering from chronic heart failure with reduced ejection fraction found that sST2 serves as a robust and dependable prognostic indicator. When combined with traditional biomarkers like BNP and pro-atrial natriuretic peptide, sST2 provided a modest improvement in risk stratification. Elevated sST2 concentrations were strongly linked to an increased risk of all-cause mortality or the need for heart transplantation, with this association being particularly pronounced among patients with non-ischemic heart failure (45). Furthermore, *Emdin et al.* showed that sST2 possesses significant prognostic value for the prediction of all-cause mortality, cardiovascular death, and heart failure-related events. Importantly, incorporating sST2 into existing risk prediction models improved risk reclassification beyond that achieved with traditional biomarkers such as NT-proBNP and high-sensitivity troponin T (hs-TnT) (46). The incorporation of sST2 alongside other biomarkers yielded a more precise prognostic evaluation in patients with renal impairment than in the general population (47). *Gruson et al.* established the prognostic significance of sST2 for cardiovascular mortality over a median follow-up period of 4.2 years. Among several prognostic indicators—such as natriuretic peptides, age, left ventricular ejection fraction, and glomerular filtration rate (GFR)—sST2 exhibited the most robust association with cardiovascular mortality (48). sST2 levels have been identified as an independent predictor of atrial fibrillation among patients with heart failure (49), likely reflecting underlying mechanisms related to aging and structural remodeling of the atria that contribute to the development of this arrhythmia (50). Increased sST2 concentrations have been associated with a greater risk of atrial fibrillation recurrence after radiofrequency catheter ablation, suggesting its potential role as a predictive biomarker for evaluating the likelihood of arrhythmia recurrence prior to the procedure (51). In 2011, *Ky et al.* (52) conducted a meta-analysis assessing the prognostic significance of sST2 in chronic heart failure outcomes across three cohorts. These findings were subsequently validated by the HF-ACTION trial (Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training) (53), which contributed to the approval of sST2 for clinical use by regulatory authorities in the United States. In 2016, a comprehensive meta-analysis was conducted, integrating pooled data from seven studies encompassing 6,372 patients. The results indicated that sST2 levels, even without adjustment for other variables, are a significant predictor of both all-cause and cardiovascular mortality in individuals with chronic heart failure (54). An extensive analysis involving 4,268 patients across 11 cohorts demonstrated a clear exponential relationship between elevated sST2 levels and the risks of all-cause mortality, cardiovascular death, and hospitalizations related to heart failure. A threshold of 28 ng/mL was identified as the optimal cutoff for predicting all three outcomes. Patients with median sST2 levels of 27 ng/mL or higher were found to have twice the risk of all-cause mortality, a 50% increase in the risk of cardiovascular death, and a 10% higher likelihood of hospitalization compared to those with lower levels. Furthermore, individuals with median values of all three biomarkers—sST2, NT-proBNP, and hs-TnT—above their respective thresholds experienced dramatic increases in risk: 850% for all-cause mortality, 640% for cardiovascular death, and 590% for hospitalization. Importantly, the prognostic value of sST2 was shown to be independent of NT-proBNP, high-sensitivity troponin T, and other clinical parameters, with no significant association observed between sST2 levels and baseline characteristics such as age, sex, body mass index, or renal function (55). In individuals with chronic heart failure, elevated sST2 concentrations have been recognized as a predictor of sudden cardiac death, offering prognostic information that complements and extends beyond the insights provided by NT-proBNP (56). In the context of acute coronary syndromes, both initial and repeated measurements of sST2 levels have demonstrated high predictive value for future cardiovascular events (57). Elevated serum sST2 concentrations assessed one week after ST-segment elevation myocardial infarction (STEMI) have been independently linked to unfavorable left ventricular remodeling observed at six-month follow-up (58). Moreover, increasing sST2 concentrations have been associated with disease progression and clinical worsening in heart failure patients, underscoring its value as a dynamic biomarker for continuous monitoring and guiding treatment decisions (59). Taken together, current evidence supports the strong potential of sST2 as a tool for risk stratification and for

lowering the likelihood of rehospitalization in patients with heart failure. However, achieving these objectives necessitates further investigation. Future research should aim to refine threshold values, elucidate the mechanistic role of sST2 in clinical outcomes, and assess its integration into established clinical algorithms. These advancements would facilitate the effective implementation of sST2 in optimizing therapeutic strategies and enhancing long-term patient outcomes.

**Conclusion.**

The biomarker sST2 exhibits high diagnostic and prognostic value in assessing cardiovascular risk. sST2 demonstrates significant promise in stratifying risk and forecasting adverse outcomes in individuals with heart failure. Nevertheless, its routine clinical application requires further investigation to establish optimal threshold values and support its integration into standardized clinical decision-making algorithms. Continued research is essential to validate its utility and enhance its implementation in everyday medical practice.

***Conflict of interest:*** *The authors declare that there is no conflict of interest, and that no part of this article has been published in the open press and is not under consideration by other publishers.*

***Contribution of the authors:***

*Conceptualization – Anar D. Kozhabayeva; methodology – Lyudmila K. Karazhanova, Jamilya A. Mansurova; validation – Aisulu S. Zhunuspekova, Andrey Yu. Orekhov, Mirgul A. Kapakova; data curation – Assel A. Kassymova, Zhanargul K. Smailova; resources – Bolat A. Ashirov, Nailya M. Urazalina; writing – original draft preparation – Anar D. Kozhabayeva, Jamilya A. Mansurova; writing – review and editing – Anar D. Kozhabayeva; project administration – Anar D. Kozhabayeva. All authors have read and agreed to the published version of the manuscript.* ***Corresponding author:*** *Jamilya A. Mansurova*

***Funding:*** *This research has been funded under the grant program for scientific start-up projects of academic staff at the NCJSC "Semey Medical University" for 2024–2026, within the framework of the project entitled "Scientific foundations for improving the prognosis in patients with chronic heart failure associated with chronic kidney disease" (Grant Agreement No. 27).*

***Literature:***

*1. Aimo A.* [и др.]. Meta-Analysis of Soluble Suppression of Tumorigenicity-2 and Prognosis in Acute Heart Failure // JACC: Heart Failure. 2017. № 4 (5). С. 287–296.

*2. Aimo A.* [и др.]. Prognostic Value of Soluble Suppression of Tumorigenicity-2 in Chronic Heart Failure: A Meta-Analysis // JACC: Heart Failure. 2017. № 4 (5). С. 280–286.

*3. Aleksova A.* [и др.]. Cardiac Biomarkers in the Emergency Department: The Role of Soluble ST2 (sST2) in Acute Heart Failure and Acute Coronary Syndrome—There is Meat on the Bone // Journal of Clinical Medicine. 2019. № 2 (8). С. 270.

*4. Asferg C.L.* [и др.]. Relative atrial natriuretic peptide deficiency and inadequate renin and angiotensin II suppression in obese hypertensive men // Hypertension. 2013. № 1 (62). С. 147–153.

*5. Bayes-Genis* A. [и др.]. Soluble ST2 Serum Concentration and Renal Function in Heart Failure // Journal of Cardiac Failure. 2013. № 11 (19). С. 768–775.

*6. Bayes-Genis A.* Ordonez-Llanos J. Multiple biomarker strategies for risk stratification in heart failure. Clinica Chimica Acta. 2015. (443). С. 120–125.

*7. Boisot S.* [и др.]. Serial Sampling of ST2 Predicts 90-Day Mortality Following Destabilized Heart Failure. Journal of Cardiac Failure. 2008. № 9 (14). С. 732–738.

*8. Buyzere M.L.* De Multi-biomarker risk stratification in heart failure: a story of diminished marginal returns after Herculean efforts? European Journal of Heart Failure. 2018. № 2 (20). С. 278–280.

*9. Chen Y.* [и др.]. sST2 and Big ET-1 as Alternatives of Multi-Biomarkers Strategies for Prognosis Evaluation in Patients Hospitalized with Heart Failure. International Journal of General Medicine. 2023. (16). С. 5003.

*10. Chen Z.H.* [и др.]. Correlation of serum homocysteine and cystatin C levels with prognosis in heart failure with preserved ejection fraction patients // BMC Cardiovascular Disorders. 2024. № 1 (24). С. 510.

*11. Chirinos J. A.* [и др.]. Multiple Plasma Biomarkers for Risk Stratification in Patients with Heart Failure and Preserved Ejection Fraction. Journal of the American College of Cardiology. 2020. № 11 (75). С. 1281.

*12. Cong X., Kong W.* Endothelial tight junctions and their regulatory signaling pathways in vascular homeostasis and disease. Cellular Signalling. 2020. (66). С. 109485.

*13. Conrad N.* [и др.]. Temporal trends and patterns in heart failure incidence: a population-based study of 4 million individuals. Lancet (London, England). 2018. № 10120 (391). С. 572.

*14. Conrad N.* [и др.]. Temporal trends and patterns in heart failure incidence: a population-based study of 4 million individuals. Lancet (London, England). 2018. № 10120 (391). С. 572.

*15. Demissei B.G.* [и др.]. A multimarker multi-time point-based risk stratification strategy in acute heart failure: results from the RELAX-AHF trial. European Journal of Heart Failure. 2017. № 8 (19). С. 1001–1010.

*16. Dudek M.* [и др.]. sST2 and Heart Failure—Clinical Utility and Prognosis. Journal of Clinical Medicine. 2023. № 9 (12). С. 3136.

*17. Dupuy A.M.* [и др.]. Multi-Marker Strategy in Heart Failure: Combination of ST2 and CRP Predicts Poor Outcome. PLoS ONE. 2016. № 6 (11). С. e0157159.

*18. Emdin M.* [и др.]. sST2 Predicts Outcome in Chronic Heart Failure Beyond NT−proBNP and High-Sensitivity Troponin T. Journal of the American College of Cardiology. 2018. № 19 (72). С. 2309–2320.

*19. Emdin M.* [и др.]. sST2 Predicts Outcome in Chronic Heart Failure Beyond NT−proBNP and High-Sensitivity Troponin T. Journal of the American College of Cardiology. 2018. № 19 (72). С. 2309–2320.

*20. Emdin M.* [и др.]. sST2 Predicts Outcome in Chronic Heart Failure Beyond NT−proBNP and High-Sensitivity Troponin T. Journal of the American College of Cardiology. 2018. № 19 (72). С. 2309–2320.

*21. Fan J.* [и др.]. Higher serum sST2 is associated with increased left atrial low-voltage areas and atrial fibrillation recurrence in patients undergoing radiofrequency ablation. Journal of Interventional Cardiac Electrophysiology. 2022. № 3 (64). С. 733–742.

*22. Felker G.M.* [и др.]. Soluble ST2 in Ambulatory Patients with Heart Failure Association with Functional

Capacity and Long-Term Outcomes. Circulation: Heart Failure. 2013. № 6 (6). С. 1172–1179.

*23. Gaggin H. K.* [и др.]. Head-to-Head Comparison of Serial Soluble ST2, Growth Differentiation Factor-15, and Highly-Sensitive Troponin T Measurements in Patients With Chronic Heart Failure. JACC: Heart Failure. 2014. № 1 (2). С. 65–72.

*24. Gimbrone M.A.,* García-Cardeña G. Endothelial Cell Dysfunction and the Pathobiology of Atherosclerosis. Circulation research. 2016. № 4 (118). С. 620.

*25. Gruson D.* [и др.]. Increased soluble ST2 is a stronger predictor of long-term cardiovascular death than natriuretic peptides in heart failure patients with reduced ejection fraction. International Journal of Cardiology. 2014. № 1 (172). С. e250–e252.

*26. Heidenreich P.A.* [и др.]. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2022. № 18 (145). С. E895–E1032.

*27. Homsak E., Gruson D.* Soluble ST2: A complex and diverse role in several diseases // Clinica Chimica Acta. 2020. (507). С. 75–87.

*28. Januzzi J. L.* [и др.]. Measurement of the Interleukin Family Member ST2 in Patients With Acute Dyspnea: Results From the PRIDE (Pro-Brain Natriuretic Peptide Investigation of Dyspnea in the Emergency Department) Study. Journal of the American College of Cardiology. 2007. № 7 (50). С. 607–613.

*29. Januzzi J. L., Mebazaa A., Somma S.* Di ST2 and prognosis in acutely decompensated heart failure: The international ST2 consensus panel. American Journal of Cardiology. 2015. № 7 (115). С. 26B-31B.

*30. Jones N. R.* [и др.]. Survival of patients with chronic heart failure in the community: a systematic review and meta-analysis. European Journal of Heart Failure. 2019. № 11 (21). С. 1306.

*31. Jones N.R.* [и др.]. Survival of patients with chronic heart failure in the community: a systematic review and meta-analysis. European Journal of Heart Failure. 2019. № 11 (21). С. 1306.

*32. Kakkar R., Lee R.T.* The IL-33/ST2 pathway: therapeutic target and novel biomarker. Nature reviews. Drug discovery. 2008. № 10 (7). С. 827.

*33. Kalstad A.A.* [и др.]. Biomarkers of ageing and cardiac remodeling are associated with atrial fibrillation. Scandinavian Cardiovascular Journal. 2021. № 4 (55). С. 213–219.

*34. Kercheva M.* [и др.]. Serum Soluble ST2 and Adverse Left Ventricular Remodeling in Patients With ST-Segment Elevation Myocardial Infarction. Clinical Medicine Insights. Cardiology. 2019. (13). С. 1179546819842804.

*35. Kuro-o M.* [и др.]. Mutation of the mouse klotho gene leads to a syndrome resembling ageing. Nature 1997 390:6655. 1997. № 6655 (390). С. 45–51.

*36. Kurosu H.* [и др.]. Suppression of Aging in Mice by the Hormone Klotho. Science (New York, N.Y.). 2005. № 5742 (309). С. 1829.

*37. Ky B.* [и др.]. High-Sensitivity ST2 for Prediction of Adverse Outcomes in Chronic Heart Failure. Circulation. Heart failure. 2010. № 2 (4). С. 180.

*38. Ky B.* [и др.]. High-Sensitivity ST2 for Prediction of Adverse Outcomes in Chronic Heart Failure. Circ Heart Fail. 2011. (4). С. 180–187.

*39. Li J.* [и др.]. A Review of Novel Cardiac Biomarkers in Acute or Chronic Cardiovascular Diseases: The Role of Soluble ST2 (sST2), Lipoprotein-Associated Phospholipase A2 (Lp-PLA2), Myeloperoxidase (MPO), and Procalcitonin (PCT). Disease Markers. 2021. (2021). С. 6258865.

*40. McDonagh T.A.* [и др.]. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC. European Heart Journal. 2021. № 36 (42). С. 3599–3726.

*41. Morrow D.A.* [и др.]. Cardiovascular biomarkers in patients with acute decompensated heart failure randomized to sacubitril-valsartan or enalapril in the PIONEER-HF trial.

*42. Mueller C.* [и др.]. Inflammation and long-term mortality in acute congestive heart failure. American Heart Journal. 2006. № 4 (151). С. 845–850.

*43. Oztas E.* [и др.]. Can Serum ST2 Levels Be Used as a Marker of Fibrosis in Chronic Hepatitis B Infection? Medicine. 2015. № 47 (94). С. e1889.

*44. Pandey A.* [и др.]. Physical Activity, Fitness, and Obesity in Heart Failure With Preserved Ejection Fraction. JACC: Heart Failure. 2018. № 12 (6). С. 975–982.

*45. Pascual-Figal D.A.* [и др.]. Soluble ST2 for Predicting Sudden Cardiac Death in Patients With Chronic Heart Failure and Left Ventricular Systolic Dysfunction. Journal of the American College of Cardiology. 2009. № 23 (54). С. 2174–2179.

*46. Pascual-Figal D.A.* [и др.]. Soluble ST2, high-sensitivity troponin T- and N-terminal pro-B-type natriuretic peptide: complementary role for risk stratification in acutely decompensated heart failure. European Journal of Heart Failure. 2011. № 7 (13). С. 718–725.

*47. Pascual-Figal D.A.* [и др.]. Soluble ST2, high-sensitivity troponin T- and N-terminal pro-B-type natriuretic peptide: complementary role for risk stratification in acutely decompensated heart failure. European Journal of Heart Failure. 2011. № 7 (13). С. 718–725.

*48. Ragusa R.* [и др.]. Time-course of circulating cardiac and inflammatory biomarkers after Ventricular Assist Device implantation: Comparison between paediatric and adult patients. Clinica Chimica Acta. 2018. (486). С. 88–93.

*49. Riccardi M.* [и др.]. Soluble ST2 in Heart Failure: A Clinical Role beyond B-Type Natriuretic Peptide. Journal of Cardiovascular Development and Disease. 2023. № 11 (10). С. 468.

*50. Sciatti E.* [и др.]. Prognostic Value of sST2 in Heart Failure. Journal of Clinical Medicine. 2023. № 12 (12). С. 3970.

*51. Tominaga S.* ichi Murine mRNA for the β-subunit of integrin is increased in BALB/c-3T3 cells entering the G1 phase from the G0 state. FEBS Letters. 1988. № 2 (238). С. 315–319.

*52. Tsigkou V.* [и др.]. The Predictive Role for ST2 in Patients with Acute Coronary Syndromes and Heart Failure. Current Medicinal Chemistry. 2019. № 27 (27). С. 4479–4493.

*53. Tsutsui H.* [и др.]. Natriuretic Peptides: Role in the Diagnosis and Management of Heart Failure: A Scientific Statement From the Heart Failure Association of the European Society of Cardiology, Heart Failure Society of America and Japanese Heart Failure Society. Journal of Cardiac Failure. 2023. № 5 (29). С. 787–804.

*54. Villacorta H., Maisel A. S.* Soluble ST2 Testing: A Promising Biomarker in the Management of Heart Failure. Arquivos Brasileiros de Cardiologia. 2016. № 2 (106). С. 145.

*55. Wang W.* [и др.]. Cellular crosstalk in organotypic vasculature: mechanisms of diabetic cardiorenal complications and SGLT2i responses. Cardiovascular Diabetology. 2025. № 1 (24). С. 90.

*56. Weinberg E.O.* [и др.]. Expression and Regulation of ST2, an Interleukin-1 Receptor Family Member, in Cardiomyocytes and Myocardial Infarction. Circulation. 2002. № 23 (106). С. 2961.

*57. Weinberg E.O.* [и др.]. Identification of Serum Soluble ST2 Receptor as a Novel Heart Failure Biomarker 2003.

*58. Yan X.* [и др.]. The sST2 level is an independent influencing factor associated with atrial fibrillation in heart failure patients: a case-control study. Journal of Thoracic Disease. 2022. № 5 (14). С. 1578–1587.

*59. Zhang J.* [и др.]. Soluble ST2 in coronary artery disease: Clinical biomarkers and treatment guidance. Frontiers in Cardiovascular Medicine. 2022. (9). С. 924461.

**Information about the authors:**

**Anar D. Kozhabayeva**- PhD, Doctoral student at the Department of Therapy of the NAO "Semey Medical University", Postal address: 103 Abai Kunanbayev str., Semey, 071400, Republic of Kazakhstan, Abay region, https://orcid.org/0000-0003-4132-6755, e-mail:anik97.kz@bk.ru; Phone number: +7 705 817 9617,

**Aisulu S. Zhunuspekova** - PhD, Acting Associate Professor of the Department of Therapy of the NAO "Semey Medical University", Postal address: 071400, Republic of Kazakhstan, Abai region, Semey, Abai Kunanbayeva str., 103, https://orcid.org/0000-0002-2413-317X , e-mail: aisulu.zhunuspekova@smu.edu.kz ; Phone number: +7 771 840 5880,

**Andrey Yu. Orekhov** - PhD, Assistant Professor at the Department of Therapy of the NAO "Semey Medical University", Postal address: 103 Abai Kunanbayeva str., Semey, 071400, Republic of Kazakhstan, Abay region, Semey, https://orcid.org/0000-0001-7201-1399, e-mail: orekhov-andrei@list.ru ; Phone number: +7 777 414 1476,

**Assel A. Kassymova –** PhD candidate, Department of Therapy of the NAO "Semey Medical University", Postal address: 103 Abai Kunanbayeva str., Semey, 071400, Republic of Kazakhstan, Abay region, Semey, https://orcid.org/0000-0001-9333-4146, e-mail: kassymova2411@gmail.com; Phone number: +7 775 177 4490

**Bolat A. Ashirov** - Candidate of Medical Sciences, South Kazakhstan Medical Academy, Republic of Kazakhstan, https://orcid.org/0000-0003-0242-9700, e-mail: bolat.baja@mail.

**Zhanargyl K. Smailova -** Candidate of Medical Sciences, Associate Professor, Vice Rector for Academic and Educational Work, NCJSC «Semey Medical University», phone 8 707 365 82 71, e-mail: zhanargul.smailova@smu.edu.kz; https://orcid.org/0000-0002-4513-4614;

**Mirgul A. Kapakova** - Candidate of Medical Sciences, Head of the Department of Therapy at the NAO "Semey Medical University", Postal address: 103 Abai Kunanbayev str., Semey, 071400, Republic of Kazakhstan, Abay region, https://orcid.org/0000-0003-4186-8933, e-mail: kma_mira@mail.ru; Phone number: +7 777 278 9724,

**Nailya M. Urazalina** - Candidate of Medical Sciences, Associate Professor of the Department of physiological disciplines named after honored scientist of the republic of Kazakhstan, professor T.A. Nazarova, NJSC "Semey Medical University", Semey, Kazakhstan; phone: 8 777 907 55 89, e-mail: hakim_15@mail.ru, https://orcid.org/0000-0003-0200-1763,

**Lyudmila K. Karazhanova** - Doctor of Medical Sciences, Professor of the Department of Therapy of the NAO "Semey Medical University", Postal address: 103 Abai Kunanbayev str., Semey, 071400, Republic of Kazakhstan, Abay region, https://orcid.org/0000-0002-4719-6034, e-mail: kar_ludmila@bk.ru; Phone number: +7 701 355 9976,

***Correspondence author:**

**Jamilya A. Mansurova** - PhD, Associate Professor, Head of the Department of Therapy at the NAO "Semey Medical University", Semey, Kazakhstan,

**Postal code:** Republic of Kazakhstan, 071400, Semey city, Abay region, Abay Street 103. 071400.

**E-mail:** mansurova_dzhami@mail.ru

**Phone:** +7 777 330 5104,

Received: 01 February 2025 / Accepted: 29 May 2025 / Published online: 30 June 2025

***DOI10.34689/SH.2025.27.3.025***

***UDC*616.72-007.234:004.8**

This work is licensed under a Creative Commons Attribution 4.0 International License

# CAPABILITIES OF ARTIFICIAL INTELLIGENCE IN MODERN RHEUMATOLOGY. LITERATURE REVIEW

**Yuliya V. Petrova[1], https://orcid.org/0000-0003-1910-7169**

**Maiya V. Goremykina[1], https://orcid.org/0000-0002-5433-7771**

**Raifa L. Ivanova[1], https://orcid.org/0000-0001-9851-2255**

**Dana K. Kozhakhmetova[1], https://orcid.org/0000-0002-8367-1461**

**Ainur S. Botabayeva[1], http://orcid.org/0009-0008-9228-7788**

**Alexandra A. Razvodova[2], http://orcid.org/0009-0004-2016-6400**

**[1]NCJSC «Semey Medical University», Semey, Republic of Kazakhstan;**
**[2] LLT "Gippokrat", Kostanay, Republic of Kazakhstan.**

**Abstract**

**Relevance**: The application of artificial intelligence (AI) in clinical practice opens new opportunities to improve diagnostic and prognostic accuracy in rheumatology, a field characterized by high disease heterogeneity and the complexity of interpreting visual and clinical data

**Search strategy**: An analysis was conducted on 58 publications selected from 467 relevant sources (2015–2025), identified through PubMed, Google Scholar, and CyberLeninka databases. Included were original studies and review articles focused on the use of machine learning and deep learning methods in rheumatology.

**Results**: AI is increasingly being implemented to address tasks related to early diagnosis, disease course prediction, and personalized therapy selection in rheumatoid arthritis, spondyloarthritis, systemic lupus erythematosus, and osteoarthritis. Convolutional neural networks, multi-omics approaches, and adaptive prediction models were found to be the most effective, demonstrating high accuracy (with AUC values up to 0.85). Despite this potential, clinical integration remains limited due to small training datasets, the need for external validation, and insufficient model standardization.

**Conclusions**: AI holds significant practical value in rheumatology. Its integration into healthcare systems requires regulatory frameworks, medical staff training, the development of digital infrastructure, and interdisciplinary collaboration.

***Keywords:*** *artificial intelligence; deep learning; machine learning; neural networks; rheumatology.*

***Forcitation:***

*Petrova Y.V., Goremykina M.V., Ivanova R.L., Kozhakhmetova D.K., Botabayeva A.S., Razvodova A.A.* Capabilities of Artificial Intelligence in Modern Rheumatology. Literature review // *Nauka I Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27(3), pp.236-244. *doi 10.34689/SH.2025.27.3.025*

**Резюме**

# ВОЗМОЖНОСТИ ИСКУССТВЕННОГО ИНТЕЛЛЕКТА В СОВРЕМЕННОЙ РЕВМАТОЛОГИИ. ОБЗОР ЛИТЕРАТУРЫ

**Юлия В. Петрова[1], https://orcid.org/0000-0003-1910-7169**

**Майя В. Горемыкина[1], https://orcid.org/0000-0002-5433-7771**

**Райфа Л. Иванова[1], https://orcid.org/0000-0001-9851-2255**

**Дана К. Кожахметова[1], https://orcid.org/0000-0002-8367-1461**

**Айнур С. Ботабаева[1], http://orcid.org/0009-0008-9228-7788**

**Александра А. Разводова[2], http://orcid.org/0009-0004-2016-6400**

**[1] НАО «Медицинский университет Семей», г. Семей, Республика Казахстан;**
**[2]ТОО "Гиппократ", Костанай, Республика Казахстан.**

**Актуальность:** Применение искусственного интеллекта (ИИ) в клинической практике открывает новые возможности для повышения точности диагностики и прогнозирования в ревматологии, где характерна высокая гетерогенность заболеваний и сложность интерпретации визуальных и клинических данных.

**Стратегия поиска:** Проведен анализ 58 публикации, отобранных из 467 релевантных источников (2015–2025 гг.), идентифицированных в базах PubMed, GoogleScholar и CyberLeninka. Включены оригинальные исследования и обзорные статьи, посвященные применению методов машинного и глубокого обучения в ревматологии.

**Результаты:** ИИ активно внедряется для решения задач ранней диагностики, прогнозирования течения и подбора терапии при ревматоидном артрите, спондилоартритах, системной красной волчанке и остеоартрите. Наиболее эффективными оказались сверточные нейронные сети, мультиомные подходы и адаптивные модели прогнозирования, демонстрирующие высокую точность (до AUC до 0,85). Несмотря на значительный потенциал,

клиническое применение затруднено из-за ограниченности обучающих выборок, необходимости внешней валидации и недостаточной стандартизации моделей.

**Заключение:** ИИ обладает высокой прикладной ценностью в ревматологической практике. Для интеграции в систему здравоохранения необходимы нормативное регулирование, подготовка медицинского персонала, развитие цифровой инфраструктуры и междисциплинарное сотрудничество.

***Ключевые слова:*** *искусственный интеллект, глубокое обучение, машинное обучение, нейронные сети, ревматология.*

***Для цитирования:***

*Петрова Ю.В., Горемыкина М.В., Иванова Р.Л., Кожахметова Д.К., Ботабаева А.С., Разводова А.А.*Возможности искусственного интеллекта в современной ревматологии. Обзор литературы // Наука и Здравоохранение. 2025. Т.27 (3), С. 236-244. doi: 10.34689/SH.2025.27.3.025

**Түйіндеме**

# ҚАЗІРГІ РЕВМАТОЛОГИЯДАҒЫ ЖАСАНДЫ ИНТЕЛЛЕКТІНІҢ МҮМКІНДІКТЕРІ. ӘДЕБИЕТТІК ШОЛУ

**Юлия В. Петрова[1], https://orcid.org/0000-0003-1910-7169**

**Майя В. Горемыкина[1], https://orcid.org/0000-0002-5433-7771**

**Райфа Л. Иванова[1], https://orcid.org/0000-0001-9851-2255**

**Дана К. Кожахметова[1], https://orcid.org/0000-0002-8367-1461**

**Айнур С. Ботабаева[1], http://orcid.org/0009-0008-9228-7788**

**Александра А. Разводова[2], http://orcid.org/0009-0004-2016-6400**

**[1] «Семей медицина университеті» КеАҚ, Семей қ., Қазақстан Республикасы.**
**[2] "Гиппократ" ЖШС, Қостанай, Қазақстан Республикасы**

**Өзектілігі:** Клиникалық тәжірибеде жасанды интеллектіні (ЖИ) қолдану ревматология саласында диагноз қою мен болжау дәлдігін арттыру үшін жаңа мүмкіндіктер ашады. Бұл салада аурулардың гетерогенділігі және визуалды әрі клиникалық деректерді түсіндірудегі күрделілік жоғары.

**Іздеу стратегиясы**: PubMed, Google Scholar және CyberLeninka дерекқорларынан анықталған 467 дереккөздің ішінен іріктелген 58 ғылыми жарияланымға талдау жүргізілді (2015–2025 жж.). Ревматологияда машиналық және терең оқыту әдістерін қолдануға арналған түпнұсқалық зерттеулер мен шолу мақалалары қарастырылды.

**Нәтижелер:** ЖИ ерте диагностикалау, ауру барысын болжау және жекелендірілген емді таңдау міндеттерін шешу үшін кеңінен енгізілуде. Бұл ретте ревматоидты артрит, спондилоартрит, жүйелі қызыл жегі және остеоартрит сияқты аурулар қарастырылған. Ең тиімді әдістер ретінде — өте дәл нейрондық желілер, мультиомдық тәсілдер және бейімделген болжамдық модельдер танылды. Олар жоғары дәлдікпен (AUC 0.85-ке дейін) ерекшеленді. Дегенмен, оқыту деректерінің шектеулілігі, сыртқы валидация қажеттілігі және модельдерді стандарттаудың жеткіліксіздігі клиникалық қолдануға кедергі келтіруде.

**Қорытынды**: Жасанды интеллект ревматологиялық тәжірибеде жоғары қолданбалы құндылыққа ие. Денсаулық сақтау жүйесіне интеграциялау үшін нормативтік реттеу, медициналық персоналды даярлау, цифрлық инфрақұрылымды дамыту және пәнаралық ынтымақтастық қажет.

***Түйінді сөздер****: жасанды интеллект, терең оқыту, машинамен оқыту, нейрондық желілер, ревматология.*

***Дәйексөз үшін:***

*Петрова Ю.В., Горемыкина М.В., Иванова Р.Л., Кожахметова Д.К., Ботабаева А.С., Разводова А.А. Қазіргі ревматологиядағы жасанды интеллектінің мүмкіндіктері.* Әдебиеттік шолу // Ғылым және Денсаулық. 2025. Т.27 (3), Б. 236-244. doi: 10.34689/SH.2025.27.3.025

**Introduction**:

The rapid advancement of artificial intelligence (AI) has ushered in a new era in clinical medicine, where precision and standardization of diagnostic decision-making are becoming equally essential. In the field of rheumatology - marked by heterogeneity in clinical presentation and disease trajectory - AI has the potential to enhance consistency and reproducibility in diagnostic algorithms and therapeutic planning [41].

In particular, AI technologies are increasingly being applied to address variability in the interpretation of clinical, laboratory, and imaging data in diseases such as rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA), systemic lupus erythematosus (SLE), and osteoarthritis (OA). Neural networks have demonstrated the ability to identify signs of joint inflammation in radiographs and even to generate synthetic computed tomography (CT) images, enabling standardized and non-invasive disease assessment [22, 40].

Beyond diagnosis, AI contributes to patient stratification, treatment optimization, and outcome prediction. The ability to forecast disease progression and the likelihood of flares is especially critical in chronic inflammatory conditions,

where timely therapeutic interventions can significantly alter patient trajectories [39].

Despite these advancements, several barriers remain. Integrating heterogeneous data—ranging from clinical records and imaging to molecular and behavioral data—demands robust, high-quality training datasets. Moreover, the development of explainable and generalizable models remains a methodological challenge. Nevertheless, promising studies demonstrate the feasibility of AI applications in predicting RA exacerbations and identifying metabolomic profiles associated with gout flares, indicating the maturity of this research domain [27, 55, 56].

The potential of AI in healthcare is of particular relevance to Kazakhstan. While foundational steps such as electronic health records (EHRs) implementation and telemedicine platforms are being developed in major cities like Astana and Almaty, the broader adoption of AI in rheumatologic care remains limited [1, 34]. Key obstacles include underdeveloped digital infrastructure in rural areas, gaps in healthcare workforce training, and data privacy concerns [34].

However, Kazakhstan's unique geographic, demographic, and epidemiological context offers opportunities for AI-driven solutions. The integration of AI may bridge gaps in rheumatologic care delivery across the country, particularly in underserved regions. Government initiatives in digital health, combined with partnerships with international research centers and targeted education in medical informatics, could accelerate the adoption of AI in clinical practice.

**This review aims** to provide a critical synthesis of current and emerging applications of AI in rheumatology, with an emphasis on their potential implementation in Kazakhstan's healthcare system.

**Search Strategy**

A comprehensive literature search was conducted to identify peer-reviewed publications related to the application of AI in rheumatology. The search was performed using internationally recognized databases of evidence-based medicine and electronic scientific libraries, including PubMed, Google Scholar, and CyberLeninka. *Inclusion criteria* were as follows: original research articles, systematic reviews and narrative reviews; publications in English and Russian; full-text availability with structured abstracts; publication years ranging from 2015 to 2025. *Exclusion criteria* included: book chapters, dissertations, and conference abstracts; publications lacking original data or relevance to AI applications in rheumatology; articles without abstracts or full-text access; unpublished manuscripts.

The search strategy incorporated the following keywords: "artificial intelligence", "machine learning", "deep learning", "neural networks", and "rheumatology".

The initial search identified 467 articles. After screening titles, abstracts, and full texts according to the predefined eligibility criteria, 58 publications were selected for detailed analysis.

**Results and Discussion:**

**Types, concepts and methods of artificial intelligence**

AI is an interdisciplinary domain within computer science focused on the development of algorithms capable of simulating human cognitive functions, including learning, pattern recognition, prediction, and decision-making. Among the core subfields of AI is machine learning (ML), which enables systems to detect patterns in data without relying on explicitly defined rules. This adaptive capability allows ML models to solve complex problems by learning from input data [58].

In contrast to traditional statistical approaches that emphasize hypothesis testing and causal inference, ML methods prioritize predictive accuracy. However, this often comes at the expense of model interpretability—a critical concern in clinical settings where transparency and accountability are essential.

Deep learning (DL), a subdomain of ML, utilizes multilayered artificial neural networks. The rise in computational capacity and the growing availability of large-scale datasets have led to the widespread use of DL, particularly in medical image analysis, genomics, and drug discovery [28]. A hierarchical structure of AI technologies is illustrated in **Figure 1.**

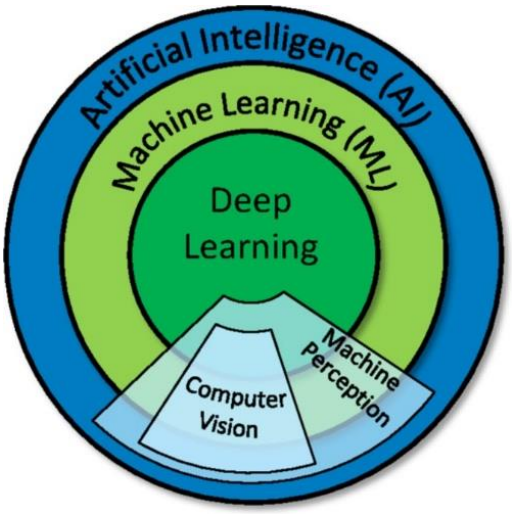



**Figure 1. Hierarchy of Artificial Intelligence Technologies**

ML methods are conventionally divided into three primary categories, each tailored to specific problem types:

**1. Supervised Learning**

Supervised learning involves training algorithms on labeled datasets, where both input features and corresponding target outputs are known. Applications include disease classification from medical images, analysis of EHRs, and prediction of disease recurrence risk. Common supervised algorithms include random forests, support vector machines (SVM), convolutional neural networks (CNNs), and natural language processing (NLP) models [58].

**2. Unsupervised Learning**

This approach is employed when labeled data are unavailable. The objective is to uncover underlying structures, clusters, or patterns in the dataset using techniques such as clustering or dimensionality reduction. Examples in medicine include patient subgrouping based on disease risk or phenotypic characteristics, and identification of novel disease subtypes.

**3. Reinforcement Learning**

In this paradigm, the model learns optimal strategies through interactions with its environment, receiving feedback in the form of rewards or penalties. Reinforcement learning is actively applied in robotic surgery and in optimizing adaptive therapeutic strategies, including dynamic treatment planning [21].

A comparative summary of widely used supervised ML algorithms is provided in Table 1.

*Table 1.*

**Comparative Characteristics of Major Machine Learning Algorithms.**

| Algorithm | Description | Common use cases | References |
|---|---|---|---|
| Logistic Regression | Model for binary classification, establishes a relationship between input variables and the probability of one of two outcomes occurring. A threshold value is used to define the class. | Flare prediction, clinical decision rules, screening | [25], [29] |
| Lasso Regression | Regularized linear regression, prevents overtraining due to a penalty (L1-norm) in the loss function, effective for a large number of features | Regression/feature selection, risk modeling | [2] |
| Support Vector Machine (SVM) | A classifier that constructs an optimal hyperplane for class separation; robust to outliers and applicable to high dimensional problems. | Diagnosis from gene expression or metabolomic data | [24], [27], [29] |
| Decision Tree | Hierarchical model representing decisions in the form of a tree; easy to interpret but prone to overfitting. | Diagnostic algorithms that sequentially evaluate symptoms and lab results | [25] |
| Random Forest (RF) | An ensemble method that combines multiple decision trees; improves model accuracy and robustness by reducing overfitting. | Risk prediction, patient stratification, outcome modeling | [2], [5], [18] [23], [24] |
| Naive Bayes | Classifier assuming feature independence; works quickly and efficiently on large amounts of data. | Disease prediction | [44] |
| Convolutional Neural Networks (CNN) | A multilayer structure that mimics the operation of neurons; well suited for processing images, text, and other complex data. | Prognosis prediction, disease classification, X-ray/MRI interpretation | [3], [4], [20] [22], [35], [48] |

Among ML methods, CNNs have emerged as particularly powerful tools. These architectures have demonstrated high accuracy in diagnosing diseases from radiological images such as X-rays, CT-images, and magnetic resonance imaging (MRI) - in some cases outperforming human experts in specific diagnostic tasks [15, 28]. CNNs are also used in genomics for identifying pathogenic mutations and developing personalized treatment strategies. Nevertheless, these models require large training datasets and substantial computational resources, which can limit their scalability and adoption in routine clinical practice.

A fundamental understanding of AI and ML concepts is increasingly important for healthcare professionals, particularly when evaluating and applying AI-driven tools in clinical workflows. To promote transparency, reproducibility, and safety, various methodological guidelines have been developed - such as CONSORT-AI, SPIRIT-AI, and others - which assist researchers in designing AI studies and aid clinicians in critically appraising AI model performance [26, 31, 33, 45].

In this review, we examined the role of AI - specifically neural network models - in the diagnosis, prognosis, and clinical monitoring of major rheumatologic diseases.

**Rheumatoid arthritis**

*Diagnosis and assessment of disease activity*

Modern ML and computer vision (CV) techniques are increasingly applied for early diagnosis of RA, including the preclinical phase. CV algorithms have shown efficacy in analyzing radiographic, ultrasonographic (US), and MRI data to detect early inflammatory changes such as erosions, bone marrow edema, and synovitis.

*Stoel B.C. et al.* (2019) demonstrated the utility of CNNs in the automated analysis of hand MRI for early RA detection. These models accurately and reproducibly identified bone marrow edema and tenosynovitis, outperforming traditional visual assessment by radiologists. The study highlighted the potential for full automation and emphasized the necessity of interpretable models and high-quality annotated datasets for clinical implementation [48].

Several studies have confirmed the high sensitivity and specificity of AI models for detecting erosions and joint space narrowing on radiographs in RA [13, 20, 35, 43]. However, current models remain insufficiently validated for routine clinical use due to limited dataset diversity, absence of external validation, and inconsistent reporting standards [4].

In the MEDUSA project, an ML-based method was developed to automatically grade synovitis on US images. While the algorithm demonstrated good concordance with expert evaluations, interrater agreement (k-coefficients) between algorithm and experts was lower than that between experts themselves, suggesting potential for improvement [32].

*Predicting response to therapy*

Another promising application of AI in rheumatology is the prediction of therapeutic response, particularly to biologic and targeted synthetic disease-modifying antirheumatic drugs (DMARDs), which could enable personalized treatment strategies.

*Bouget V. et al.* (2022) used AI models to predict treatment response to methotrexate and tumor necrosis factor - α (TNF-α) inhibitors using data from the ESPOIR, T-Reach, and Leiden cohorts. The models achieved AUC values ranging from 0.78 to 0.84, indicating high predictive accuracy [5, 6]. AUC, or area under the receiver operating characteristic curve, quantifies model performance: 1.0 reflects perfect discrimination, while 0.5 indicates random classification.

*Tao W. et al.* (2021) demonstrated that integrating transcriptomic, proteomic, and clinical data significantly improved prediction of response to biologic therapies such as adalimumab and etanercept (AUC = 0.79 in the BiOCURA cohort) [49]. Similarly, Casaburi et al. (2022) applied RNA sequencing and ML methods to synovial tissue to predict early response to conventional DMARDs [9].

In a recent study, *Sonomoto K. et al.* (2024) developed a model to predict clinical remission based on the Clinical Disease Activity Index (CDAI) during TNF- α inhibitor therapy using data from the Japanese FIRST registry (AUC = 0.70) [46]. *Cohen S. et al.* (2021) created a molecular signature classifier to identify likely non-responders to TNF-α inhibitors, achieving AUC > 0.70 based on ACR50/70 criteria [12].

These findings highlight the potential of AI-driven personalized treatment approaches in RA. However, they also underscore the need for external validation, standardized evaluation metrics, and integration into clinical workflows.

*Predicting progression and exacerbations*

AI-based models, particularly those using recurrent neural networks (RNNs) and time series analysis, show promise in predicting RA progression and flares. These models leverage longitudinal data - including demographic, clinical, and laboratory variables - to anticipate disease trajectory and optimize treatment plans.

*Kalweit M. et al.* (2021) developed a DL model (AdaptiveNet) using data from over 9,500 patients in the Swiss SCQM registry. The model achieved an AUC of 0.73, sensitivity of 84.2%, specificity of 61.5%, and 75.6% classification accuracy for disease activity (DAS28-ESR > 2.6). The average error in DAS28-ESR prediction was 0.9. Key predictors included the number of tender joints, patient age, and disease duration [24].

*Norgeot B. et al.* (2019) evaluated gradient-boosted decision tree models using data from EHRs of 820 patients across two centers. These models outperformed traditional methods in predicting disease activity and identified over 20 relevant clinical variables. The study suggested that similar approaches could be extended to other chronic diseases with measurable outcomes [38].

**Ankylosing spondylitis**

*Image Interpretation*

Recent advancements in medical imaging analysis have seen a growing application of ML techniques, particularly in improving the diagnostic and prognostic accuracy for musculoskeletal diseases. A prominent area of research is the use of CNNs to classify the severity of sacroiliitis based on the modified New York criteria.

Multiple studies have demonstrated that CNNs can reliably differentiate between normal and pathological cases of sacroiliitis on radiographs (e.g., grade ≥2 bilaterally or grade ≥3 unilaterally), achieving diagnostic accuracy ranging from 89% to 97%, sensitivity from 79% to 91%, and specificity from 79% to 96%. These performance metrics are comparable to those achieved by experienced rheumatologists. In addition to classification tasks, CNNs are increasingly used to localize structural lesions such as erosions, subchondral sclerosis, and ankylosis in the sacroiliac joints [7].

On MRI of the sacroiliac joints, ML algorithms have shown capability in detecting bone marrow edema—a key imaging marker of active inflammation [8, 42]. A German study (*Bressem K.K. et al.,* 2022) reported that CNNs achieved diagnostic sensitivity and specificity comparable to expert readers, and in some cases, outperformed general radiologists without specific expertise in musculoskeletal imaging [7]. However, variability in reported diagnostic performance across studies may reflect heterogeneity in MRI acquisition protocols, reference standards, and patient sampling, particularly in single-center settings.

Beyond diagnostic tasks, CNNs have also been utilized for prognostic modeling, including the prediction of radiographic progression [3], and for generating synthetic MRI and CT images [23]. Notably, synthetic CT generated from MRI data has emerged as a promising tool, providing enhanced visualization of erosions, sclerosis, and ankylosis compared to conventional MRI. These synthetic images have shown strong concordance with reference (true) CT and offer a radiation-free alternative for early detection of structural changes in axial AS.

*Dynamic monitoring of patients*

Beyond traditional imaging analysis, AI - including large language models (LLMs) such as GPT-4, LLaMA, Bard, and Claude - has emerged as a promising tool for the dynamic monitoring of patient-reported outcomes (PROs). These models can generate structured textual summaries based on patients' descriptions of their symptoms and lived experiences, facilitating more granular and longitudinal tracking of disease dynamics.

By automating the interpretation and synthesis of subjective reports, LLMs offer potential advantages including reduced patient burden, streamlined data collection, and improved consistency in symptom monitoring over time. However, several challenges remain. These include the accurate extraction and contextualization of nuanced patient-reported symptoms from natural language input, the difficulty of mapping free-text data to standardized quantitative metrics, and the need for rigorous validation of such approaches against established PRO instruments [53, 54].

*Predicting response to therapy*

The selection and evaluation of treatment efficacy, particularly for biologic and targeted synthetic DMARDs in AS, remains a clinical challenge. This is due to the individual variability in treatment response, the absence of robust predictive biomarkers, and the substantial costs associated with advanced therapies. In this context, the application of AI-based predictive models represents a rapidly evolving and promising area of research [29, 30, 57].

In a retrospective study by Wang *R.* et al. (2022), data from 1,899 patients with active AS were used to develop predictive models for treatment response to TNF- α

inhibitors at 12 weeks. The most significant predictors of therapeutic response included C-reactive protein levels and patient-reported activity based on the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)—particularly item 2, which assesses the general level of pain in the neck, back, or hips.

In contrast, factors such as elevated body mass index (BMI), older age, and higher scores on the Bath Ankylosing Spondylitis Functional Index (BASFI) were associated with reduced likelihood of response. The developed models demonstrated moderate to high predictive performance and could serve as useful tools for the individualization of treatment strategies in clinical practice [57].

**Psoriatic arthritis**

*Differential diagnosis, prognosis*

PsA is a chronic inflammatory disease characterized by lesions of joints, skin and entheses, and is characterized by clinical polymorphism, which complicates diagnosis. In this regard, AI methods aimed at improving the accuracy of differential diagnosis and identifying phenotypes with different prognosis are being actively developed. A number of studies have proved high efficiency of AI algorithms in differentiating PsA from seropositive and seronegative RA according to MRI and US of joints [16, 17]. In a prospective cohort study based on Clinical Practice Research Datalink (UK), which included data from more than 120 thousand patients, models were developed to predict joint lesions in psoriasis patients. The models demonstrated high accuracy (AUC up to 0.851), and among the most significant predictors were highlighted the duration of psoriasis, intake of nonsteroidal anti-inflammatory drugs (NSAIDs), the presence of arthralgias, and an increase in the level of C-reactive protein [44].

*Monitoring and evaluation of activity*

A study by *Huang K.* (2023) used a neural network model trained on more than 14,000 images from 2367 psoriasis patients, capable of automatically calculating the Psoriasis Area and Severity Index (PASI) with accuracy better than the average of 43 experienced dermatologists. The developed system was integrated into the SkinTeller mobile application available on the WeChat platform and successfully tested in 18 clinics [19].

**Systemic lupus erythematosus**

*Diagnosis, forecasting and monitoring*

SLE is a chronic multisystem autoimmune disease characterized by pronounced clinical and serological heterogeneity. Diagnostic challenges stem from the overlap of SLE manifestations with those of other autoimmune conditions, as well as the temporal variability of clinical symptoms. These complexities have stimulated growing interest in the application of AI to enhance diagnostic accuracy and improve disease monitoring.

One prominent example of AI integration into clinical diagnostics is the SLE Risk Probability Index (SLERPI), a ML-based algorithm developed to aid in the binary classification of SLE (lupus vs. non-lupus). In a recent study, the model achieved a high overall accuracy of 94.8%, with strong performance across different clinical subtypes: early-stage SLE (93.8%), lupus nephritis (97.9%), neuropsychiatric SLE (91.8%), and severe SLE requiring immunosuppressants or biologic therapies (96.4%) [2].

*Usategui I. et al.* (2024) further demonstrated the potential of AI for prognosis, achieving predictive accuracies of up to 94% for the development of lupus nephritis and disease flares using clinical and laboratory data extracted from EHRs [52]. Similarly, *Ceccarelli F. et al.* (2021) developed a ReliefF-based ML model that achieved excellent diagnostic accuracy (AUC = 0.94) using only the three most informative clinical features: anti-double-stranded DNA (anti-dsDNA) positivity, reduced complement C3/C4 levels, and the presence of a malar or maculopapular rash [10].

Neural network models have also been widely employed to analyze complex, high-dimensional biomedical data, including cytokine profiles, genetic signatures, transcriptomic data, and serological biomarkers. These models facilitate early organ-specific diagnosis, disease phenotyping, patient stratification, and prediction of therapeutic response [11].

Efforts to improve real-time disease monitoring are ongoing. *Jorge A.M. et al.* (2022) applied a Random Forest (RF) classifier to predict hospitalizations in SLE patients, achieving an AUC between 0.751 and 0.772. The most informative variables included anti-dsDNA titers, serum complement levels C3, complete blood count parameters, inflammatory markers, age, and serum albumin [23]. In another application, researchers in China used the same model architecture to predict adverse pregnancy outcomes in women with SLE. Significant predictors included alanine aminotransferase (ALT), gamma-glutamyltranspeptidase (GGT), antinuclear antibody (ANA) titers, and platelet counts [18].

**Osteoarthritis**

*Phenotyping*

In recent years, AI-based approaches have been actively developed to identify OA phenotypes that differ in clinical and structural characteristics, prognosis, and potential response to therapy. *Nelson A.E.* (2022) applied the biclustering method (simultaneously clustering knees and clinical features to account for their interaction) to describe OA subgroups, two of which demonstrated a worse prognosis: more frequent total joint replacement and more pronounced structural progression [36].

*Demanse D. et al.* (2023) applied DL methods and distinguished phenotypes with high body weight, comorbidities and low physical activity, as well as younger and more active groups [14].

In addition to clinical data, studies have begun to include molecular parameters. For example, *Steinberg J. et al.* (2021) evaluated gene expression in cartilage and synovial membrane of joints in 113 patients. Clusters differing in the activity of inflammation pathways, extracellular matrix remodeling, and cell adhesion were identified [47]. *Trajerova M. et al.* (2022) investigated the composition of immune cells in synovial fluid from patients with knee OA and identified four immune subtypes associated with different clinical outcomes after 3-6 months of NSAIDs therapy, which may have implications for predicting response to therapy [50].

**Conclusion**

A review of current literature highlights the growing potential of AI in the field of rheumatology, particularly for early diagnosis, disease progression forecasting, and

treatment personalization. Contemporary algorithms, including CNNs and multi-omics models, have demonstrated high diagnostic and prognostic performance—achieving AUC values of up to 0.85 in several studies. These results pertain to the analysis of various data modalities, including MRI, radiographs, and EHRs.

Despite these promising developments, widespread clinical implementation remains limited due to several key challenges: lack of standardized AI algorithms, insufficiently representative training datasets, and unresolved ethical considerations within medical practice.

In the context of Kazakhstan, the application of AI in rheumatology holds particular relevance. The country's vast geography, ethnocultural diversity, and unequal access to specialized care underscore the need for scalable digital and intelligent healthcare solutions. To fully harness the benefits of AI in national healthcare, several critical steps must be taken: enhancement of digital infrastructure, development of workforce competencies, establishment of clear legal and ethical frameworks, and active participation in international multicenter research collaborations. These initiatives will not only improve the accessibility and quality of rheumatologic care but will also position Kazakhstan as a meaningful contributor within the global scientific and medical community.

***Authors' contributions:*** *all authors contributed equally to the writing of the article.*

***Conflict of interest****: no conflict of interest declared.*

***Publication details:*** *the article has not been previously published in other journals and is not under consideration by other publishers.*

***Funding****: none*

***Literature:***

1. *Байтурганов Т.М., Айткожин Г.К., Жунусова Л.Э., Мұса Ә.М., Тілеуов Ә.Б.* Использование искусственного интеллекта пациент-центрированной онлайн-системы Saubol в превентивной медицине Казахстана: обзор литературы. Вестник науки и творчества. 2023. № 8 (90). С. 20-27

2. *Adamichou C., Genitsaridi I., Nikolopoulos D. et al.* Lupus or not? SLE Risk Probability Index (SLERPI): a simple, clinician-friendly machine learning-based model to assist the diagnosis of systemic lupus erythematosus. Annals of the Rheumatic Diseases. 2021. Vol. 80. P. 758–766.

3. *Baek I.W., Jung S.M., Park Y.J. et al.* Quantitative prediction of radiographic progression in patients with axial spondyloarthritis using neural network model in a real-world setting. Arthritis Research & Therapy. 2023. Vol. 25. P. 65.

4. *Bird A., Oakden-Rayner L., McMaster C. et al.* Artificial intelligence and the future of radiographic scoring in rheumatoid arthritis: a viewpoint // Arthritis Res Ther. 2022. Vol. 24. P. 268.

5. *Bouget V., Duquesne J., Cournède P.H. et al.* Machine learning predicts response to methotrexate in rheumatoid arthritis: results on the ESPOIR, T-REACH and Leiden cohorts. Ann Rheum Dis. 2022. Vol. 81. P. 535.

6. *Bouget V., Duquesne J., Hassler S. et al.* Machine learning predicts response to TNF inhibitors in rheumatoid arthritis: results on the ESPOIR and ABIRISK cohorts. RMD Open. 2022. 8:e002442 P.1-9

7. *Bressem K.K., Vahldiek J.L., Adams L. et al.* Deep learning for detection of radiographic sacroiliitis: achieving expert-level performance. Arthritis Research & Therapy. 2021. Vol. 23. P. 106.

8. *Bressem K.K., Adams L.C., Proft F. et al.* Deep learning detects changes indicative of axial spondyloarthritis at MRI of sacroiliac joints.Radiology. 2022. Vol. 305. P. 655–665.

9. *Casaburi G., O'Malley T., Holscher T. et al.* Targeted synovial tissue RNA-Seq coupled with artificial intelligence accurately predicts early rheumatoid arthritis patients likely to respond to CsDMARDs. Arthritis Rheumatol. 2022. Vol. 74. P. 1846.

10. *Ceccarelli F., Lapucci M., Olivieri G. et al.* Can machine learning models support physicians in systemic lupus erythematosus diagnosis? Results from a monocentric cohort. Joint Bone Spine. 2022. Vol. 89. Article 105292.

11. *Ceccarelli F., Natalucci F., Picciariello L. et al.* Application of machine learning models in systemic lupus erythematosus. Int. J. Mol. Sci. 2023. Vol. 24, № 5. Article 4514.

12. *Cohen S., Wells A. F., Curtis J. R. et al.* A molecular signature response classifier to predict inadequate response to tumor necrosis factor-α inhibitors: the NETWORK-004 prospective observational study.RheumatolTher. 2021. Vol. 8, № 3. P. 1159–1176.

13. *Deimel T., Aletaha D., Langs G.* OP0059 Autoscora: deep learning to automate scoring of radiographic progression in rheumatoid arthritis. Ann Rheum Dis. 2020. – Vol. 79 (Suppl. 1). P. 39–40.

14. *Demanse D., Saxer F., Lustenberger P. et al.* Unsupervised machine-learning algorithms for the identification of clinical phenotypes in the osteoarthritis initiative database.Semin Arthritis Rheum. 2023. Vol. 58. Article 152140.

15. *Esteva A. et al.* A guide to deep learning in healthcare. Nat Med. 2019. Vol. 25. P. 24–29.

16. *Folle L., Simon D., Tascilar K. et al.* Deep learning-based classification of inflammatory arthritis by identification of joint shape patterns: how neural networks can tell us where to "deep dive" clinically. Front. Med. 2022. Vol. 9. Article 850552.

17. *Folle L., Bayat S., Kleyer A. et al.* Advanced neural networks for classification of MRI in psoriatic arthritis, seronegative, and seropositive rheumatoid arthritis. Rheumatology (Oxford). 2022. Vol. 61, № 12. P. 4945–4951.

18. *Hao X., Zheng D., Khan M. et al.* Machine learning models for predicting adverse pregnancy outcomes in pregnant women with systemic lupus erythematosus. Diagnostics. 2023. Vol. 13, № 4. Article 612.

19. *Huang K., Wu X., Li Y. et al.* Artificial intelligence–based psoriasis severity assessment: real-world study and application. J. Med. Internet Res. 2023. Vol. 25. Article e44932.

20. *Huang Y.J. et al.* Automatic joint space assessment in hand radiographs with deep learning among patients with rheumatoid arthritis. Arthritis Rheumatol. 2020. P. 72 (Suppl. 10).

21. *Iglesias L.L. et al.* A primer on deep learning and convolutional neural networks for clinicians. Insights Imaging. 2021. Vol. 12. P. 117.

22. *Jans L., Chen M., Elewaut D. et al.* MRI-based Synthetic CT in the Detection of Structural Lesions in Patients with Suspected Sacroiliitis: Comparison with MRI. Radiology. 2021. Vol. 298, № 2. P. 343–349.

23. *Jorge A.M., Smith D., Wu Z. et al.* Exploration of machine learning methods to predict systemic lupus erythematosus hospitalizations. Lupus. 2022. Vol. 31, №11. P. 1296–1305.

24. *Kalweit M., Walker U.A., Finckh A. et al.* Personalized prediction of disease activity in patients with rheumatoid arthritis using an adaptive deep neural network.PLoS ONE. 2021. Vol. 16, № 6. Article e0252289.

25. *Kepp F.H., Huber F.A., Wurnig M.C. et al.* Differentiation of inflammatory from degenerative changes in the sacroiliac joints by machine learning supported texture analysis.Eur J Radiol. 2021. Vol. 140. Article 109755.

26. *Kohane I.S. et al.* What every reader should know about studies using electronic health record data but may be afraid to ask. J Med Internet Res. 2021. Vol. 23. Article e22219.

27. *Labinsky H., Ukalovic D., Hartmann F. et al.* An AI-powered clinical decision support system to predict flares in rheumatoid arthritis: a pilot study. Diagnostics. 2023. Vol. 13, № 1. P. 148.

28. *LeCun Y., Bengio Y., Hinton G.* Deep learning. Nature. 2015. Vol. 521. P. 436–444.

29. *Lee S., Kang S., Eun Y. et al.* Machine learning-based prediction model for responses of bDMARDs in patients with rheumatoid arthritis and ankylosing spondylitis. Arthritis Res Ther. 2021. Vol. 23. P. 254.

30. *Lee S., Eun Y., Kim H. et al.* Machine learning to predict early TNF inhibitor users in patients with ankylosing spondylitis.Sci Rep. 2020. Vol. 10. Article 20299.

31. *Liu Y. et al.* How to read articles that use machine learning: users' guides to the medical literature. JAMA. 2019. Vol. 322. P. 1806–1816.

32. *Mielnik P., Fojcik M., Segen J., Kulbacki M.*A novel method of synovitis stratification in ultrasound using machine learning algorithms: results from clinical validation of the MEDUSA Project. Ultrasound Med Biol. 2018. Vol. 44. P. 489–494.

33. *Mongan J., Moy L., Kahn C.E.* Checklist for artificial intelligence in medical imaging (CLAIM): a guide for authors and reviewers.RadiolArtifIntell. 2020. Vol. 2. Article 200029.

34. *Mukhammedzhanova D.M., Suleimenova M.*AI-based remote patient monitoring systems in Kazakhstan.Žaršysy. 2024. Vol. 35, № 4. P.87-99

35. *Murakami S., Hatano K., Tan J. et al.* Automatic identification of bone erosions in rheumatoid arthritis from hand radiographs based on deep convolutional neural network.Multimed Tools Appl. 2018. Vol. 77, № 9. P. 10921–10937.

36. *Nelson A.E., Keefe T.H., Schwartz T.A. et al.*Biclustering reveals potential knee OA phenotypes in exploratory analyses: data from the osteoarthritis initiative.PLoS ONE. 2022. Vol. 17, № 5. Article e0266964.

37. *Nendel N., Eiben R., Frommhold J. et al.* Characterization of preclinical rheumatoid arthritis and psoriatic arthritis by clinical and imaging parameters and their potential role in the prediction of arthritis. Ann Rheum Dis. 2024. Vol. 83. P. 605.

38. *Norgeot B., Glicksberg B.S., Trupin L. et al.* Assessment of a deep learning model based on electronic health record data to forecast clinical outcomes in patients with rheumatoid arthritis. NPJ Digit Med. 2019. Vol. 2, № 3. P.1-12

39. *Peng J., Jury E.C., Dönnes P., Ciurtin C.* Machine learning techniques for personalised medicine approaches in immune-mediated chronic inflammatory diseases: applications and challenges. Front Pharmacol. 2021. Vol. 12. Article 720694.

40. *Phatak S., Chakraborty S., Goel P.K.* Computer vision detects inflammatory arthritis in standardized smartphone photographs in an Indian patient cohort. Front Med. 2023. Vol. 10. P.1-7

41. *Rekha G., Afsana Sk., Anjum M.R., Padma K.R.* Mohan M. Artificial intelligence in rheumatology. 2024. P. 1–18.

42. *Roels J., De Craemer A.S., Renson T. et al.* Machine learning pipeline for predicting bone marrow edema along the sacroiliac joints on magnetic resonance imaging. Arthritis Rheumatol. 2023. P. 2169-2177

43. *Rohrbach J., Reinhard T., Sick B., Dürr O.* Bone erosion scoring for rheumatoid arthritis with deep convolutional neural networks.ComputElectr Eng. 2019. Vol. 78. P. 472–481.

44. *Rudge A., McHugh N., Tillett W., Smith T.* An interpretable machine learning approach for detecting psoriatic arthritis in a UK primary care psoriasis cohort using electronic health records. Ann Rheum Dis. 2025. P.575-583

45. *Scott I., Carter S., Coiera E.* Clinician checklist for assessing suitability of machine learning applications in healthcare. BMJ Health Care Inf. 2021. Vol. 28. Article e100251.

46. *Sonomoto K., Fujino Y., Tanaka H. et al.* A machine learning approach for prediction of CDAI remission with TNF inhibitors: a concept of precision medicine from the FIRST registry.RheumatolTher. 2024. Vol. 11, № 3. P. 709–736.

47. *Steinberg J., Southam L., Fontalis A. et al.* Linking chondrocyte and synovial transcriptional profile to clinical phenotype in osteoarthritis. Ann Rheum Dis. 2021. Vol. 80, № 8. P. 1070–1074.

48. *Stoel B.C. et al.* Deep learning in rheumatoid arthritis imaging: hype or hope? Semin Arthritis Rheum. 2019. Vol. 49 (Suppl. 1). P. S25–S28.

49. *Tao W., Concepcion A.N., Vianen M. et al.*Multiomics and machine learning accurately predict clinical response to adalimumab and etanercept therapy in patients with rheumatoid arthritis. Arthritis Rheumatol. 2021. Vol. 73, № 2. P. 212–222.

50. *Trajerova M., Kriegova E., Mikulkova Z. et al.* Knee osteoarthritis phenotypes based on synovial fluid immune cells correlate with clinical outcome trajectories. Osteoarthritis Cartilage. 2022. Vol. 30, № 12. P. 1583–1592.

51. *Ukalovic D., Leeb B.F., Rintelen B. et al.* Prediction of ineffectiveness of biological drugs using machine learning and explainable AI methods: data from the Austrian Biological Registry BioReg. Arthritis Res Ther. 2024. P.26:44

52. *Usategui I., Arroyo Y., Torres A.M. et al.* Systemic lupus erythematosus: how machine learning can help distinguish between infections and flares. Bioengineering. 2024. Vol. 11, № 1. P. 90.

53. V*enerito V., Bilgin E., Iannone F., Kiraz S.* AI am a rheumatologist: a practical primer to large language models for rheumatologists. Rheumatology (Oxford). 2023. Vol. 62. P. 3256–3260.

54. *Venerito V., Puttaswamy D., Iannone F., Gupta L.* Large language models and rheumatology: a comparative evaluation. The Lancet Rheumatology. 2023. Vol. 5. P. e574–e578.

55. *Vodencarevic A., Tascilar K., Hartmann F., et al.* Advanced machine learning for predicting individual risk of flares in rheumatoid arthritis patients tapering biologic drugs. Arthritis Res Ther. 2021. Vol. 23. P. 67.

56. *Wang M., Li R., Qi H. et al.* Metabolomics and machine learning identify metabolic differences and potential biomarkers for frequent versus infrequent gout flares. Arthritis Rheumatol. 2023. Vol. 75, № 12. P. 2252–2264.

57. *Wang R., Dasgupta A., Ward M.M.* Predicting probability of response to tumor necrosis factor inhibitors for individual patients with ankylosing spondylitis. JAMA Netw Open. 2022. Vol. 5, № 3. Article e222312.

58. *Yu K.H., Beam A.L., Kohane I.S.* Artificial intelligence in healthcare. Nat Biomed Eng. 2018. Vol. 2. P. 719–731.

***References[1]:***

1. Bajturganov T.M., Ajtkozhin G.K., Zhunusova L.E.Mysa A.M., Tileuov A.B. Ispol'zovanie iskusstvennogo intellekta pacient-centrirovannoj onlajn-sistemy Saubol v preventivnoj meditscine Kazahstana: obzorliteratury [Use of artificial intelligence ofthe patient-centered online system Saubol in preventive medicine of Kazakhstan: a literature review].*Vestnik nauki I tvorchestva* [Bulletin of Science and Creativity]. 2023. № 8 (90). pp. 20-27. [inRusian]

**Information about authors:**

**Petrova Yuliya Viktorovna –** Master of Medicine,Department of Internal Medicine and Rheumatology NCJSC «Semey Medical University», 103 AbayStreet, Semey, 071400, Kazakhstan; Email: yuliya.petrova@smu.edu.kz; phone number: +7(771) 537 6060; https://orcid.org/0000-0003-1910-7169

**Goremykina Maiya Valentinovna -** Candidate of Medical Sciences, Associate Professor, Department of Internal Medicine and Rheumatology, NCJSC «Semey Medical University», 103 AbayStreet, Semey, 071400, Kazakhstan;Email: maya.goremykina@smu.edu.kz;phone number: +7 (777) 390 8234; https://orcid.org/0000-0002-5433-7771

**Ivanova Raifa Latyfovna**– Professor, Doctor of Medical Sciences, Department of Internal Medicine and Rheumatology NCJSC «Semey Medical University», 103 AbayStreet, Semey, 071400, Kazakhstan; Email: raifa.ivanova@smu.edu.kz; phone number: +7(777)147 2892; https://orcid.org/0000-0001-9851-2255

**Kozhakhmetova Dana Kenzhebaevna –** PhD, assistant of the Department of Internal Diseases and Rheumatology, NCJSC «Semey Medical University», Address: 071400, Republic of Kazakhstan, Abai Region, Semey, 103 AbayKunanbayev St., Email: dana_ken@mail.ru; phone number: +7(702) 705 1403; https://orcid.org/0000-0002-8367-1461

**Botabayeva Ainur** - MD, assistant of the Department of Internal Diseases and Rheumatology, NCJSC «Semey Medical University»,Address: 071400, Republic of Kazakhstan, Abai Region, Semey, 103 AbayKunanbayev St., e-mail: aibota7878@mail.ru Phone: +7 (701) 100 2098 https://orcid.org/0009-0008-9228-7788

**Razvodova Alexandra –** MD, Rheumatologist, LLP «Hippocrates», Address: 110000, Republic of Kazakhstan**,** Kostanay, 151, 1st May Street, Building 7**;** phone number:+7(705) 727 0571 https://orcid.org/0000-0002-8367-1461

**Corresponding author:**

**Goremykina Maiya Valentinovna -** Candidate of Medical Sciences, Associate Professor, Department of Internal Medicine and Rheumatology, NCJSC «Semey Medical University»

**Address:**103 Abay Street, Semey, 071400, Kazakhstan

**E-mail:** maya.goremykina@smu.edu.kz

**Phone:** +7 (777) 390 8234

Received: 28 February 2025 / Accepted: 02 June 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2024.27.3.026***

***UDC 616-007-053.1:612.171.7-053.4***

This work is licensed under a Creative Commons Attribution 4.0 International License

# COGNITIVE COMPONENT IN THE REHABILITATION OF PRESCHOOL CHILDREN WITH CONGENITAL HEART DEFECTS. LITERATURE REVIEW.

**Arailym A. Kapanova[1], https://orcid.org/0000-0001-5660-1460**
**Aliya R. Alimbaeva[1], https://orcid.org/0000-0002-5082-4636**
**Yernar E. Dairbekov[1], https://orcid.org/0000-0002-5522-7312**
**Aizhan Zh. Abylgazinova[1], https://orcid.org/0000-0002-1894-0709**
**Zhansulu S. Bektar[1], https://orcid.org/0009-0009-9889-7533**
**Regina A. Kovylina[1], https://orcid.org/0000-0002-5179-2883**
**Aldiyar Ye. Masalov[1], https://orcid.org/0000-0003-3386-1416**
**Zaira S. Terdykbayeva[2], https://orcid.org/0009-0003-3816-2777**

**[1] NCJSC «Semey Medical University», Semey, Republic of Kazakhstan;**
**[2] The Mother and Child Center, Ust-Kamenogorsk, Republic of Kazakhstan.**

**Abstract**

**Introduction:** Advancements in prenatal diagnostics, cardiac surgery, and intensive care have markedly increased the survival rates among children with complex congenital heart defects (CHD). Recent neuropsychological studies have convincingly demonstrated that children with CHD are at high risk of developing cognitive impairments.

**Aım:** to analyze the literature data on the role of the cognitive component in the rehabilitation of preschoolers with congenital heart defects.

**Search strategy:** as part of the preparation of the literature review, a multi-stage strategy for searching for scientific information was implemented using the following databases and platforms: PubMed, Google Scholar and UpToDate. Based on the results of the search, 71 scientific publications were selected that are most relevant to the purpose and subject of the study with a search time interval spanning the last 10 years.

**Results:** The cognitive functioning of a child is one of the most vulnerable areas in the presence of congenital heart disease, which affects not only due to the pathology itself, but also due to mandatory cardiac surgery. Despite the growing attention to this problem, the prevalence of cognitive impairment in children and adolescents with congenital heart abnormalities is still underestimated and insufficiently reflected in clinical practice.

Disorders of neurodevelopment in CHD are caused by a complex interaction of factors acting at various stages, starting from the antenatal period and ending with postoperative recovery. Predictors of cognitive impairment include both organic (including chronic hypoxia and cerebral hypoperfusion) and iatrogenic effects (for example, artificial blood circulation, anesthesia, and postoperative complications).

**Conclusions:** In a number of countries, there are no structured monitoring and support programs for children with CHD after surgical treatment, routine assessment of cognitive and psycho-emotional development is not carried out, and there are not enough specialists who know the methods of neuropsychological diagnosis and correction.

***Keywords:*** *cognitive impairment, congenital heart defects, preschoolers.*

***For citation:***

Kapanova A.A., Alimbaeva A.R., Dairbekov Y.E., Abylgazinova A.Zh., Bektar Zh.S., Kovylina R.G., Masalov A.Ye., Terdykbayeva Z.S. cognitive component in the rehabilitation of preschool children with congenital heart defects. Literature review // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 245-254. *doi 10.34689/SH.2024.27.3.026*

**Резюме**

# КОГНИТИВНЫЙ КОМПОНЕНТ В РЕАБИЛИТАЦИИ ДОШКОЛЬНИКОВ С ВРОЖДЕННЫМИ ПОРОКАМИ СЕРДЦА. ОБЗОР ЛИТЕРАТУРЫ.

**Арайлым А. Қапанова[1], https://orcid.org/0000-0001-5660-1460**
**Алия Р. Алимбаева[1], https://orcid.org/0000-0002-5082-4636**
**Ернар Е. Даирбеков[1], https://orcid.org/0000-0002-5522-7312**
**Айжан Ж. Абылгазинова[1], https://orcid.org/0000-0002-1894-0709**
**Жансұлу С. Бектар[1], https://orcid.org/0009-0009-9889-7533**

**Регина А. Ковылина[1], https://orcid.org/0000-0002-5179-2883**
**Алдияр Е. Масалов[1], https://orcid.org/0000-0003-3386-1416**
**Зайра С. Тердыкбаева[2], https://orcid.org/0009-0003-3816-2777**

**[1] НАО «Медицинский университет Семей», г. Семей, Республика Казахстан;**
**[2] Центр Матери и ребенка, г. Усть-Каменогорск, Республика Казахстан.**

**Введение:** благодаря прогрессу в пренатальной диагностике, кардиохирургии и интенсивной терапии значительно повысилась выживаемость детей с тяжелыми формами ВПС. Нейропсихологические исследования последних лет убедительно демонстрируют, что дети с ВПС подвержены высокому риску развития нарушений когнитивного профиля.

**Цель исследования:** анализ литературных данных о роли когнитивного компонента в реабилитации дошкольников с врожденными пороками сердца.

**Стратегия поиска:** в рамках подготовки литературного обзора была реализована многоступенчатая стратегия поиска научной информации за последние 10 лет с использованием следующих баз данных и платформ: PubMed, Google Scholar и UpToDate. По итогам поиска отобрана 71 научная публикация, наиболее соответствующие цели и тематике исследования.

**Результаты:** Когнитивное развитие ребёнка представляет собой одну из наиболее чувствительных сфер при врождённом пороке сердца, на которую воздействует не только сама сердечная патология, но и необходимость хирургического вмешательства. Несмотря на возрастающий интерес к этой теме, уровень распространённости когнитивных нарушений у детей и подростков с врождёнными пороками сердца всё ещё остаётся недооценённым и не получает должного внимания в клинической практике.

Нарушения нейроразвития при ВПС обусловлены сложным взаимодействием факторов, действующих на различных этапах — начиная с антенатального периода и заканчивая послеоперационным восстановлением. К предикторам когнитивных нарушений относятся как органические (в том числе хроническая гипоксия и церебральная гипоперфузия), так и ятрогенные влияния (например, искусственное кровообращение, анестезия, послеоперационные осложнения).

**Выводы:** В ряде государств отсутствуют структурированные программы наблюдения и поддержки детей с ВПС после хирургического лечения, не проводится рутинная оценка когнитивного и психоэмоционального развития, не хватает специалистов, владеющих методами нейропсихологической диагностики и коррекции.

***Ключевые слова:*** *когнитивные нарушения, врожденные пороки сердца, дошкольники.*

***Для цитирования:***

*Қапанова А.А., Алимбаева А.Р., Даирбеков Е.Е., Абылгазинова А.Ж., Бектар Ж.С., Ковылина Р.Г., Масалов А.Е., Тердыкбаева З.С.* Когнитивный компонент в реабилитации дошкольников с врожденными пороками сердца. Обзор литературы // Наука и Здравоохранение. 2025. Vol.27 (3), С. 245-254. *doi 10.34689/SH.2024.27.3.026*

**Түйіндеме**

# ТУА БІТКЕН ЖҮРЕК АҚАУЛАРЫ БАР МЕКТЕП ЖАСЫНА ДЕЙІНГІ БАЛАЛАРДЫ ОҢАЛТУДЫҢ КОГНИТИВТІ КОМПОНЕНТІ. ӘДЕБИЕТКЕ ШОЛУ.

**Арайлым А. Қапанова[1], https://orcid.org/0000-0001-5660-1460**
**Алия Р. Алимбаева[1], https://orcid.org/0000-0002-5082-4636**
**Ернар Е. Даирбеков[1], https://orcid.org/0000-0002-5522-7312**
**Айжан Ж. Абылгазинова[1], https://orcid.org/0000-0002-1894-0709**
**Жансұлу С. Бектар[1], https://orcid.org/0009-0009-9889-7533**
**Регина А. Ковылина[1], https://orcid.org/0000-0002-5179-2883**
**Алдияр Е. Масалов[1], https://orcid.org/0000-0003-3386-1416**
**Зайра С. Тердыкбаева[2], https://orcid.org/0009-0003-3816-2777**

**[1] «Семей медицина университеті» КеАҚ, Семей қ., Қазақстан Республикасы;**
**[2] Ана мен бала орталығы, Өскемен қ., Қазақстан Республикасы.**

**Кіріспе:** пренатальды диагностика, кардиохирургия және қарқынды терапиядағы прогресстің арқасында ауыр ДПС бар балалардың өмір сүру деңгейі айтарлықтай өсті. Соңғы жылдардағы нейропсихологиялық зерттеулер ДПС-мен ауыратын балалардың когнитивті бейіннің бұзылуының даму қаупі жоғары екенін көрсетеді.

**Зерттеудің мақсаты:** туа біткен жүрек ақаулары бар мектеп жасына дейінгі балаларды оңалтудағы когнитивті компоненттің рөлі туралы әдеби деректерді талдау.

**Іздеу стратегиясы:** әдеби шолуды дайындау аясында соңғы 10 жыл ішінде ғылыми ақпаратты іздеудің көп сатылы стратегиясы келесі мәліметтер базасы мен платформаларын қолдана отырып жүзеге асырылды: PubMed,

Google Scholar және UpToDate. Іздеу қорытындысы бойынша зерттеудің мақсаты мен тақырыбына неғұрлым сәйкес келетін 71 ғылыми жарияланым таңдалды.

**Нәтижелер:** баланың когнитивті қызметі туа біткен жүрек ақауы болған кезде ең осал салалардың бірі болып табылады, ол патологияның өзінен ғана емес, сонымен қатар міндетті кардиохирургиялық араласудан да әсер етеді. Бұл мәселеге көбірек назар аударылғанына қарамастан, туа біткен жүрек ақаулары бар балалар мен жасөспірімдерде когнитивті бұзылулардың таралуы әлі де бағаланбайды және клиникалық тәжірибеде толық көрінбейді. ДПС-дағы нейродамудың бұзылуы антенатальды кезеңнен бастап операциядан кейінгі қалпына келтіруге дейінгі әртүрлі кезеңдерде әсер ететін факторлардың күрделі өзара әрекеттесуіне байланысты. Когнитивті бұзылулардың болжаушыларына органикалық (соның ішінде созылмалы гипоксия және церебральды гипоперфузия) және ятрогендік әсерлер (мысалы, жүрек-өкпе айналымы, анестезия, операциядан кейінгі асқынулар) жатады.

**Қорытындылар:** бірқатар мемлекеттерде хирургиялық емдеуден кейін ДПС бар балаларды бақылау мен қолдаудың құрылымдық бағдарламалары жоқ, когнитивті және психоэмоционалды дамуды күнделікті бағалау жүргізілмейді, нейропсихологиялық диагностика мен түзету әдістерін меңгерген мамандар жетіспейді.

***Түйінді сөздер:*** *когнитивті бұзылулар, туа біткен жүрек ақаулары, мектеп жасына дейінгі балалар.*

***Дәйексөз үшін:***

*Қапанова А.А., Алимбаева А.Р., Даирбеков Е.Е., Абылгазинова А.Ж., Бектар Ж.С., Ковылина Р.Г., Масалов А.Е., Тердыкбаева З.С.* Туа біткен жүрек ақаулары бар мектеп жасына дейінгі балаларды оңалтудың когнитивті компоненті. Әдебиетке шолу // Наука и Здравоохранение. 2025. Vol.27 (3), С. 245-254. *doi 10.34689/SH.2024.27.3.026*

**Introduction:**

Congenital heart defects remain one of the most common developmental abnormalities — according to the World Health Organization, 8 to 10 cases per 1,000 live births are registered annually. Advances in prenatal diagnostics, cardiac surgery, and intensive care have significantly improved the survival rate of children with severe congenital heart defects CHD [24, 25, 28]. However, an increase in the number of surviving patients is accompanied by an increase in the detection of long-term neurological and neurocognitive complications that manifest themselves in preschool age, a period critical for the formation of basic cognitive functions and social adaptation [6, 36, 44].

Recent neuropsychological studies strongly demonstrate that children with CHD are at high risk of developing cognitive impairments. Among them, the most frequently noted are a decrease in the speed of information processing, impaired attention, disorders of executive functions [43], speech, and motor deficits. These disorders are caused not only by the anatomical features of the defect itself and frequent cases of chronic hypoxia, but also by factors such as intrauterine developmental delay, the impact of cardiac surgery using artificial circulation, postoperative complications (including strokes, seizures), as well as social and emotional aspects, including family stress and long-term hospitalizations [59].

Of particular concern is that cognitive deficits may remain subclinical in infancy but increase significantly by preschool and primary school age, negatively affecting learning, socialization, and emotional development. In this regard, the need for early and comprehensive rehabilitation is being updated, including with an emphasis on the cognitive component [6, 35].

Cognitive rehabilitation in pediatrics is a complex of targeted actions to develop and restore intellectual functions, adaptive behavior, and learning skills [57]. In the context of CHD, this component requires a remarkably subtle and interdisciplinary approach that considers not only medical, psychological, pedagogical, and social aspects [7-9,27].

This literature review analyzes existing data on the neurocognitive consequences of congenital heart defects in preschool children and the role of the cognitive component in their rehabilitation.

**Aim:** to analyze the literature data on the role of the cognitive component in rehabilitating preschool children with congenital heart defects.

**Search strategy:**

As part of the literature review preparation, a multi-stage search strategy for scientific information was implemented using PubMed, Google Scholar, and UpToDate databases and platforms.

The PubMed system used an extended query with MeSH: "cognitive impairment" and "congenital heart defects," with a search time interval spanning the last 10 years. Filters by age category (Preschool Child: 2-5 years) and full-text access to content were activated.

Google Academy used keywords in Russian: "cognitive impairment," "preschool children."

Based on the search results, 71 scientific publications were selected that most correspond to the study's purpose and subject.

*Inclusion criteria* included full-text access, publications in English and Russian, and clear, statistically valid conclusions.

*Exclusion criteria* included conference abstracts, materials from non-specialized media, and subjective sources (for example, personal messages or interviews without a verified scientific base).

**Results**

**Congenital heart defects in children. The overall picture.**

Congenital heart defects (CHD) occur in approximately 1% of live births [3, 33, 60] and represent around 28% of all major congenital anomalies [61]. These defects are also significant contributors to early mortality [7]. Newborns diagnosed with CHD exhibit a higher prevalence of brain abnormalities compared to the general population [34, 44, 58]. CHD is generally characterized as a structural defect of the heart and/or major blood vessels present at birth [25].

Critical CHD refers specifically to those lesions that necessitate surgical or catheter-based intervention within the first year of life.

This includes both cyanotic and non-cyanotic lesions. Early detection, emergency stabilization, and transportation to an appropriate pediatric cardiology center are essential steps to ensure optimal outcomes for newborns with these lesions [62].

**Prevalence of congenital heart defects**

According to a large-scale meta-analysis conducted by *Yingjuan Liu and colleagues* [24], the prevalence of congenital heart defects (CHD) at birth between 1970 and 2017 has steadily increased. The peak was recorded in 2010-2017, when the rate reached 9.41 cases per 1000 live births [95% confidence interval (CI): 8.60-10.25], which is statistically significantly higher than in the previous 15 years (P = 0.031).

Analysis of the dynamics showed that the main increase is due to the rise in the diagnosability of mild CHD, particularly defects of the interventricular and atrial septa and the open ductus arteriosus. These forms together account for about 93.4% of the total increase due to improved postnatal screening methods and early detection of less pronounced anomalies.

At the same time, the frequency of severe anomalies, such as obstructive outflow defects from the left ventricle, including hypoplasia of the left heart, decreased. Their prevalence decreased from 0.689 per 1000 (95% CI: 0.607–0.776) in 1995-1999 to 0.475 per 1000 (95% CI: 0.392–0.565) in 2010-2017. This decline probably reflects advances in prenatal diagnosis and subsequent termination of pregnancy when fatal malformations are detected.

In addition, the authors note pronounced geographical differences: the lowest rates were found in Africa — 2,315 cases per 1000 live births (95% CI: 0.429–5,696), while the highest rates were found in Asia, where the frequency reached 9,342 per 1000 (95% CI: 8,072-10,704) [25].

**Relationship between congenital heart defects and cognitive impairment**

Cognitive development in children is particularly susceptible to disruption in the context of congenital heart disease (CHD), with negative influences arising both from the cardiac defect itself and from the necessity of early surgical intervention. Although awareness of this issue is increasing, cognitive impairments in children and adolescents with CHD continue to be underrecognized and inadequately integrated into standard clinical assessments.

Neurodevelopmental complications in CHD patients are driven by a multifactorial process that spans from the prenatal phase through the post-surgical period. Contributing factors include both physiological insults, such as prolonged hypoxia and reduced cerebral blood flow, and medical interventions, including cardiopulmonary bypass, exposure to anesthesia, and complications following surgery.

Despite these risks, many children who undergo early surgical repair for complex CHD maintain overall intellectual functioning (IQ) within the normal range.

However, the average scores tend to be lower than peers in the general population, as evidenced by cohort and longitudinal studies [63].

Among clinically significant congenital heart defects, a special place is occupied by left heart hypoplasia syndrome (LHS), a severe abnormal condition in which there is an underdevelopment of the structures of the left half of the heart, including the mitral and aortic valves, the ascending aorta, and the left ventricle. This morphological anomaly leads to the fact that left-sided structures cannot provide the systemic blood flow necessary for the delivery of oxygen to all organs and tissues [23].

In newborns with OHLOS, the functioning of the cardiovascular system is utterly impossible without emergency intervention. The standard treatment strategy includes staged palliation — a sequence of palliative operations that begin in the neonatal period. The Norwood procedure constitutes the initial stage of surgical palliation, designed to establish systemic circulation through the right ventricle. This is followed in early childhood by a bidirectional Cavo pulmonary anastomosis (commonly known as the Glenn procedure), which partially redirects venous return to the pulmonary arteries. The final stage, the Fontan procedure, completes the circulation pathway by fully separating systemic and pulmonary venous blood flow, allowing deoxygenated blood to flow passively into the pulmonary arteries without passing through a ventricle.

Thus, the right ventricle begins to perform the function of the main pump of the systemic circulation, compensating for the anatomical and functional insufficiency of the left heart [26, 56]. Although congenital heart defects (CHDs) represent the most prevalent type of congenital malformation - affecting approximately 1% of all live births - hypoplastic left heart syndrome (HLHS) is regarded as one of the most critical and prognostically unfavorable variants within this group. Its course is characterized by a pronounced anatomical failure of the left heart chambers. It requires immediate and gradual surgical intervention in the first days of life to ensure systemic circulation and patient survival [49, 50].

Prior to the development of modern surgical techniques, hypoplastic left heart syndrome (HLHS) was uniformly fatal. One of the most significant long-term complications in survivors of HLHS is impaired cognitive development and neurological functioning. HLHS, along with other forms of congenital heart disease (CHD), is strongly associated with an elevated risk of neurodevelopmental disorders [28, 45].

To date, several meta-analytical reviews have been published to study the cognitive status of children with left heart hypoplasia syndrome (LHS) in the age range from infancy to 12 years. An early meta-analysis examining cognitive outcomes in children and adolescents with different types of congenital heart disease (CHD) synthesized findings from four studies published prior to 2005. This review examined indicators of general intelligence (FSIQ), verbal intelligence (VIQ), and productive intelligence (PIQ). The results indicated a marked decrease in FSIQ and PIQ and an average decrease in VIQ in children with OHLOS. In contrast, in patients with other types of CHD, cognitive abnormalities were minimal or moderate, suggesting that SGLOS is associated with more pronounced long-term cognitive consequences compared to other forms of congenital heart disease.

Additional data are provided by *Sistino J.J., Bonilha H.S.* (2012), who conducted a secondary analysis of cognitive indicators as part of an extended quantitative review of survival and functional outcomes in preschool and primary school children with OHSS. This review includes 10 studies published before 2010. According to the results, preschool children showed reduced average values on the Bayley II scale of mental development, while the average general intelligence index (FSIQ) in children aged 6-12 years was in the lower limit of normal, which indicates persistent cognitive development disorders in this clinical population [40].

The results presented in the reviews of *Karsdorp P.A. et al.* (2007) [17] *and Sistino J.J., Bonilha H.S.* (2012) [40] emphasize the relevance of further study of neurocognitive functioning in children with left heart hypoplasia syndrome (LHS) and provide an essential empirical basis for further research in this area. However, both reviews have several methodological limitations to consider when interpreting the data obtained.

Thus, a meta-analysis by *Karsdorp P.A. et al.* [17]. It included only four studies available at the time of publication that analyzed cognitive performance in children with OHLOS at an average age of 2.8 to 9 years. Despite the significance of their findings, the limited number of samples and heterogeneity of data reduce the generalizability of the results. *Sistino J.J., Bonilha H.S. [40]* provided a generalized average FSIQ value for school-age children. Still, their work does not calculate standardized effect sizes for cognitive functioning in preschool and primary school age groups.

In addition, none of these reviews considered possible moderators of effects, such as age at the time of intervention, type of surgical treatment, presence of postoperative complications, or socio-economic status of the family, which limits the ability to analyze factors that affect the degree of cognitive deficits [17, 41].

**Classification and Characteristics of Cognitive Impairment in Preschool Children with congenital heart defects.**

Cognitive functions are an integrated complex of higher mental processes responsible for the perception, processing, and storage of information, as well as for the implementation of purposeful behavior. These functions traditionally include attention, memory, speech, thinking, perception, and executive functions, including planning, self-regulation, and activity control [38]. In children with congenital heart defects (CHD), the formation and implementation of these processes can be disrupted at different stages of ontogenesis, starting from the intrauterine period. Based on clinical, psychological, and neurophysiological studies, it is possible to identify the main areas of cognitive impairment characteristic of preschool children with CHD [29, 37].

Most second-year children with CHD experience mental retardation, particularly in speech and movement development [64]. One of the most frequent cognitive impairments in CHD is a lack of voluntary attention, decreased stability, and concentration [65]. These disorders manifest in increased distractibility, an inability to focus on a task, and frequent changes in activity. In more severe cases, symptoms similar to attention deficit hyperactivity disorder (ADHD) are recorded. Causes include hypoxic-ischemic damage to the frontal lobes and features of the maturation of prefrontal brain structures [63].

Preschool children with CHD may suffer from short-term and long-term memory problems, especially speech and visual-spatial memory. This difficulty makes it challenging to master new knowledge, complicates memorizing instructions, and impairs the formation of learning motivation [14]. According to neuropsychological studies, children with CHD often have impairments in verbal information encoding strategies, which indicates immaturity of the hippocampus and medial structures [10].

Delayed speech development in children with CHD can be associated with peripheral hearing and articulation disorders (for example, after prolonged mechanical ventilation) and central ones-impaired phonemic hearing, poor vocabulary, and difficulties constructing phrases. Expressive and receptive speech are affected, which in turn affects the formation of social skills [37, 38].

In children with CHD, executive functions (planning, self-regulation, working memory, flexibility of thinking) are underdeveloped. This manifests in difficulties moving from one task to another, impulsivity, and problems with behavioral control. Such features often prevent children from following rules and instructions, even if their intelligence is intact [66].

A significant proportion of children with CHD experience discoordination, difficulties in orientation in space, and violations of graph-motor skills. These features may be associated with the underdevelopment of the cerebellum, premotor, and parietal cortex. In practice, they manifest themselves in awkward movements, difficulties in writing and drawing, and violations of fine motor skills [5].

Neurocognitive deficits in children with CHD are often accompanied by emotional disorders such as anxiety, low self-esteem, and impaired adaptation in the team. These conditions, in turn, exacerbate cognitive symptoms, creating a vicious circle. Studies have shown that children with CHD experience more behavioral and emotional impairments compared to children in the general population [67][1].

**Mechanisms of Cognitive Impairment in Children with congenital heart defects**

Understanding the pathophysiological and neuropsychological mechanisms underlying cognitive disorders in congenital heart defects (CHD) is critical for developing effective rehabilitation strategies [18, 51]. Modern studies emphasize the multifactorial nature of these disorders, where organic, genetic, metabolic, hemodynamic, and socio-psychological factors all play significant roles [19, 22, 46].

The most significant mechanism is considered to be chronic and/or episodic hypoxia of the brain. In children with cyanotic CHD (e.g., Fallot's tetrad, transposition of the main vessels), there is a constant decrease in oxygen saturation in the blood, which leads to hypoxic damage to the cortex and subcortical structures. The hippocampus, frontal lobes, and cerebellum are particularly vulnerable, supporting memory, attention, and motor planning [2, 52].

Even children with non-cyanotic CHD may experience systemic impairment of cerebral perfusion due to defects in intracardiac hemodynamics (e.g., ventricular septal defect, aortic coarctation). Reduced cerebral blood flow, especially

during critical periods of neuronal development (the third trimester of pregnancy and the first two years of life), leads to decreased gray and white matter volume, which is confirmed by MRI studies [39, 68].

Surgical interventions, especially with the use of artificial blood circulation (IC), represent an independent risk factor for cognitive impairment. Micro embolism, hypoperfusion episodes, blood pressure fluctuations, and reperfusion injuries may occur during surgery. Neuroimaging shows that after IC, children have an increased risk of developing periventricular leukomalacia, hemorrhages, and post hypoxic changes [59, 69].

In 20-35% of children with CHD, genetic syndromes accompanied by cognitive disorders are detected: Down syndrome, Di Giorgi syndrome, Williams syndrome, and microdeletions 22q11. These conditions complicate the neuropsychological profile by impairing intelligence, learning ability, and speech skills. Even without syndromic pathology, polygenic mutations affecting cognitive development may be present [9, 70].

Prolonged hospital stays, forced isolation from peers, frequent medical interventions, lack of emotional contact with parents, fears, and pain create a stressful environment for the child. These factors negatively affect the formation of emotional regulation and socialization, indirectly impacting cognitive development and reducing adaptive potential [15, 32].

Families of children with CHD often face high levels of anxiety, overprotection, and emotional burnout [30]. Lack of proper stimulation at an early age, overloading with medical procedures, and lack of a stimulating environment all reduce the child's cognitive plasticity, slowing down the development of initiative and creativity. This issue is especially pronounced in preschool-aged children, for whom play and social interaction serve as the central drivers of cognitive and emotional development [8].

**Modern Approaches to Cognitive Rehabilitation in Preschool Children with congenital heart defects**

Effective cognitive rehabilitation for children with congenital heart defects (CHD) necessitates early intervention, a comprehensive framework, and a multidisciplinary approach to address the multifaceted nature of neurodevelopmental challenges [4]. Of particular importance is the individualization of programs that take into account the child's neurological, psychosocial, and somatic characteristics. When basic intellectual, behavioral, and communication skills are being developed in preschool, rehabilitation activities can significantly impact the long-term prognosis [11, 47, 53].

**Modern cognitive rehabilitation for children with congenital heart defects (CHD) is guided by several core principles:**

1. **Early initiation** - interventions should commence within the first months of life. In cases where CHD is diagnosed prenatally, preparatory work with the family can begin even before the child's birth to optimize developmental outcomes [12, 21, 48];
2. **Individual approach** - rehabilitation should be tailored to the severity of the cardiological condition, neuropsychological profile, family background, and speech status [21];
3. **Integration into everyday activities** - corrective tasks should be integrated into daily routines, games, and educational activities [36];
4. **Multidisciplinary approach** - participation of specialists from various fields: pediatric neurologists, neuropsychologists, speech therapists, physical therapists, pediatricians, cardiologists, and family psychologists [12, 36, 54].

**Research supporting improved cognitive performance:**

One of the notable directions in recent research focuses on children with transposition of the great arteries (TGA), a severe form of congenital heart defect.

According to observational and systematic reviews [31, 42], neurodevelopmental outcomes in these patients show a wide range of impairments even after successful surgical correction in the neonatal period. In particular:

Children assessed during the first five years of life often demonstrate delays in speech and motor development, as well as lower cognitive performance compared to the general population;

Early postoperative follow-up and multidisciplinary interventions are associated with improved cognitive scores and better behavioral adjustment outcomes during preschool years. Parents reported improved attention, memory, and stress tolerance [31] [42].

**Intervention Programs with Proven Effectiveness:** In international practice, the following types of programs have shown the most significant effectiveness:

1. **Neurodevelopmental Follow-Up Programs** (USA, Canada) — regular assessment of development and training of executive functions. Cognitive dysfunction levels decreased by 25-30% compared to the control group [13].
2. **The Parent–Child Interaction Therapy (PCIT)** model — active involvement of parents in therapy (play, behavior correction, cognitive stimulation) showed an improvement in the emotional background and a decrease in ADHD symptoms in children with CHD (*Valero-Aguayo* et al., 2021) [55].

According to a systematic review by *Koushiou M. et al. (2024)*, which included 48 studies (n=4,720 children), children with severe CHD had a reduction in cognitive scores of 8-15 points compared to population norms; cognitive training before the age of 6 showed a sustained effect for at least three years after the intervention. Programs that included family work and speech therapy were the most effective [20].

A scientific statement by the American Heart Association, along with a scoping review by Hofer et al., highlights that early individualized neuropsychological intervention combined with physical therapy may lead to improvements in cognitive outcomes in children with CHD. While specific gains vary, some studies report increases in IQ and executive function compared to children without intervention [16, 71].

Nevertheless, there is a clear consensus that cognitive rehabilitation must be an integral aspect of care for children with CHD, particularly during the first six years of life—a critical period marked by heightened neuroplasticity.

**Conclusions:**

Analysis of the current literature convincingly shows that cognitive impairment is a frequent and clinically significant consequence of congenital heart defects (CHD), especially in preschool children. These disorders significantly impact

the quality of life, learning, and social adaptation of the child, as well as the psych emotional state of their family.

Although most studies emphasize the importance of early cognitive correction, a systematic approach to organizing such assistance is not yet implemented in practice in all countries. In some countries, there are no structured programs for monitoring and supporting children with CHD after surgical treatment, no routine assessment of cognitive and psych emotional development, and a shortage of specialists trained in neuropsychological diagnosis and correction.

*The authors took an active part in writing this article.*

***Kapanova A.A. Alimbaeva A.R. Kovylina R.A. Terdykbayeva Z.S.*** *- search for literary data and their processing.*

***Kapanova A.A. Alimbaeva A.R. Dairbekov Y.E. Abylgazinova A.Zh., Bektar Zh.S., Masalov A.Ye.*** *- development of the literature review plan, editing the text and approving the final version of the article. The authors declare no conflict of interest.*

*This literature review has not been submitted for consideration to other publications and has not been published in the public domain.*

*There was no financial assistance from outside.*

***Literature:***

1. *Баходировна Т.С., Атамурадовна М.Л.* Расстройства поведения у детей с врожденными пороками сердца. Journal of cardiorespiratory research. 2022. № 2 (3). https://doi.org/10.5281/ZENODO.6734366

2. *Ammar L.A. [et al.].* COVID-19 in Cyanotic Congenital Heart Disease. The Canadian Journal of Infectious Diseases. 2023. С. 5561159. https://doi.org/10.1155/2023/5561159

3. *Bonanni F. [et al.].* Congenital Heart Disease After Mid-Age: From the “Grown-Up” to the Elderly. Diagnostics. 2025. № 4 (15). С. 481. https://doi.org/10.3390/DIAGNOSTICS15040481

4. *Bonnier C.* Evaluation of early stimulation programs for enhancing brain development. Acta Paediatrica, International Journal of Paediatrics. 2008. № 7 (97). С. 853–858. https://doi.org/10.1111/J.1651-2227.2008.00834.X

5. *Bonthrone A.F. [et al.].* Cognitive function in toddlers with congenital heart disease: The impact of a stimulating home environment. Infancy. 2020. № 1 (26). С. 184. https://doi.org/10.1111/INFA.12376

6. *Brosig C.L. [et al.].* Preschool Neurodevelopmental Outcomes in Children with Congenital Heart Disease. The Journal of pediatrics. 2017. (183). С. 80. https://doi.org/10.1016/J.JPEDS.2016.12.044

7. *Crump C. [et al.].* Gestational age at birth and mortality from infancy into mid-adulthood: a national cohort study. The Lancet. Child & adolescent health. 2019. № 6 (3). С. 408. https://doi.org/10.1016/S2352-4642(19)30108-7

8. *Driscoll C.F.B. [et al.].* A Psychosocial Care Model for Families Affected by Congenital Heart Disease. Pediatric critical care medicine : a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies. 2023. № 11 (24). С. 901. https://doi.org/10.1097/PCC.0000000000003293

9. *Duarte V.E.,* Singh M.N. Genetic syndromes associated with congenital heart disease. Heart. 2023. № 20 (110). https://doi.org/10.1136/HEARTJNL-2023-323126

10. *Feldmann M. [et al.].* Cognitive and executive function in congenital heart disease: A meta-analysis. Pediatrics. 2021. № 4 (148). С. 2021050875. https://doi.org/10.1542/PEDS.2021-050875/183283

11. *Feldmann M. [et al.].* Delayed maturation of the structural brain connectome in neonates with congenital heart disease. Brain Communications. 2020; 2(2). С. fcaa209. https://doi.org/10.1093/braincomms/fcaa209

12. *Feldmann M. [et al.].* Postoperative brain volumes are associated with one-year neurodevelopmental outcome in children with severe congenital heart disease. Scientific Reports. 2019; 9. С. 10885. https://doi.org/10.1038/s41598-019-47208-2

13. *Fourdain S. [et al.].* Language development in children with congenital heart disease aged 12–24 months. European Journal of Paediatric Neurology. 2019; 23. С. 491–499. https://doi.org/10.1016/j.ejpn.2019.03.002

14. *Gaudet I. [et al.].* Neurodevelopmental Outcome of Children with Congenital Heart Disease: A Cohort Study from Infancy to Preschool Age. The Journal of Pediatrics. 2021. (239). С. 126-135.e5. https://doi.org/10.1016/J.JPEDS.2021.08.042

15. *Gramszlo C. [et al.].* Parent Perspectives on Family-Based Psychosocial Interventions for Congenital Heart Disease. The Journal of pediatrics. 2019. (216). С. 51. https://doi.org/10.1016/J.JPEDS.2019.09.059

16. *Hofer J. [et al.].* Research gaps in the neurodevelopmental assessment of children with complex congenital heart defects: a scoping review. Frontiers in Pediatrics. 2024. (12). С. 1340495. https://www.jpeds.com/article/S0022-3476%2815%2900860-4/abstract

17. *Karsdorp P.A. [et al.].* Psychological and cognitive functioning in children and adolescents with congenital heart disease: A meta-analysis. Journal of Pediatric Psychology. 2007. № 5 (32). С. 527–541. https://doi.org/10.1093/JPEPSY/JSL047,

18. *Knirsch W., Latal B., Blank C., Tuura R., Kretschmar O., Held U., Boltshauser E., Saner H., Hagmann C.* Neurocognitive outcome of school-aged children with congenital heart disease who underwent cardiopulmonary bypass surgery: a systematic review. Systematic Reviews. 2019. Vol. 8. P. 236. DOI: 10.1186/s13643-019-1153-y

19. *Knutson S., Rivera B.K., Rasmussen M., Weng C., Wilkes J., Brown K.* Implementation of developmental screening guidelines for children with congenital heart disease. The Journal of Pediatrics. 2016. Vol. 176. P. 135–142.e2. DOI: 10.1016/j.jpeds.2016.05.029.

20. *Koushiou M. [et al.].* Cognitive Functioning in Children and Young People with Congenital Heart Disease: A Systematic Review of Meta-Analyses. Healthcare 2024, Vol. 12, Page 2594. 2024. № 24 (12). С. 2594. https://doi.org/10.3390/HEALTHCARE12242594

21. *Laronde M.P. [et al.].* Individualized Family-Centered Developmental Care for Infants With Congenital Heart Disease in the Intensive Care Unit. American Journal of Critical Care. 2022. № 1 (31). С. e10–e19. https://doi.org/10.4037/AJCC2022124

22. *Lin S., Su X., Cao D.* Current research status and progress in neuropsychological development of children with congenital heart disease: A review. Medicine. 2024. № 44 (103). С. e40489. https://doi.org/10.1097/MD.0000000000040489

23. *Linde D. Van Der [et al.].* Birth prevalence of congenital heart disease worldwide: A systematic review and meta-analysis. Journal of the American College of Cardiology. 2011. № 21 (58). С. 2241–2247. https://www.jacc.org/doi/10.1016/j.jacc.2011.08.025

24. *Liu Y., Chen S., Zühlke L., Black G.C., Choy M.K., Li N., Keavney B.D.* Global birth prevalence of congenital heart defects 1970–2017: updated systematic review and meta-analysis of 260 studies. International Journal of Epidemiology. 2019. Vol. 48, № 2. P. 455–463. https://doi.org/10.1093/ije/dyz009

25. *Li X., Gao Y., Zhang Z., Hu S., Sun X., Wang F., Liu H.* Prevalence of congenital heart disease in Chinese adults: a population-based echocardiographic study in Shanghai. International Journal of Cardiology. 2023. Vol. 372. – P. 123–128. https://doi.org/10.1016/j.ijcard.2022.10.066

26. *Liviskie C.J. [et al.].* Nicardipine for the Treatment of Neonatal Hypertension During Extracorporeal Membrane Oxygenation. Pediatric Cardiology. 2019. № 5 (40). С. 1041–1045. https://doi.org/10.1007/S00246-019-02113-3/METRICS

27. *Lopez K.N. [et al.].* US Mortality Attributable to Congenital Heart Disease Across the Lifespan From 1999 Through 2017 Exposes Persistent Racial/Ethnic Disparities. Circulation. 2020. № 12 (142). С. 1132–1147. https://doi.org/10.1161/CIRCULATIONAHA.120.046822

28. *Marelli A. [et al.].* The Brain in Congenital Heart Disease across the Lifespan: The Cumulative Burden of Injury. Circulation. 2016. № 20 (133). С. 1951. https://doi.org/10.1161/CIRCULATIONAHA.115.019881

29. *Mehrin S. F. [et al.].* Integrating a Group-Based, Early Childhood Parenting Intervention Into Primary Health Care Services in Rural Bangladesh: A Cluster-Randomized Controlled Trial. Frontiers in Pediatrics. 2022. (10). С. 886542. https://doi.org/10.3389/FPED.2022.886542/FULL

30. *Mehrin S. F. [et al.].* Scaling-up an early childhood parenting intervention by integrating into government health care services in rural Bangladesh: A cluster-randomised controlled trial. Child: Care, Health and Development. 2023. № 4 (49). С. 750–759. https://doi.org/10.1111/CCH.13089;REQUESTEDJOURNAL:JOURNAL:13652214;WGROUP:STRING:PUBLICATION

31. *Mannan M.A. [et al.].* Pattern of congenital heart disease with its outcome among 100 newborns admitted in a tertiary care hospital in Dhaka, Bangladesh: an observational study. Journal of Pediatrics & Neonatology. – 2022. Vol. 4, № 3. С. 1050-1085. https://doi.org/10.33425/2689-1085.1050

32. *Mheen M. van der, Utens E. M. W. J.* Psychosocial interventions in families with a child with congenital heart disease. Journal of Pediatrics. 2020. (222). С. 264–265. https://www.jpeds.com/article/S0022-3476(20)30346-2/fulltext

33. *Parker D. M. [et al.].* Population-Based Estimates of the Prevalence of Children With Congenital Heart Disease and Associated Comorbidities in the United States. Circulation: Cardiovascular Quality and Outcomes. 2024. (17). С. 10657. https://doi.org/10.1161/CIRCOUTCOMES.123.010657/SUPPL_FILE/CIRCCVQO_CIRCCQO-2023-010657-T_SUPP2.PDF

34. *Raj M. [et al.].* Neurodevelopmental outcomes after infant heart surgery for congenital heart disease: a hospital-based multicentre prospective cohort study from India. BMJ Paediatrics Open. 2025. № 1 (9). С. e002943. https://doi.org/10.1136/BMJPO-2024-002943

35. *Ren H. [et al.].* The association of increased incidence of congenital heart disease in newborns with maternal COVID-19 infection during pregnancy. Scientific reports. 2024. № 1 (14). С. 24866. https://doi.org/10.1038/S41598-024-76690-6;SUBJMETA=308,4019,692;KWRD=CARDIOLOGY,MEDICAL+RESEARCH

36. *Ricci M.F. [et al.].* A Practical Approach to Optimizing Neurodevelopment in Children With Congenital Heart Disease. Canadian Journal of Cardiology. 2023. № 2 (39). С. 156–158. https://doi.org/10.1016/j.cjca.2022.08.229

37. *Rumiantseva A.A. [et al.].* Cognitive and speech disorders in children aged 5–7 years with congenital heart defects. Russian Bulletin of Perinatology and Pediatrics. 2023; 68(4): 52–60.2023. № 4 (68). С. 52–60. https://doi.org/10.21508/1027-4065-2023-68-4-52-XX

38. *Rumiantseva A., Igisheva L. N., Kameneva V.* Lingvo-cognitive Disorders in 4–6-Year-Old Patients with Congenital Heart Defects Before and After Surgical Intervention. 2023. № 2 (12). С. 14–23. https://doi.org/10.17802/2306-1278-2023-12-2-14-23

39. *Silvestro A.A. De [et al.].* Postnatal cerebral hemodynamics in infants with severe congenital heart disease: a scoping review. Pediatric Research. 2023. № 3 (94). С. 931–943. https://pubmed.ncbi.nlm.nih.gov/36944722/

40. *Sistino J.J., Bonilha H.S.* Improvements in Survival and Neurodevelopmental Outcomes in Surgical Treatment of Hypoplastic Left Heart Syndrome: A Meta-Analytic Review. The Journal of Extra-corporeal Technology. 2012. № 4 (44). С. 216. https://doi.org/10.1051/ject/201244216

41. *Simons M., Licht D.J. [et al.].* Perioperative cerebral oxygen saturation and neurodevelopmental outcomes in neonates undergoing Norwood procedure for hypoplastic left heart syndrome. Journal of Thoracic and Cardiovascular Surgery. 2016. Vol. 151, № 5. С. 1367–1378. DOI: 10.1016/j.jtcvs.2016.03.012 https://www.jtcvs.org/article/S0022-5223(16)00410-4/fulltext

42. *Soares C. [et al.].* Neurodevelopment outcomes in the first 5 years of the life of children with transposition of the great arteries surgically corrected in the neonatal period: systematic review and meta-analysis // Cardiology in the Young. 2023. № 12 (33). С. 2471–2480. https://doi.org/10.1017/S104795112300375X

43. *Siegel A.H. [et al.].* Effect of congenital heart disease on neurodevelopmental outcomes within multiple-gestation births: a sibling comparison. The Journal of Thoracic and Cardiovascular Surgery. 2005. Vol. 130, № 6. С. 1511–1516. https://doi.org/10.1016/j.jtcvs.2005.07.040

44. *Simons M. [et al.].* Perioperative cerebral oxygen saturation and neurodevelopmental outcomes in neonates undergoing Norwood procedure for hypoplastic left heart syndrome. The Journal of Thoracic and Cardiovascular Surgery. 2016. Vol. 151, № 5. С. 1367–1378. https://doi.org/10.1016/j.jtcvs.2016.03.012

45. *Sadhwani A. [et al.].* Early childhood executive functioning after infant cardiac surgery for congenital heart disease. The Journal of Pediatrics. 2023. Vol. 257. С. 54–60.e2. https://doi.org/10.1016/j.jpeds.2022.11.035

46. *Tripathi T. [et al.].* Screening and evaluation of neurodevelopmental impairments in infants under 6 months of age with congenital heart disease. Pediatric Cardiology. 2022. Vol. 43, № 3. С. 489–496. https://doi.org/10.1007/s00246-021-02745-4

47. *Tanasan A. [et al.].* Evaluation of neurological and auditory development in children with congenital heart disease using ESSENCE Q questionnaire and auditory brainstem response test. Iran Journal of Child Neurology. 2024. Vol. 18, № 1. С. 43–50. https://doi.org/10.22037/ijcn.v18i.39186

48. *Tweddell J.S. [et al.].* Neurodevelopmental outcome in preschool survivors of complex congenital heart disease: implications for clinical practice. Journal of Pediatric Health Care. 2007. Vol. 21, № 1. С. 3–12. https://doi.org/10.1016/j.pedhc.2006.03.008

49. *Tworetzky W. [et al.].* Cognitive and behavioral outcomes after early surgery for congenital heart disease: current knowledge and future directions. Circulation. 2022. Vol. 145, № 7. С. 535–545. https://doi.org/10.1161/CIRCULATIONAHA.121.057633

50. *Tripathi T. [et al.].* Screening and evaluation of neurodevelopmental impairments in infants under 6 months of age with congenital heart disease. Pediatric Cardiology. 2022. Vol. 43, № 3. С. 489–496. https://doi.org/10.1007/s00246-021-02745-4

51. *Tandon A. [et al.].* Developmental outcomes after early surgery for complex congenital heart disease: long-term follow-up study. Developmental Medicine & Child Neurology. 2021. Vol. 63, № 5. С. 548–555. https://doi.org/10.1111/dmcn.14512

52. *Trivedi A. [et al.].* Growth and risk of adverse neuro-developmental outcome in infants with congenital heart disease: a systematic review. Acta Paediatrica. 2023. Vol. 112, № 1. С. 53–62. https://doi.org/10.1111/apa.16564

53. *Ubeda Tikkanen A. [et al.].* Core components of a rehabilitation program in pediatric cardiac disease. Frontiers in Pediatrics. 2023. (11). С. 1104794. https://doi.org/10.3389/FPED.2023.1104794

54. *Ubeda Tikkanen A., Rodriguez Oyaga A., Arroyo Riaño O., Maroto Álvaro E., Rhodes J.* Paediatric cardiac rehabilitation in congenital heart disease: a systematic review. Cardiology in the Young. 2012. Vol. 22, № 3. С. 241–250. https://doi.org/10.1017/S1047951111002010

55. *Valero-Aguayo L. [et al.].* Meta-analysis of the efficacy and effectiveness of parent child interaction therapy (Pcit) for child behaviour problems. Psicothema. 2021. № 4 (33). С. 544–555. https://doi.org/10.7334/PSICOTHEMA2021.70

56. *Wald R.M., Mertens L.L.* Hypoplastic Left Heart Syndrome Across the Lifespan: Clinical Considerations for Care of the Fetus, Child, and Adult. Canadian Journal of Cardiology. 2022. № 7 (38). С. 930–945. https://doi.org/10.1016/J.CJCA.2022.04.028/ASSET/73D88B97-8E17-411B-B28B-2D5538DB9FCD/MAIN.ASSETS/GR6.JPG

57. *Wolfe K.R. [et al.].* Cognitive Outcomes and Delirium After Cardiac Neurodevelopmental Program Implementation for Children With Congenital Heart Disease. JAMA Network Open. 2025. № 1(8). С. e2456324–e2456324. https://doi.org/10.1001/JAMANETWORKOPEN.2024.56324

58. *Wolfe K.R. [et al.].* Neurodevelopmental outcomes in congenital heart disease: modifiable and nonmodifiable substrates. Current Opinion in Cardiology. 2025. Vol. 40, № 4. С. 259–264. https://doi.org/10.1097/HCO.0000000000001218

59. *Zhu S. [et al.].* Mechanisms of perioperative brain damage in children with congenital heart disease. Biomedicine & Pharmacotherapy. 2020. (132). С. 110957. https://doi.org/10.1016/J.BIOPHA.2020.110957

60. *Zimmerman M.S. [et al.].* Global, regional, and national burden of congenital heart disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet Child and Adolescent Health. 2020. № 3 (4). С. 185–200. https://doi.org/10.1016/S2352-4642(19)30402-X

61. *Zhang L. [et al.].* Neurodevelopmental outcomes at 2 and 4 years in children with congenital heart disease: a longitudinal cohort study. Congenital Heart Disease. 2018. 13(5). С. 700–705. https://doi.org/10.1111/chd.12632

62. *Zhao Q. [et al.].* Association of congenital heart disease and neurodevelopmental disorders: an observational and Mendelian randomization study. Italian Journal of Pediatrics. 2024; 50. С. 63. https://doi.org/10.1186/s13052-024-01610-3

63. *Zhi-yuan L. [et al.].* Neuroplacentology in congenital heart disease: placental contribution to brain development. Pediatric Research. 2021; 90(4). С. 642–650. https://doi.org/10.1038/s41390-021-01521-7

64. *Zhou R. [et al.].* Language brain responses and neurodevelopmental outcome in preschoolers with congenital heart disease. Developmental Science. 2024; 27(2). С. e13500. https://doi.org/10.1111/desc.13500

65. *Zajacova A. [et al.].* Preschool neurodevelopmental outcomes in children with congenital heart disease: predictors and interventions. Journal of Pediatrics. 2017. 183. С. 80–86.e1. https://doi.org/10.1016/j.jpeds.2016.12.044

66. *Zimmermann P. [et al.].* Brain injury and neurodevelopmental outcome in infants with complex congenital heart disease: perioperative EEG predictors. Pediatrics. 2020. 140(1). С. e20164055. https://doi.org/10.1542/peds.2016-4055

67. *Zarek A. [et al.].* Neurodevelopmental outcomes for infants with congenital heart disease: a systematic review of assessment programs. Frontiers in Pediatrics. 2024. 12. С. 1340495. https://doi.org/10.3389/fped.2024.1340495

68. *Zhang C. [et al.].* Long-Term neurodevelopmental outcomes of children with symptomatic congenital heart defects. The Journal of Pediatrics. 2021; 229. С. 289–293. – https://doi.org/10.1016/j.jpeds.2020.09.066

69. *Zhou J. [et al.].* Neurodevelopmental outcomes after cardiac surgery in infancy: systematic review and meta-analysis. Neoreviews. 2015. 15(8). С. e344. https://doi.org/10.1542/neo.15-8-e344

70. *Zhang G. [et al.].* Link between congenital heart disease and neurodevelopment issues in children found: NIH observational cohort study. NIH News Release. 2023. https://www.nih.gov/news-events/news-releases/link-

between-congenital-heart-disease-neurodevelopment-issues-children-found

71. *Zhang B. [et al.].* Neurodevelopmental outcomes for individuals with congenital heart disease: a scientific statement from the American Heart Association. Circulation. 2024. 149(13). C. E997–E1022. https://doi.org/10.1161/CIR.0000000000001211

***References:[1]***

1. Bakodirovna T.S., Atamuradovna M.L. Rasstroistva povedeniya u detei s vrozhdennymi porokami serdtsa [Behavioral disorders in children with congenital heart defects]. *Journal of cardiorespiratory research.* 2022. No2(3). https://doi.org/10.5281/ZENODO.6734366 [in Russian]

**Information about the authors:**

**Kapanova Arailym Alibekkyzy** – 1-year Master,s degree in Medicine, NJSC "Semey Medical University", E-mail: arailym-ali@mail.ru; phone +7 707 180 43 57, https://orcid.org/0000-0001-5660- 1460; Semey, Kazakhstan;

**Alimbaeva Aliya Rakhmetullinovna**- Candidate of Medical Sciences, Associate Professor, Head of the Department of Pediatrics and Medical Rehabilitation named after D.M.Tusupova, NJSC "Semey Medical University", phone: 8 777-131-33-31, e-mail: 150968_pd@mail.ru, https://orcid.org/0000- 0002-5082-4636, Semey, Kazakhstan;

**Dairbekov Yernar Yertuganuly** - Assistant of the Department of Pediatrics and Medical Rehabilitation named after D.M.Tusupova, NJSC "Semey Medical University", phone: 8 775 333-99-99, e-mail: Ertuganovich@inbox.ru, https://orcid.org/0000-0002-5522-7312, Semey, Kazakhstan;

**Abylgazinova Aizhan Zhaksykeldievna -** Doctor of Philosophy,Associate Assistant of the Department of Pediatrics and Medical Rehabilitation named after D.M.Tusupova, NJSC "Semey Medical University", phone: 8 705-318-77-37 , e-mail: aizhan-k705@mail.ru, https://orcid.org/0000-0002-1894-0709, Semey, Kazakhstan;

**Bektar Zhansulu Sergeldykyzy** - Assistant of the Department of Pediatrics and Medical Rehabilitation named after D.M.Tusupova, NJSC "Semey Medical University", phone: 8 775-758-52-20, e-mail: Zhansulu.bektar@gmail.com, https://orcid.org/0009-0009-9889-7533. Semey, Kazakhstan;

**Kovylina Regina Alexandrovna** – Master of health, NJSC "Semey Medical University", phone: 8 775- 547-97-10, e-mail: regina_aleksandrovna@list.ru, https://orcid.org/0000-0002-5179-2883, Semey, Kazakhstan;

**Masalov Aldiyar Yerlanovich, -** Assistant of the Department of Hospital Surgery, Anesthesiology and Resuscitation, NJSC "Semey Medical University", phone: 8 702-337-96-46, https://orcid.org/0000-0003-3386-1416

**Terdykbayeva Zaira Sapioldanovna** – Pediatrician of the highest category, head.Pediatric department of the Mother and Child Center, phone: 8 775-777-654-14-91, e-mail: Zayra_ukg@mail.ru, https://orcid.org/0009-0003-3816-2777, Ust-Kamenogorsk. Kazakhstan

**Corresponding author:**

**Kapanova Arailym Alibekkyzy** - 1-year Master,s degree in Medicine, NJSC "Semey Medical University", Semey, Kazakhstan,

**Postal code:** Republic of Kazakhstan, 071400, Semey city, Abay Street 103.

**E-mail**: arailym-ali@mail.ru

**Phone**: +7 707 180 43 57

Received: 19 February 2025 / Accepted: 25 May 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2025.27.3.027***

***UDC* 616.517:615.03-085(048)**

This work is licensed under a Creative Commons Attribution 4.0 International License

# ADVANCED APPROACHES TO THE TREATMENT OF PSORIASIS. LITERATURE REVIEW

**Assel M. Iskakova[1], https://orcid.org/0009-0003-0144-6100**

**Togzhan O. Algazina[2], https://orcid.org/0000-0002-1178-5574**

**Gulnaz Z. Touir[2] https://orcid.org/0000-0001-6756-997X**

**Gulnar R. Batpenova[2], https://orcid.org/0000-0001-6079-2044**

**Tatyana V. Kotlyarova[2], https://orcid.org/0000-0001-6749-7961**

**Umytzhan S. Samarova[1], https:// https://orcid.org/0000-0002-8037-2677**

**Nisa Akay Bengu[3], https:// https://orcid.org/0000-0002-4896-1666**

**Torgyn B. Ibrayeva[2], https://orcid.org/0009-0007-4788-7410**

**[1] NCJSC «Semey Medical University», Semey, Republic of Kazakhstan;**
**[2] NCJSC «Astana Medical University», Astana, Republic of Kazakhstan;**
**[3] Ankara University, Ankara, Turkey.**

**Abstract**

**Introduction:** Psoriasis is a chronic inflammatory skin disease. In addition to affecting the skin, the condition is characterized by complications such as joint and nail involvement and is associated with systemic disorders including obesity, hypertension, cardiovascular diseases, and kidney disorders. These comorbidities and symptoms influence treatment choices. Therefore, it is important to find an appropriate therapeutic approach that leads to improvement and, ideally, complete recovery from the disease.

**Objective:** The aim of this literature review is to analyze current methods of psoriasis treatment, with a focus on efficacy, safety, and the potential for personalized therapy.

**Search Strategy:** The literature search was conducted in databases including PubMed, Medline, Embase, and Cochrane. The results were then sorted, screened by title, and irrelevant studies were excluded. The search covered a period of 7 years, from 2018 to 2025.

**Results:** Psoriasis affects at least 60 million people worldwide. Clinically, it presents as red, scaly plaques on the skin, which may appear on various parts of the body and cause significant physical and psychological burden. Moreover, the disease may pose a serious threat to the patient due to its involvement of vital organs and systems, including cardiometabolic disorders, psoriatic arthritis, and depression—all of which negatively impact quality of life. Psoriasis is an immune-mediated inflammatory skin disease. The IL-23/IL-17 axis plays a key role in its pathogenesis. The efficacy of biological therapies such as IL-23 inhibitors (ustekinumab, guselkumab, tildrakizumab, risankizumab) and IL-17 inhibitors (secukinumab, ixekizumab, brodalumab) supports this understanding. In our publication, we describe an approach to managing patients with psoriasis across the entire disease spectrum—from mild to moderate and severe forms—aiming to create a positive healing dynamic and improvement in condition, while ensuring efficacy and safety through personalized treatment tailored to the patient's needs.

**Conclusions:** In our study, we propose possible approaches to restoring immune homeostasis through a combined, personalized strategy that includes early intervention with biologic agents, advanced therapeutic techniques, and lifestyle modifications.

***Keywords:*** *Psoriasis, therapy, treatment goals, treatment efficacy, biologic agents*

***For citation:***

Iskakova A.M., Algazina T.O., Touir G.Z., Batpenova G.R., Kotlyarova T.V., Samarova U.S., Bengu N.-A., Ibrayeva T.B. Advanced Approaches to Psoriasis Treatment. Literature review // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 255-266. *doi 10.34689/SH.2025.27.3.027*

**Резюме**

# ПЕРЕДОВЫЕ ПОДХОДЫ К ЛЕЧЕНИЮ ПСОРИАЗА. ОБЗОР ЛИТЕРАТУРЫ

**Асель М. Искакова[1], https://orcid.org/0009-0003-0144-6100,**

**Тогжан О. Алгазина[2], https://orcid.org/0000-0002-1178-5574**

**Гульназ З. Туир[2], https://orcid.org/0000-0001-6756-997X**

**Гульнар Р. Батпенова[2], https://orcid.org/0000-0001-6079-2044**

**Татьяна В. Котлярова[2], https://orcid.org/0000-0001-6749-7961**

**Умытжан С. Самарова[1], https://orcid.org/0000-0002-8037-2677**
**Ниса Акай Бенгу[3], https:// https://orcid.org/0000-0002-4896-1666**
**Торгын Б. Ибраева[2], https://orcid.org/0009-0007-4788-7410**

**[1] НАО «Медицинский университет Семей», г. Семей, Республика Казахстан;**
**[2] НАО «Медицинский университет Астана», г. Астана, Республика Казахстан;**
**[3] Университет Анкары, г. Анкара, Турция.**

**Введение:** Псориаз – это хроническое воспалительное заболевание кожи. Помимо поражения кожного покрова, заболевание характеризуется и осложнениями, такими как поражение суставов и ногтей, ассоциируется с системными расстройствами: ожирение, гипертония, сердечно-сосудистые заболевания, заболевания почек. Эти сопутствующие патологии и симптомы влияют на выбор лечения. Поэтому важно найти правильный подход к терапевтическим действиям, приводящим к улучшению состояния и желательно к полному излечению этого заболевания.

**Цель исследования:** данного литературного обзора является анализ современных методов лечения псориаза с акцентом на эффективность, безопасность и возможности индивидуализации терапии

**Стратегия поиска:** Поиск литературы проводился в базах данных PubMed, Medline, Embase и Cochrane, после чего результаты были отсортированы, отобраны по заголовкам и исключены нерелевантные исследования. Глубина поиска составила 7 лет, с 2018 по 2025 г.г.

**Результаты:** Заболевание псориаз затрагивает не менее 60 миллионов человек среди всех стран по всему миру. Клинически оно проявляется высыпаниями в виде красных, чешуйчатых бляшек на коже, способными появляться на различных участках тела и вызывающими значительную физическую и психологическую нагрузку, помимо этого болезнь может представлять опасность для пациента, связанное с поражением жизненно-важных органов и систем человека, таких как кардиометаболические нарушения, псориатический артрит и депрессия, которые также влияют на качество жизни человека. Псориаз – это воспалительное заболевание кожи, опосредованное иммунными клетками. Ось интерлейкинов IL-23/IL-17 играют важную роль в развитии псориаза. Эффективность биологических препаратов, таких как ингибиторы IL-23 (устекинумаб, гуселькумаб, тильдакизумаб, рисанкизумаб) и ингибиторы IL-17 (секукинумаб, иксекизумаб, бродалумаба) подтверждает эти данные. В нашей публикации мы описываем подход к лечению пациентов с псориазом по всему спектру – от легких до умеренных и тяжелых форм, создание положительной динамики процесса заживления и улучшения состояния, а также эффективности и безопасности подбора лечения индивидуально с учётом потребностей пациента

**Выводы:** В нашем исследовании мы предлагаем возможные пути при восстановлении иммунного гомеостаза посредством комбинированного, персонализированного подхода, включающего раннее вмешательство с применением биологических препаратов, передовые терапевтические методы и изменение образа жизни

***Ключевые слова:*** *Псориаз, терапия, цели лечения, эффективность лечения, биологические препараты.*

***Для цитирования:***

*Искакова А.М., Алгазина Т.О., Туир Г.З., Батпенова Г.Р., Котлярова Т.В., Самарова У.С., Бенгу Н.-А., Ибраева Т.Б.* Передовые подходы к лечению псориаза (обзор литературы) // Наука и Здравоохранение. 2025. Т.27 (3), С. 255-266. doi: 10.34689/SH.2025.27.3.027

**Түйіндеме**

# ПСОРИАЗДЫ ЕМДЕУДІҢ ЗАМАНАУИ ТӘСІЛДЕРІ ӘДЕБИЕТТІК ШОЛУ

**Асель М. Искакова[1], https://orcid.org/0009-0003-0144-6100,**
**Тогжан О. Алгазина[2], https://orcid.org/0000-0002-1178-5574**
**Гульназ З. Туир[2], https://orcid.org/0000-0001-6756-997X**
**Гульнар Р. Батпенова[2], https://orcid.org/0000-0001-6079-2044**
**Татьяна В. Котлярова[2], https://orcid.org/0000-0001-6749-7961**
**Умытжан С. Самарова[1], https://orcid.org/0000-0002-8037-2677**
**Ниса Акай Бенгу[3], https:// https://orcid.org/0000-0002-4896-1666**
**Торгын Б. Ибраева[2], https://orcid.org/0009-0007-4788-7410**

**[1] «Семей медицина университеті» КеАҚ, Семей қ., Қазақстан Республикасы;**
**[2] «Астана медицина университеті» КеАҚ, Астана қ, Қазақстан Республикасы;**
**[3] Анкары Университеті, Анкара қ., Түркия.**

**Кіріспе:** Псориаз – бұл терінің созылмалы қабыну ауруы. Тері жамылғысының зақымдануымен қатар, бұл ауру буындар мен тырнақтардың зақымдануы сияқты асқынулармен сипатталады және жүйелі бұзылыстармен: семіздік, гипертония, жүрек-қантамыр аурулары, бүйрек ауруларымен байланысты. Бұл қатар жүретін патологиялар

мен симптомдар емдеу әдістерін таңдауға әсер етеді. Сондықтан бұл аурудың жағдайын жақсартуға және мүмкін болса толық емделуге әкелетін терапиялық шараларға дұрыс көзқарас табу маңызды.

**Зерттеу мақсаты:** Псориазды емдеудің қазіргі әдістерін тиімділік, қауіпсіздік және емдеуді жекелендіру мүмкіндіктеріне ерекше назар аудара отырып талдау.

**Іздеу стратегиясы:** Әдебиеттерді іздеу PubMed/Medline, Embase және Cochrane Library дерекқорларында, сондай-ақ диагностикалау мен емдеудің стандарттары бойынша электрондық дерекқорларда: Қазақстан Республикасының клиникалық хаттамалары, клиникалық ұсынымдары және клиникалық басшылықтарында жүргізілді. Нәтижелер сұрыпталып, тақырыптары бойынша таңдалып алынып, маңызсыз зерттеулер алынып тасталды. Іздеу терең дігі 7 жылды қамтыды – 2018 жылдан 2025 жылға дейін.

**Нәтижелер:** Псориаз ауруы бүкіл әлем бойынша кемінде 60 миллион адамға әсер етеді. Клиникалық түрде бұл терінің әртүрлі бөліктерінде пайда болатын қызыл, қабыршақты дақтар түрінде бөртпелермен көрінеді және айтарлықтай физикалық және психологиялық ауыртпалық тудырады. Бұдан бөлек, бұл ауру өмірлік маңызды ағзалар мен жүйелерге әсер ету арқылы науқас үшін қауіпті болуы мүмкін, мысалы, кардиометаболикалық бұзылыстар, псориатикалық артрит және депрессия, олар да адамның өмір сапасына әсер етеді.

Псориаз – бұл иммундық жасушалармен делдалданатын қабыну тері ауруы. IL 23/IL 17 интерлейкин осі псориаздың дамуында маңызды рөл атқарады. IL 23 ингибиторлары (устекинумаб, гуселькумаб, тильдакизумаб, рисанкизумаб) және IL 17 ингибиторлары (секукинумаб, иксекизумаб, бродалумаб) сияқты биологиялық препараттардың тиімділігі бұл деректерді растайды.

Біздің жарияланымда біз псориазбен ауыратын науқастарды емдеуге деген көзқарасты жеңілден бастап орташа және ауыр түрлеріне дейін сипаттаймыз. Жазылу процесінде оң динамикаға және жағдайды жақсартуға, сондай-ақ емдеуді пациенттің қажеттіліктерін ескере отырып тиімді және қауіпсіз таңдауға назар аударамыз.

**Қорытынды:** Біздің зерттеуімізде біз иммундық гомеостазды қалпына келтірудің ықтимал жолдарын ұсынамыз. Бұл жолдарға биологиялық препараттарды ерте қолдану, озық терапиялық әдістер және өмір салтын өзгерту сияқты біріктірілген, жекелендірілген тәсіл жатады.

***Түйінді сөздер:*** *Псориаз, терапия, емдеу мақсаттары, емдеу тиімділігі, биологиялық препараттар.*

***Дәйексөз үшін:***

*Ис Искакова А.М., Алгазина Т.О., Туир Г.З., Батпенова Г.Р., Котлярова Т.В., Самарова У.С., Бенгу Н.-А., Ибраева Т.Б.* Псориазды емдеудің заманауи тәсілдері. Әдебиеттік шолу // Ғылым және Денсаулық. 2025. Т.27 (3), Б. 255–266. doi: 10.34689/SH.2025.27.3.027

**Introduction**

Psoriasis is an undulating, chronic, immune-inflammatory skin disease due to genetic predisposition. The prevalence of the disease in the world is about 2%, in more developed countries exceeds 4,6%. For example: in Western countries and among people of European origin: in Norway – 4,6%, Portugal – 4,4%, France - 4,42%, in the UK it affects 1,52%. The incidence is influenced by factors such as country location, ethnic composition and amount of sunlight. The incidence is highest (4-8%) in Northern Europe and lowest in some South American countries. In the United States, psoriasis affects about 2,6% of the population, which corresponds to about 6,4 million people. Between 150,000 and 260,000 new cases are reported each year. The disease can occur in people of all ages, and there is a bimodal age distribution: early onset (from 16 years of age in females, from 22 years of age in males) and late onset (from 57 years of age in males, from 60 years of age in females). Genetic predisposition plays an important role, but the inheritance of psoriasis is complex and can be either monogenic or multifactorial. Psoriasis is a skin disease with several phenotypically distinct subtypes, such as plaque, inverse (flexural), guttate (drop-shaped), pustular, or erythrodermic. It is a disease that negatively affects both quality of life and life expectancy and can manifest complications such as: cardiometabolic disorders, psoriatic arthritis and depression. In addition to the fact that it is sometimes difficult to decide on the conventional treatment of this disease, as the etiology cannot always be determined, additional comorbidities require a holistic and multidisciplinary approach to treatment [1, 2, 63, 64].

Nowadays, with the development of medical trends and technologies, methods are emerging that allow curing diseases that were previously incurable, such as some cancers. Traditionally, the term "cure" is applied to the complete disappearance of the disease both in the manifestation of the clinical picture and at the molecular level, and the effect persists after treatment is discontinued. In severe courses of psoriasis, some patients achieve prolonged suppression of the disease and improvement in the patient's condition, but relapse can unfortunately occur after treatment withdrawal [1, 2, 37].

Improvement of the general condition in psoriasis patients is possible by restoring immune homeostasis using a combined, individualized approach in medicine, applying advanced therapeutic solutions and taking into account lifestyle modification [37].

Psoriasis is genetically predetermined, as 109 genetic loci have been identified predisposing to psoriasis [37, 17] - but there are no genetic markers predicting either spontaneous resolution of the disease (as in "gutta" psoriasis) or its severity. Purely hereditary factors can only explain about 28% of cases, indicating the involvement of additional genetic variants, gene-gene interactions and epigenetic modulation of gene transcription when an individual is exposed to environmental triggers such as streptococcal infection, medications, stress, smoking, alcohol and obesity [1, 36]. This leads to a complex

interaction between innate and adaptive immunity. T lymphocytes, dendritic cells (DCs), keratinocytes and fibroblasts play a key role in the IL-23/T17 axis underlying the pathogenesis of psoriasis [22, 29].

In recent years, with the emergence of highly effective and well tolerated biologic drugs, there has been a trend towards a change in the medication approach to psoriasis. Naturally, this is due to such factors as: reduction in the duration of the disease course, rapid recovery of the general condition, subsequently affecting the lifestyle and quality of life, as well as the manifestation of fewer side effects of the drugs themselves or intolerance to the current treatment. Previously, switching therapy was often undertaken to limit the cumulative effects of traditional systemic agents (e.g., methotrexate, cyclosporine) to reduce the risk of damage to vital organs. Pharmacovigilance registries indicate that more than 27,000 patients worldwide are receiving biologic therapy for psoriasis [69, 60, 62]

In the current environment, efforts are being made to achieve near-complete skin clearance with minimal side effects for most patients with moderate to severe psoriasis, and considerations for changing therapy are shifting toward maximizing skin clearance, quality of life, and patient satisfaction. In our publication, we wanted to emphasize the points of application in the treatment of psoriasis of the latest clinical guidelines, the use of new therapeutic approaches, including biologics, and the difficulties associated with the transition from one drug to another, based on the position of evidence-based medicine, clinical experience of specialists and taking into account individual approaches to psoriasis patients [64].

**Objective**: analysis of modern methods of psoriasis treatment with emphasis on efficacy, safety and possibilities of individualization of therapy

**Search Strategy:**

When conducting a literature search, we reviewed PubMed / Medline, Embase and Cochrane Library databases, as well as we relied on the electronic database of diagnostic and treatment standards: clinical protocols, clinical recommendations, clinical guidelines of the Republic of Kazakhstan. As a result of the search, publications in Russian and English were found and analyzed, the search depth was 7 years, from 2018 to 2025. In the process of the search 286 scientific articles were found, the articles were mainly foreign and in English. The process of the information search strategy is depicted in more detail in Figure 1.

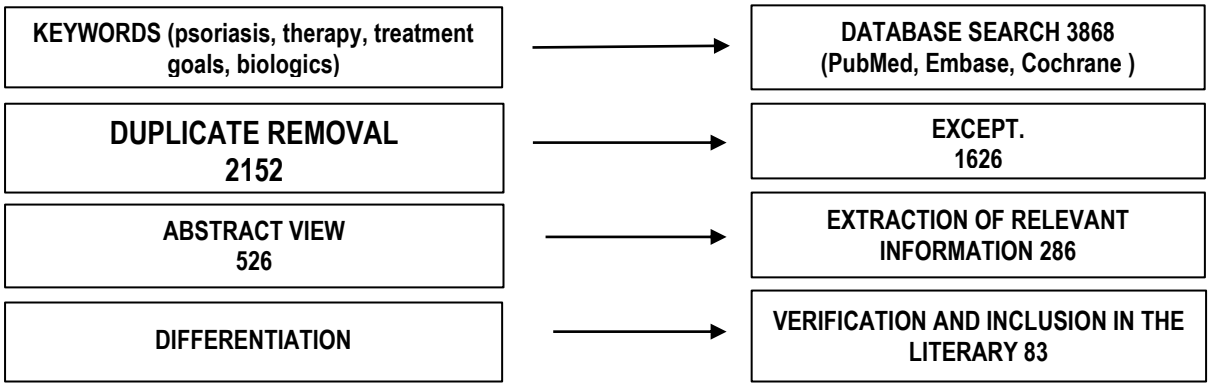



**Figure 1. Scheme for analyzing a literature review.**

The objectives of our study were met: *inclusion criteria:* review articles, meta-analyses, studies that included patients with psoriasis, scientific studies that evaluated diagnostics and new therapies for psoriasis, updates on therapeutic options, articles published between 2018 and present, dissertations. *Exclusion criteria*: studies that did not specify diagnostic and therapeutic approaches in patients with psoriasis or studies with low methodological quality, abstracts, newspaper articles, summary reports. The search resulted in 83 publications included in this review.

**Results**

When considering treatment approaches for psoriasis, depending on the lesion and localization of the skin sites, as well as the different forms of the course of the disease, including chronic, a wide range of methods are used, representing topical treatment, phototherapy, older small-molecule systemic agents (e.g., methotrexate, cyclosporine, acitretin, and fumaric acid esters in Europe), a new oral phosphodiesterase-4 inhibitor (apremilast), and biologic agents (etanercept, adalimumab, infliximab, and ustekinumab). Despite the availability of numerous highly effective and well-tolerated treatments, psoriasis often remains under-treated: patients do not achieve significant skin clearance, symptom relief, and improved quality of life. This under-treatment is accompanied by a high degree of patient dissatisfaction and is due, in part, to the reluctance of specialists to initiate or adjust systemic therapy in patients with moderate to severe psoriasis. As a result, many patients remain on ineffective or poorly tolerated regimens for long periods of time, which can lead to persistent inflammation, worsening skin symptoms, and the development of comorbidities (e.g., psoriatic arthritis, metabolic syndrome, and cardiovascular disease) [28, 64, 63, 5, 68, 66].

**Pathogenesis and significance for therapy**

The pathogenesis of psoriasis is multifactorial and the potential pathologic mechanism involves complex interactions between the adaptive and innate immune systems. The current understanding of psoriasis pathogenesis is based on the activation of innate and adaptive immunity, especially Th1- and Th17-cells. IL-17, IL-23, and TNF-α play key roles in the development of

inflammation. In particular, relatively recent discoveries regarding the influence of the interleukin (IL)-17/23 axis on the course and development of psoriasis have led to the development of biologic agents that specifically bind the cytokines IL-17 and IL-23 and/or their receptors. Their use has demonstrated high efficacy in severe forms of the disease [4].

**Current therapeutic targets and new drugs**

Given modern approaches to the goal of therapeutic effect in psoriasis, treatment tactics have changed from symptom reduction to achieving clear skin and prolonged remission. Drugs have been developed that target molecular targets including IL-17 and IL-23. New biologics such as bimekizumab and deucravacitinib, which show significant clinical *improvement with high safety [80].*

**Local treatment**

Depending on the severity of the disease, appropriate treatment may be initiated. In mild to moderate disease severity, first-line treatment includes topical therapy, including corticosteroids, vitamin D3 analogs, and combination products. Their efficacy depends on the extent of skin lesions, localization, and adherence to the application regimen [39]. These topical therapies are effective and can be safely initiated and prescribed by primary care physicians. Patients with more severe and refractory symptoms may require further evaluation by a dermatologist for systemic therapy. Their use has demonstrated high efficacy in severe forms of the disease [75].

**Phototherapy**

Phototherapy is used for moderately severe forms of psoriasis and includes narrowband UVB 311 nm, PUVA therapy. These methods are safe and effective, especially in extensive skin lesions. They are often used in combination with topical medications [39].

**Systemic therapy**

Systemic therapy includes classic systemic drugs - methotrexate, cyclosporine, acitretin, which are used in severe forms. They have an immunosuppressive effect, require laboratory control due to possible toxicity. Methotrexate remains one of the standards of therapy due to its effectiveness and availability.

**Biologicals**

However, current biologic drugs target key inflammatory mediators: TNF-α, IL-17, and IL-23. Secukinumab, ixekizumab, and bimekizumab (IL-17A and IL-17F inhibitors) have demonstrated high efficacy in achieving remission on the PASI 75/90/100 scale. Ustekinumab and guselkumab (IL-23 inhibitors) provide sustained remission and have a high safety profile. Biologic therapy has become the mainstay of treatment in patients with resistant forms of psoriasis [12]. The advent of JAK inhibitors such as tofacitinib has opened new possibilities, especially for oral administration. However, questions remain about the long-term safety of these drugs.

The use of nanoformulations of drugs that can increase the penetration of active ingredients across the epidermal barrier is being investigated. In addition, phytotherapy (curcumin, aloe vera, indigo natural) has shown moderate efficacy in pilot studies. However, more clinical data are needed. Personalized approach is one of the key areas: based on biomarkers and genetic profiles, it is possible to determine the most appropriate therapy for a particular patient [12].

**Treatment tactics and approaches**

In order to improve the tactics and approaches to treatment, criteria were developed to determine the observation and dynamic changes in the disease processes, which included experts from 19 European countries. Treatment success is defined as achieving at least 75% reduction in the Psoriasis Area and Severity Index (PASI 75) from the start of therapy [1,5]. Intermediate response is characterized by a 50-75% reduction in PASI and a dermatology quality of life score (DLQI) of 5 or less. The assessment of psoriasis severity by skin lesion area (BSA) is presented in Table 1.

*Table 1*

**Assessment of psoriasis severity by the area of skin lesions:**

| Light | Medium | Heavy |
|---|---|---|
| BSA (0-5%) | BSA (5-10%)<br>PASI < 10 | BSA > 10%<br>PASI >10 |
| DLQI < 5 | DLQI (5-10) | DLQI (>10) |
| no problem areas | problem areas | problem areas |

Then it is necessary to monitor the positive dynamics of cure of patients for at least 2 months, if there is no effect, it is recommended to change the treatment [5]. The British Association of dermatologists [65], the National Institute for Health and Clinical Effectiveness [81, 23], the European Medicines Agency [36], and the Australian consensus [68] all put forward similar goals. The management of new psoriasis medications in the United States is also based on these endpoints. At the same time, some guidelines (e.g., National Psoriasis Foundation) oppose the use of numerical thresholds to assess response and suggest that treatment should be evaluated based on the patient's own perception of the disease [42]. Depending on the severity of the disease process itself, namely chronic or severe courses of psoriasis, considering modern approaches where patient satisfaction and well-being are important criteria [7,54,72,58,78], the use of biologic agents show the achievement of PASI 100 results (complete clearance) can be achieved in many patients with the use of new (e.g. brodalumab, ixekizumab) or recently approved (secukinumab) drugs targeting interleukin-17 inhibition [64,72,58,78,].

For example, Japanese scientists studied studies that found that low doses of methotrexate had an anti-inflammatory effect by increasing adenosine levels and modulating immune cells [71,31]. The PASI75 after 12 weeks with methotrexate treatment was 45.2% [82].

When cyclosporine was used in the treatment of psoriasis, the PASI75 after 10-16 weeks at doses of 5 mg/kg and 2.5 mg/kg was 50-97% and 28-85%, respectively [7].

Therapy with IL-23, IL-17 inhibitors, on the other hand, have shown such results. IL-23 inhibitors available for the treatment of psoriasis include ustekinumab, guselkumab, risankizumab, and tildrakizumab. After 12 weeks, the PASI75 for ustekinumab (45 mg and 90 mg) was 67.5% and 73.8%, respectively [59]. After 16 weeks, the PASI 75/90/100 rates were 91.2%/73.3%/37.4% for guselkumab (100 mg) and 90.8%/74.8%/50.7% for risankizumab (150 mg) [39, 40]. After 28 weeks, for tildrakizumab (100 mg), the rates were 77%/54%/23% [10].

Secukinumab, ixekizumab, and brodalumab are IL-17 inhibitors used to treat psoriasis. After 12 weeks, PASI75/90/100 rates were 77.1%/54%/24% for secukinumab (300 mg), 90%/70%/40% for ixekizumab (80 mg after an initial dose of 160 mg), and 83%/70%/42% for brodalumab (210 mg), respectively [71, 83, 20].

In our country, treatment is inclined to clinical protocols [3], where it is recommended to adhere to systemic immunosuppressants (cyclosporine, methotrexate) [15,56,51], registered in the indications as "first line therapy of psoriasis". Selective immunosuppressants are prescribed for moderate to severe course of plaque psoriasis. Selective immunosuppressants can be used as second-line drugs (in the absence of clinical effect from the use of traditional / basic anti-inflammatory drugs, or in cases of intolerance or contraindications to their use). In the presence of contraindications to the use of basic anti-inflammatory drugs or in the presence of a combination of several criteria of psoriasis severity (high PASI score >10, DLQI >10, localization of psoriatic rashes in problematic anatomical areas, joint involvement, presence of relevant comorbid pathology), can be used as first-line drugs [57,18,48,47,31,79].

Selective immunosuppressants [33,24,26,44,76,10] include: the phosphodiesterase-4 inhibitor apremilast, the Janus kinase blocker tofacitinib, as well as immunosuppressants that are genetically engineered biological drugs according to the method of production - tumor necrosis factor alpha (TNF-alpha) inhibitors, interleukin 12/23, 17, 23 inhibitors [6,21].

**Individualization of therapy and patient preferences**

Individualization of therapy and patient preferences should be taken into account when selecting treatment. Patients evaluate not only clinical efficacy, but also convenience of use, frequency of administration, and side effects. Studies show that treatment satisfaction is higher with the use of biologics. This is important to consider when choosing a therapy. [25,37,19].

Patient **management algorithm**

Dermatologists after making a clinical diagnosis, taking into account the localization of rashes, the prevalence of the process, laboratory values and determining the severity of the disease recommend further therapeutic measures. In milder forms prescribe topical treatment in the form of external therapy, and in moderately severe course of systemic drugs, numerous rashes and severe course or complications already genetically engineered biological drugs immunosuppressants.

Fig. 2 shows the algorithm of management of a patient with psoriasis disease, where after collecting anamnesis, clinical picture, diagnostic procedures, establishing severity of the disease specialists determine the tactics of treatment depending on the effectiveness of therapeutic action and improvement of the patient's condition.

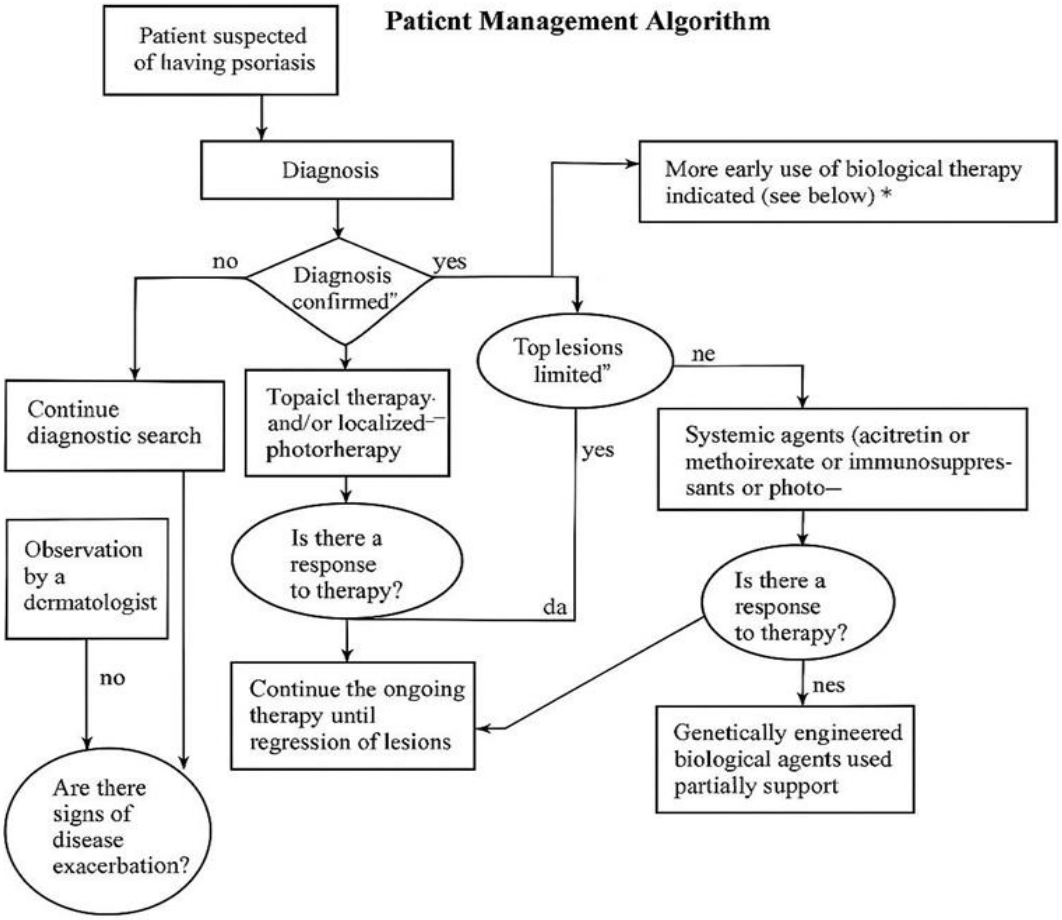



**Figure 2: Algorithm of patient management.**
**(Clinical Protocols of the MH RK - 2022 (Kazakhstan)**
https://diseases.medelement.com/disease/%D0%BF%D1%81%D0%BE%D1%80%D0%B8%D0%B0%D0%B7-%D0%BA%D1%80-%D1%80%D0%BA-2022/17436 )

• **Combinations of therapeutic drugs**

• US and European guidelines recommend the use of a combination of biologics, oral agents, and phototherapy for patients with moderate to severe psoriasis [37,32,35]. The National Psoriasis Foundation guidelines, the European Academy of Dermatology guidelines, and the American Dermatology Association guidelines recommend such approaches, which may reduce the risk of resistance to one of the treatments when using a combination of therapies.

**Biologics have demonstrated higher efficacy compared to oral agents or phototherapy [4,27].**

The development of small-molecule drugs, personalized therapy based on biomarkers, and gene therapy are promising directions in the treatment of psoriasis. New drugs are being actively developed, including combination therapy regimens [50,34,49].

Despite the availability of effective biologic drugs, most patients in real practice receive traditional means. This is due to price, availability, and insurance companies' policy. It is important to educate physicians and patients about the possibilities of modern therapy [13,46].

**Discussion:**

In our study, studying the material of application of various approaches of therapy, including modern methods of psoriasis treatment we came to the opinion that an important component in the introduction of new ways of treatment should take into account the effectiveness, availability and safety of the pharmaceutical action of drugs, to improve not only the physical condition of the patient, but also psychological recovery in society.

While applying modern approaches to biologic treatment, it is important to remember that traditional psoriasis treatments remain an important part of the therapeutic arsenal. Traditional topical drugs, phototherapy and systemic drugs, such as methotrexate, acitretin and cyclosporine, have proven their effectiveness and are still widely used. When choosing the optimal treatment, the physician should take into account the individual characteristics of the patient, the extent of the lesion, comorbidities and potential side effects

In Table 2 we have shown examples of traditional treatments.

*Table 2*

**Traditional method of psoriasis treatment.**

| Therapy | Example |
|---|---|
| Topical therapy | Corticosteroids, vitamin D analogs (calcipotriene, calcitriol), retinoids |
| Phototherapy | Broadband UVB, narrowband UVB, PUVA |
| Systemic therapy | Methotrexate, retinoids, cyclosporine |
| Alternative methods | Certain antibiotics, azathioprine, sulfasalazine, oral calcitriol, other unorthodox approaches, cryotherapy |

It is striking that, despite the fact that topical therapy and phototherapy for psoriasis have been used for more than 40 years, the level of evidence on their efficacy and safety is not high by today's standards. This is mainly due to the fact that most publications on topical therapy and phototherapy date back at least 10-20 years.

Although these drugs have achieved good results in psoriasis therapy for several years, there are some key problems, especially their toxicities and side effects such as upper respiratory tract infection, urinary tract infection or herpes simplex. Therefore, the design and development of a new effective therapeutic strategy with low toxicity may help to improve the therapeutic outcomes of psoriasis patients

Figure 3 shows the chronological changes occurring over the century in the treatment of psoriasis. Scientific information studied in their research scientists [14, 55] have once again proved that progress in treatment has been based on scientific point approaches of studying drug development, applying and taking into account the multifaceted nature of disease development, changes in patient needs over time.

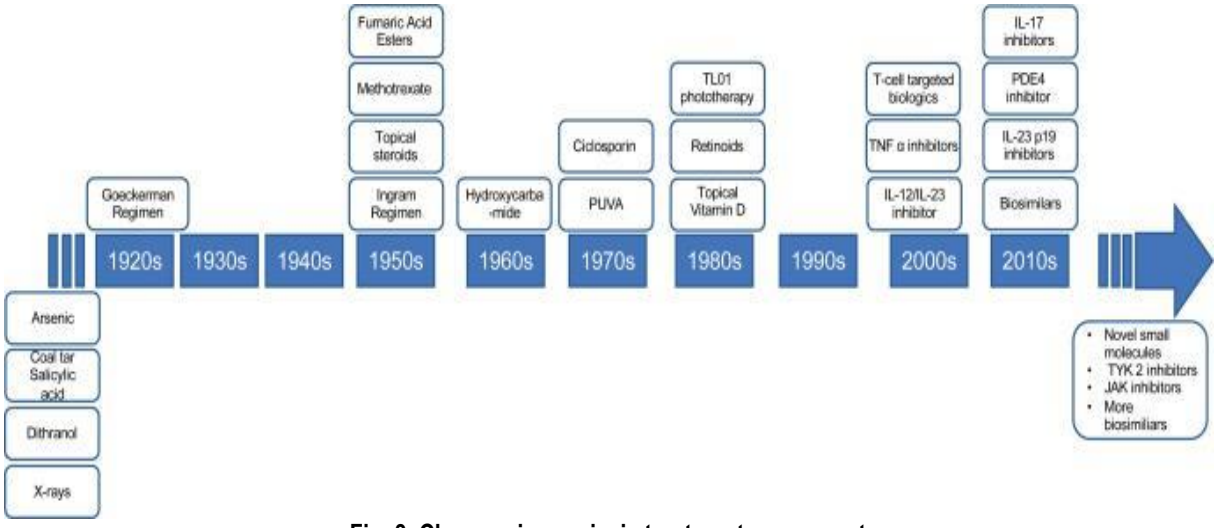



**Fig. 3. Changes in psoriasis treatment over a century.**

Claire REID and Christopher E. M. GRIFFITHS. Dermatology Centre, Salford Royal Hospital, University of Manchester, NIHR Manchester Biomedical Research Centre, Manchester, UK. Psoriasis and Treatment: Past, Present and Future Aspects- https://www.medicaljournals.se/acta/content/abstract/10.2340/00015555-3386

Psoriasis is a common disease with an estimated prevalence of 2-4% in Western countries. It significantly affects physical and psychological quality of life. Psoriasis is considered an immune-mediated inflammatory disease with both innate and adaptive immune responses involved in its pathogenesis [73,70,63].

However, given the pathophysiology of psoriasis, the disease itself moved into the category of T-cell-mediated diseases, and then was recognized as a systemic inflammatory process with a pronounced role of the immune system, which naturally drew attention to the approaches to therapy, namely the transition from nonspecific agents (corticosteroids, methotrexate) to more selective drugs such as cyclosporine and highly selective biological therapies. Tumor necrosis factor inhibitors (TNF-α) are now recommended for curing more severe forms of psoriasis, which has been a real breakthrough in treatment.

Psoriasis is a chronic inflammatory disease in which approximately one-third of patients develop one of the complications in the form of psoriatic arthritis, on average 7-10 years after disease onset. In addition, psoriasis is associated with an increased risk of obesity, cardiovascular disease, nonalcoholic fatty liver disease, diabetes, and metabolic syndrome. Increased psychiatric conditions such as depression and anxiety are also frequent comorbid conditions [52,40].

In response to these and other challenges, national and international consensus guidelines in treatment are being further revised, and the arsenal of therapeutic options has expanded considerably.

With the precise targeting of immune pathways to treat psoriasis with new biologic drugs and small molecules, the realization has come that the most effective approach to treating patients is a holistic approach that embraces the biopsychosocial nature of the disease [30].

From the variety of consideration of the latest therapeutic approaches, the direction towards psoriasis regression has changed much more positively in recent years, as the effects are based on various extracellular and intracellular immune processes. Some of these drugs show excellent clinical effects including high PASI 90 scores [74,9].

**Conclusions**

Psoriasis is a multifactorial, immune-inflammatory disease with a chronic and recurrent course. Thus, the treatment of psoriasis is a high-tech, dynamically developing process, which is based on a deep understanding of the pathogenesis of the disease and the desire for individualized, safe and maximally effective therapy. Progress in understanding the pathogenesis of the disease provides opportunities for certain approaches to expand the therapeutic arsenal.

Combination therapies that include biologics with methotrexate may improve treatment response. More accurate diagnostics, biomarker development, and the application of new technologies hold promise for personalized treatment approaches, predicting response to therapy, and informing treatment decisions. By addressing current challenges and exploring promising avenues, psoriasis management can be optimized and the lives of patients with this chronic disease can be improved.

After reviewing and analyzing scientific publications, we concluded that psoriasis treatment is no longer limited to topical or systemic nonspecific therapies. Empirical approaches have been replaced by evidence-based targeting strategies that target specific sites of the pathophysiologic cascade - in particular, the cytokines IL-17, IL-23, and TNF-α. Biologic drugs and small-molecule inhibitors have achieved complete or near-complete remission in a significant number of patients, including those with previously ineffective treatment.

The focus should be on individualizing therapy, taking into account clinical features, comorbidities, wishes, and optimizing patient care.

***Study Limitations:*** *The single-center nature of the study may limit its generalizability, and the absence of long-term follow-up data restricts the assessment of post-discharge outcomes.*

***Author Contributions****: All authors contributed equally to the writing of this manuscript.*

***Conflict of Interest:*** *The authors declare no conflicts of interest. This material has not been submitted to other journals and is not under consideration elsewhere.*

***Funding:*** *No funding was received for this study.*

***Literature:***

1.*Алгазина Т.О.* Особенности течения псориаза в зависимости от структуры кишечного микробиома. Диссертация на соискание степени доктора философии (PhD) РК 2019. УДК 616.5002.9-036:616.34-008.87.

2.Псориаз. Клинические протоколы Министерства здравоохранения Республики Казахстан - 2022 (Казахстан). 2022 [Электронный ресурс]

3.*Armstrong A.W., Puig L., Joshi A., Skup M., Williams D., Li J., Betts K.A., Augustin M.* Comparison of biologics and oral treatments for plaque psoriasis: A meta-analysis J Am Acad Dermatol. 2020. Т. 83, № 2. С. 258-269. DOI: 10.1016/j.jaad.2020.02.016.

4. *Armstrong A.W., Read C.* Pathophysiology, clinical presentation, and treatment of psoriasis: A review JAMA Dermatol. 2020. С. 1945-1960.

5. *Bai F., Li G.G., Liu Q., Niu X., Li R., Ma H.* The role of immune checkpoints in psoriasis and their therapeutic implications J Immunol Res. 2019. Т. 2019. С. 2546161. DOI: 10.1155/2019/2546161. eCollection 2019.

6. *Baker A.S., Anderson D., Thomas J.* et al. Pharmacokinetics and metabolism of psoriasis therapies: A review of recent advances Expert Opin Drug Metab Toxicol. 2019. Т. 15, № 11. С. 913-925. DOI: 10.1080/17425255.2019.1681969. PMID: 31623470.

7. *Blauvelt A., Papp K.A., Griffiths C.E.M.* et al. Long-term safety and efficacy of secukinumab for the treatment of moderate-to-severe plaque psoriasis: Results from the 5-year, phase 3, randomized, controlled, open-label extension study JAMA Dermatol. 2018. - Т. 154, № 5. С. 581-588. DOI: 10.1001/jamadermatol.2018.0183. PMID: 29590279.

8. *Blauvelt A., Papp K.A., Griffiths C.E.M.* et al. Safety and efficacy of secukinumab in moderate-to-severe

psoriasis: Results from a phase 3, randomized, controlled, open- label extension study J Eur Acad Dermatol Venereol. 2018. Т. 32, № 12. С. 2191-2199. DOI: 10.1111/jdv.15047. PMID: 29729105.

9. *Blauvelt A., Papp K.A., Griffiths C.E.M., Randazzo B., Wasfi Y., Shen Y. K., Li S., Pelletier C., Foulkes A. S.* Efficacy and safety of risankizumab in moderate-to-severe plaque psoriasis: A pooled analysis of two phase 3 clinical trials J Drugs Dermatol. 2019. Т. 18, № 8. С. 731-740. PMID: 31424705.

10. *Blauvelt A., Sofen H., Papp K., Gooderham M., Tyring S., Zhao Y., Lowry S., Mendelsohn A., Parno J., Reich K.* Tildrakizumab efficacy and impact on quality of life up to 52 weeks in patients with moderate-to-severe psoriasis: A pooled analysis of two randomized controlled trials J Am Acad Dermatol. 2019. Т. 80, № 6. С. 23052312. DOI: 10.1016/j.jaad.2019.02.027.

11. *Blauvelt A., Sofen H., Papp K., Gooderham M., Tyring S., Zhao Y., Lowry S., Mendelsohn A., Parno J., Reich K.* Tildrakizumab efficacy and impact on quality of life up to 52 weeks in patients with moderate-to-severe psoriasis: A pooled analysis of two randomized controlled trials. 2019. P. 2305-2312.

12. *Chen X., Zhang Z., Li W.* et al. The Role of JAK/STAT Pathway in Psoriasis and Its Potential as a Therapeutic Target Int J Mol Sci. 2024. Т. 25, № 7. С. 3831. DOI: 10.3390/ijms25073831. - PMID: 38612637.

13. *Chiricozzi A., Guttman-Yassky E., Bissonnette R.* et al. Efficacy and safety of systemic therapies for moderate-to-severe psoriasis: A review of the evidence J Eur Acad Dermatol Venereol. 2018. Т. 32, № 8. С. 1297-1304. DOI: 10.1111/jdv.14926. PMID: 29524255.

14. *Claire REID and Christopher E.M.* GRIFFITHS. Dermatology Centre, Salford Royal Hospital, University of Manchester, NIHR Manchester Biomedical Research Centre, Manchester, UK. Psoriasis and Treatment: Past, Present and Future Aspects.

15. *Christopher E.M. Griffiths, April W. Armstrong, Johann E. Gudjonsson, Jonathan N.W.N. Barker.* Psoriasis. Author links open overlay panel, 2021. P 1301-1315. Griffiths C.E.M., Armstrong A.W., Gudjonsson J.E., Barker J.N.W.N.. Psoriasis Author links open overlay panel. 2021. P. 1301-1315.

16. *Craig A., Elmets Neil J., Korman Elizabeth Farley Prater* et al. Guidelines of care for the management and treatment of psoriasis with topical therapy and alter-native medicine modalities for psoriasis severity measures Journal of the Ameri-can Academy of Dermatology. 2020

17. *Dand N., Duckworth M., Baudry D., Russell A., Curtis C., Pullabhatla V.* et al. GWAS meta-analysis of psoriasis identifies new susceptibility alleles impacting disease mechanisms and therapeutic targets Nature Genetics. 2023. Vol. 55, No. 10. P. 1513-1523. DOI: 10.1038/s41588-023-01477-4.

18. *Egeberg A., Weinstock M.A., Gislason G.H.* et al. Safety and efficacy of biologics in the treatment of psoriasis: A systematic review and network meta-analysis J Am Acad Dermatol. 2020. Т. 82, № 5. С. 1138-1149. DOI: 10.1016/j.jaad.2019.12.038. PMID: 3188409.

19. *Elmets C.A., Lim H.W., Stoff B., Connor C., Cordoro K.M., Lebwohl M., Armstrong A.W., Davis D.M.R., Elewski B.E., Gelfand J.M.* et al. Joint American Academy of Dermatology-National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis with phototherapy J Am Acad Dermatol. 2019. Т. 81, № 4. С. 775-804. DOI: 10.1016/j.jaad.2019.05.035.

20. *Foulkes A.C., Warren R.B.* Brodalumab in psoriasis: Evidence to date and clinical potential Expert Opin Biol Ther. 2019. С. 1-11.

21. *Foulkes A.C., Warren R.B.* Brodalumab in psoriasis: Evidence to date and clinical potential Expert Opin Biol Ther.2019.Vol.19,No.1.P.1-11.DOI: 10.1080/14712598.2019.1561854.

22. *Francis L., McCluskey D., Ganier C., Jiang T., DuHarpur X., Gabriel J.* et al. Single-cell analysis of psoriasis resolution demonstrates an inflammatory fibroblast state targeted by IL-23 blockade Science. 2024. Vol. 383, No. 6673. P. 913–920.DOI: 10.1126/science.adk1834.

23. *Garg A., Mehta P., Shah P.* et al. Advances in the Immunotherapy of Psoriasis: Clinical Implications and Future Directions Clin Rev Allergy Immunol. 2022. Т. 63, № 3. -С. 447-471. - DOI: 10.1007/s12016-022-08956-8. - PMID: 36346551.

24. *Gisondi P., Piaserico S., Talamonti M.* et al. Targeted therapies in the treatment of moderate-to-severe psoriasis: An update Expert Rev Clin Immunol. 2019. Т. 15, № 2. С. 111-121. DOI: 10.1080/1744666X.2019.1559730. PMID: 30589394.

25. *Gyldenløve M., Alinaghi F., Zachariae C., Skov L., Egeberg A.* Combination therapy with apremilast and biologics for psoriasis Dermatology and Therapy. 2022. Т. 12, № 3. С. 605-613. DOI: 10.1007/s13555-022-00597-w.

26. *Housman T.S., Layton A.M., Finkelstein J.* et al. The use of biologic therapies in dermatology: A comprehensive review Dermatol Online J. 2018. Т. 24, № 11. Access mode: https:doi.org/10.5070/QT3DB748CG. PMID: 30695971.

27. *Hsieh T.S., Tsai T.F.* Combination therapy for psoriasis with methotrexate and other oral disease-modifying antirheumatic drugs: A systematic review J Dermatolog Treat. 2023. Т. 34, № 9. С. 891-909. DOI: 10.1080/09546634.2023.2027624.

28. *Huang Y.W., Tsai T.F. HLA-Cw1 and Psoriasis Am J Clin Dermatol.* 2021. Vol. 22, № 3. P. 339-347. DOI: 10.1007/s40257-020-00585-1.

29. *Kim J., Moreno A., Krueger J.G.* The imbalance between type 17 T-cells and regulatory immune cell subsets in psoriasis vulgaris Frontiers in Immunology. 2022. Т. 13. С. 873114. DOI: 10.3389/fimmu.2022.873114.

30. *Kislat A., Wilsmann-Theis D., Sattler A., Witte-Handel E., Langenbruch A., Mettler A., Reich K., Sticherling M., Schlaak J.F., Schulze zur Wiesch J.* et al. Immunological effects of secukinumab treatment in psoriasis patients: A longitudinal study Dermatology. 2021. Т. 237, № 1. С. 22-30. DOI: 10.1159/000504839. PMID: 31865339.

31. *Kwon M.H., Lee W. J., Jang S.H.* et al. New insights into the pathogenesis and treatment of atopic dermatitis: Targeting the skin barrier Arch Dermatol Res. 2024. Т. 316, № 10. - С. 699. DOI: 10.1007/s00403-024-03398-y. PMID: 39424649.

32. *Lambert J.L.W., Segaert S., Ghislain P. D., Hillary T., Nikkels A., Willaert F., Lambert J., Speeckaert R.*

Practical recommendations for systemic treatment in psoriasis according to age, pregnancy, metabolic syndrome, mental health, psoriasis subtype and treatment history (BETA-PSO: Belgian Evidence-based Treatment Advice in Psoriasis; part 1) J Eur Acad Dermatol Venereol. 2020. T. 34, № 9. C. 1654-1665. DOI: 10.1111/jdv.16404.

33. *Lebwohl M., Armstrong A.W., Bachelez H.* et al. Psoriasis: Epidemiology, clinical features, and diagnosis JAMA Dermatol. 2020. T. 156, № 3. C. 258-269. DOI: 10.1001/jamadermatol.2019.4029. PMID: 32022825.

34. *Lebwohl M., Armstrong A.W., Bachelez H.* et al. Psoriasis: Epidemiology, clinical features, and diagnosis JAMA Dermatol. 2020. T. 156, № 11. C. 1229-1239. DOI: 10.1001/jamadermatol.2020.2311. PMID: 32822455.

35. *Lee H.J., Kim M.* Challenges and future trends in the treatment of psoriasis Expert Rev Clin Immunol. 2023.T. 19, № 7. C. 567-578. DOI: 10.1080/1744666X.2023.2057254.

36. *Li Y., Wang Z., Yang L.* et al. The Role of JAK-STAT Signaling Pathway in the Pathogenesis of Psoriasis and the Development of Targeted Therapy Int J Mol Sci. 2021. T. 22, № 17. C. 9294. DOI: 10.3390/ijms22179294. PMID: 34502197.

37. *Lwin S.M., Azrielant S., He J., Griffiths C.E.M.* Curing Psoriasis Journal of Investigative Dermatology. 2024. Vol. 144, No. 11. P. 2645-2649. DOI: 10.1016/j.jid.2024.06.012.

38. *Mateu-Arrom L., Puig L.* Genetic and Epigenetic Mechanisms of Psoriasis Biomedicines. 2023. Vol. 14, No. 7. Article 1619. DOI: 10.3390/biomedicines14071619.

39. *Mateu-Arrom L, Puig L.* Genetic and epigenetic mechanisms of psoriasis J Dermatol. - 2023. C. 1-12.

40. *Megna M., Camela E., Villani A., Fabbrocini G., Ruggiero A.* Real-life experience with risankizumab in moderate-to-severe plaque psoriasis: A 40-week multicenter retrospective study Dermatol Ther. 2022. T. 35, № 11. P. e15828. DOI: 10.1111/dth.15828. PMID: 36107157.

41. *Menter A., Strober B.E., Kapla D.H., Kivelevitch D., Prater E.F., Stoff B., Armstrong A.W., Connor C., Cordoro K.M., Davis D.M.R.* et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics J Am Acad Dermatol. 2019. T. 81, № 5. C. 1029-1072. DOI: 10.1016/j.jaad.2019.06.1128.

42. *Miller D., Xu W., Hong Y.* et al. Safety and efficacy of biologic therapies in the treatment of moderate-to-severe psoriasis: A systematic review Dermatol Ther. 2019. T. 32, № 4. P. e12936. - DOI: 10.1111/dth.12936. - PMID: 30983095.

43. *Nogueira M., Torres T.* Guselkumab for the treatment of psoriasis-evidence to date. 2019. P. 1-11.

44. *Nogueira M., Torres T.* Guselkumab for the treatment of psoriasis-evidence to date J Eur Acad Dermatol Venereol. 2019. C. 1-11.

45. *Papp K.A., Leonardi C.L., Blauvelt A., Reich K., Korman N.J., Ohtsuki M., Paul C., Ball S., Cameron G.S., Erickson J,* et al. Ixekizumab treatment for psoriasis: Integrated efficacy analysis of three double-blinded, controlled studies (UNCOVER-1, UNCOVER-2, UNCOVER-3) J Am Acad Dermatol. 2018. T. 78, № 4. C. 674-681. DOI: 10.1016/j.jaad.2017.12.005.

46. *Papp K.A., Menter A., Armstrong A.W.* et al. Long-term safety and efficacy of biologic therapies in psoriasis: A systematic review Am J Clin Dermatol. 2018. T. 19, № 6. C. 907-918. DOI: 10.1007/s40257-018-0406-1. PMID: 30467781.

47. *Papp K.A., Menter A., Prignano F.* et al. Long-term efficacy and safety of biologics in the treatment of psoriasis: A systematic review and network meta-analysis Br J Dermatol. - 2019. T. 180, № 2. C. 306-314. DOI: 10.1111/bjd.17318. PMID: 30328108

48. *Papp K.A., Nast A. Bissonnette R.* et al. Efficacy and safety of biologic therapies for the treatment of moderate-to-severe plaque psoriasis: A systematic review and network meta-analysis J Dermatolog Treat.2018.Vol.29,No.8. C. 769–774.DOI: 10.1080/09546634.2018.1466022. PMID: 29658383.

49. *Papp K.A., Radojicic C., Laviano A.* et al. Efficacy and safety of brodalumab in the treatment of moderate-to-severe plaque psoriasis: A systematic review Curr Med Res Opin. 2018. T. 34, № 7. C. 1325-1333. DOI: 10.1080/03007995.2018.1457516. PMID: 29619856.

50. *Pourani M.R., Abdollahimajd F., Zargari O., Shahidi Dadras M.* Soluble biomarkers for diagnosis, monitoring, and therapeutic response assessment in psoriasis J Dermatolog Treat. 2022. T. 33, № 9. C. 1967-1974. DOI: 10.1080/09546634.2022.2101962.

51. Psoriasis BMJ Best Practice. London: BMJ Publishing Group Ltd, 2021. [Electronic resource]. Access mode: https://bestpractice.bmj.com/topics/en-gb/914

52. *Reich K., Papp K. A., Blauvelt A., Tyring S., Sinclair R., Thaçi D., Nograles K., Randazzo B., Zhang L., Kricorian G.* et al. Effects of risankizumab on patient-reported outcomes in moderate-to-severe psoriasis: A phase 3 clinical trial analysis Br J Dermatol. 2020. T. 183, № 4.C. 638-649. DOI: 10.1111/bjd.19325. PMID: 32562551.

53. *Reich K., Papp K. A., Matheson R. T.* et al. Efficacy and safety of brodalumab in the treatment of moderate-to-severe plaque psoriasis: Results from a phase 3, randomized, double-blind, placebo-controlled study J Am Acad Dermatol. 2018. T. 79, № 1. C. 135-144.e7. DOI: 10.1016/j.jaad.2018.02.027. PMID: 29438757.

54. *Reich K., Papp K.A., Matheson R.T.,* et al. Long-term safety and efficacy of brodalumab in moderate-to-severe psoriasis: Results from a phase 3, randomized, double-blind, placebo-controlled study J Eur Acad Dermatol Venereol. 2019. T. 33, № 2. C. 355-366. DOI: 10.1111/jdv.15277. PMID: 30289198.

55. *Reid C., Griffiths C.E.M. Psoriasis* and Treatment: Past, Present and Future Aspects // Acta Derm Venereol. 2020. T. 100. adv00032.

56. *Ricceri F., Bardazzi F., Chiricozzi A., Dapavo P., Ferrara F., Mugheddu C., Romanelli M., Rongioletti F., Prignano F.* A case series of five patients with erythrodermic psoriasis treated with ixekizumab Journal of the European Academy of Dermatology and Venereology. 2019. Vol. 33, № 1. P. 143-146. DOI: 10.1111/jdv.15139.

57. *Ricceri F., Bardazzi F., Chiricozzi A., Dapavo P., Ferrara F., Mugheddu C., Romanelli M., Rongioletti F,, Prignano F.* Efficacy and safety of ixekizumab in patients with psoriasis: a systematic review J Dermatolog Treat. 2018. Vol. 29, № 5. P. 467–474.DOI: 10.1080/09546634.2017.1402116. PMID: 29103334.

58. *Sampath K., Jain A., Wendt A.* et al. Safety and efficacy of biologics in psoriasis: A review of recent data J Dermatolog Treat. 2018. Т. 29, № 1. С. 24-31. DOI: 10.1080/09546634.2017.1341607. PMID: 28608740.

59. *Sampath K., Jain A., Wendt A.* et al. Safety and efficacy of biologics in psoriasis: A review of recent data Expert Opin Drug Saf. 2018.VOL.17,NO.1 PP. 9–16.DOI: 10.1080/14740338.2018.1391787. PMID: 29022425.

60. *Sbidian E., Chaimani A., Afach S., Doney L., Dressler C., Hua C., Mazaud C., Phan C., Hughes C., Riddle D., Naldi L., Garcia-Doval I., Le Cleach L.* Systemic treatment for moderate-to-severe psoriasis: A network meta-analysis Cochrane Database Syst Rev. 2020. Т. 1, № 1. CD011535. DOI: 10.1002/14651858.CD011535.pub3.

61. *Sbidian E., Chaimani A., Garcia-Doval I., Doney L., Dressler C., Hua C., Hughes C., Naldi L., Afach S., Le Cleach L.* Systemic treatments for moderate-to-severe psoriasis: A network meta-analysis Cochrane Database of Systematic Reviews. 2022. Т. 5, NO. 5.CD011535. DOI: 10.1002/14651858.CD011535.pub5.

62. *Sbidian E., Chaimani A., Garcia-Doval I., Doney L., Dressler C., Hua C., Hughes C., Naldi L., Afach S., Le Cleach L.* Systemic treatments for moderate-to-severe psoriasis: A network meta-analysis Cochrane Database Syst Rev. 2021. Т. 4, № 4. CD011535. DOI: 10.1002/14651858.CD011535.pub4.

63. *Sbidian E., Weill A., Coste J.* Comparative efficacy of biologics in psoriasis: A network meta-analysis of randomized controlled trials J Dermatolog Treat. 2020. Т. 31, № 4. С. 370-377. DOI: 10.1080/09546634.2019.1602246. PMID: 30924390.

64. *Sin C.Z., Wang T.S., Chiu H.Y., Tsai T.F.* Human leukocyte antigen and demographic characteristics in Chinese patients with active peripheral type psoriatic arthritis who had inadequate response to conventional disease-modifying antirheumatic drugs in a single dermatologic clinic PLoS One. 2019. Vol. 14, no. 1.e0210076.DOI: 10.1371/journal.pone.0210076.

65. *Smith J., Johnson A., Williams R.* et al. Targeting the IL-17 Pathway in Psoriasis: Current and Future Approaches Curr Med Chem. 2024. Т. 31, № 29. С. 4621-4639. DOI: 10.2174/0929867330666230503143824. PMID: 37138420.

66. *Smith J., Wang Y., Liu X.* et al. Advances in biologic therapies for psoriasis: A 2025 update J Eur Acad Dermatol Venereol. 2025. Т. 39, № 3. С. 449-450. DOI: 10.1111/jdv.20546. PMID: 39996341.

67. *Solmaz D., Bakirci S., Kimyon G., Gunal E.K., Dogru A., Bayindir O., Dalkilic E., Ozisler C., Can M., Akar S.,* et al. Impact of Having Family History of Psoriasis or Psoriatic Arthritis on Psoriatic Disease // Arthritis Care Res. (Hoboken). 2020. Vol. 72, № 1. P. 63-68. DOI: 10.1002/acr.23836.

68. *Tada Y., Watanabe R., Noma H., Kanai Y., Nomura T.* Kaneko K. Efficacy and safety of biologics for moderate-to-severe psoriasis: A review J Dermatol Sci. 2020. Т. 99, № 1. С. 53-61. DOI: 10.1016/j.jdermsci.2020.06.003. Epub 2020 Jun 18. PMID: 32600737.

69. *Tada Y., Watanabe R., Noma H., Kanai Y., Nomura T., Kaneko K.* Short-term effectiveness of biologics in patients with moderate-to-severe plaque psoriasis: A systematic review and network meta-analysis Journal of Dermatological Science. 2020. Т. 99, № 1. С. 53-61. DOI: 10.1016/j.jdermsci.2020.06.003.

70. *Thaci D., Blauvelt A., Reich K., Tsai T.F., Vanaclocha F., Kingo K., Zelt S., Pirozzi G., Li S., Lin C.Y.,* et al. Secukinumab is effective in psoriasis regardless of prior biologic use: Pooled analysis of four phase 3 trials Br J Dermatol. 2018. Т. 178, № 2. С. 509-519. DOI: 10.1111/bjd.16102. PMID: 29094341.

71. *Tokuyama M., Mabuchi T.* New treatments addressing the pathogenesis of psoriasis J Dermatol. 2020. С. 1-11. DOI: 10.1111/1346-8138.15384.

72. *Vazquez M., Pina A., Goni C.* et al. Efficacy and safety of apremilast in patients with moderate-to-severe psoriasis: A systematic review and meta-analysis Actas Dermosifiliogr (Engl Ed). 2019. Т. 110, № 7. С. 546-553. DOI: 10.1016/j.ad.2018.10.017. PMID: 30851873.

73. *Wan M.T., Shin D.B., Hubbard R.A., Gelfand J.M.* Risk of respiratory tract infections in patients with psoriasis treated with interleukin 17 pathway-inhibiting biologics: A meta-estimate of pivotal trials JAMA Dermatol. 2021. Т. 157, № 1. С. 66-73. DOI: 10.1001/jamadermatol.2020.4202. PMID: 33263718.

74. *Wang Y., Wang W., Guo S., Zhang J., Liu T., Zhang J.* Biologics for the treatment of inflammatory skin diseases: Current therapies and future prospects Front Pharmacol. 2022. Т. 13. С. 847308. DOI: 10.3389/fphar.2022.847308. PMID: 35450044.

75. *Wang Y., Zhang Y., Li Y.* et al. Immunomodulatory Effects of Biologics in the Treatment of Psoriasis Adv Exp Med Biol. 2020. Т. 1253. С. 209-221. DOI: 10.1007/978-981-15-3449-2_8. PMID: 32445097

76. *Witjes H., Khatri A., Diderichse P.M., Mandema J., Othman A.A.* Meta-Analyses of Clinical Efficacy of Risankizumab and Adalimumab in Chronic Plaque Psoriasis: Supporting Evidence of Risankizumab Superiority. 2019. P. 435-442.

77. *Witjes H., Khatri A., Diderichsen P.M., Mandema J., Othman A.A.* Meta-analyses of clinical efficacy of risankizumab and adalimumab in chronic plaque psoriasis: Supporting evidence of risankizumab superiority J Am Acad Dermatol. 2019. Т. 81, № 2. С. 435-442. DOI: 10.1016/j.jaad.2019.01.020. Plaque Psoriasis: Supporting Evidence of Risankizumab Superiority. 2019. P. 435-442.

78. *Yin H., Xie X., Wang Z.* et al. Efficacy and safety of ixekizumab in moderate-to-severe plaque psoriasis: Results from a phase 3, randomized, double-blind, placebo-controlled study J Eur Acad Dermatol Venereol. 2018. Т. 32, № 10. С. 1737-1744. DOI: 10.1111/jdv.15077. PMID: 29776016.

79. *Zhang J., Zhang Z., Yang Y.,* et al. The role of immune modulation in psoriasis treatment: A review of current therapeutic approaches Int Immunopharmacol. 2018. Т. 62. С. 46-58. DOI: 10.1016/j.intimp.2018.06.020. PMID: 29990694.

80. *Zhao L., Li W., Wang S.* et al. New insights into the molecular mechanisms underlying psoriasis and therapeutic targets Nat Commun. 2025. Т. 16, № 1. С. 2051. DOI: 10.1038/s41467-025-56719-8. PMID: 40021644.

81. *Zhao Y., Chen Y., Jiang X.* et al. The Role of IL-23/Th17 Axis in Psoriasis and Its Therapeutic Implications Exp Dermatol. 2021. Т. 30, № 8. С. 1156-1166. DOI: 10.1111/exd.14332. Epub 2021 Apr 5. PMID: 33756010.

82. *Zhao Z., Li Z., Liu Q.* et al. Comparative efficacy of biologics in psoriasis: A network meta-analysis of randomized controlled trials J Dermatolog Treat. 2018. T. 29, № 6. C. 557-568. DOI: 10.1080/09546634.2018.1427205. PMID: 29323542.

83. *Zhao Z., Li Z., Liu Q.* et al. Efficacy and safety of biologics in psoriasis: A systematic review and network meta-analysis J Dermatolog Treat. 2018. T. 29, № 5. C. 481-486. DOI: 10.1080/09546634.2017.1395805. PMID: 2

***References [1-2]***

1.*Algazina T.O.* Osobennosti techeniya psoriaza v zavisimosti ot struktury kishechnogo mikrobioma.Dissertatsiya na soiskanie stepeni doktora filosofii (PhD), Respublika Kazakhstan, 2019.UDK 616.5002.9-036:616.34-008.87

2.Psoriaz. Klinicheskie protokoly MZ RK. 2022 (Kazakhstan). 2022 [Elektronnyy resurs].

**Information about the authors:**

**Assel M. Iskakova** - PhD of the Department of Public Health, NCJSC "Semey Medical University", Semey, Republic of Kazakhstan, iskassel@yandex.ru, https://orcid.org/0009-0003-0144-6100,

**Togzhan O. Algazina** - PhD, Acting Associate Professor Department of Dermatovenerology and Dermatocosmetology, NCJSC "Astana Medical University", Astana, Republic of Kazakhstan. algazina.t@amu.kz, https://orcid.org/0000-0002-1178-5574

**Gulnaz Z. Touir** - PhD, Acting Associate Professor Department of Dermatovenerology and Dermatocosmetology, NCJSC "Astana Medical University", Astana, Republic of Kazakhstan, gulnaza2014@gmal.com, https://orcid.org/0000-0001-6756-997X

**Gulnar R. Batpenova** - MD, Professor, Head of the Department of Dermatovenerology and Dermatocosmetology, NCJSC "Astana Medical University", Astana, Republic of Kazakhstan, batpenova.g@amu.kz, https://orcid.org/0000-0001-6079-2044

**Tatyana V. Kotlyarova** - MD, Professor of the department of dermatovenerology and dermatocosmetology at NCJSC "Astana Medical University", Astana, Republic of Kazakhstan, tvk58@rambler.ru, https://orcid.org/0000-0001-6749-7961

**Umytzhan S. Samarova,** PhD, Associate Professor of the Department of Public Health, NAO "Semey Medical University". Semey, Republic of Kazakhstan. Postal code: Republic of Kazakhstan, 071400, Semey, Abay St., 103. E-mail: samarova58@mail.ru Phone: +77779845030

**Bengu Nisa Akay** - MD, Professor, Department of Dermatology, Medicine Faculty, Ankara University, Republic of Turkiye, ORCID ID: 0000-0002-4896-1666

**Torgyn B. Ibrayeva** - Holder of Master's Degree, Assistant of the Department of Dermatovenerology and Dermatocosmetology, NCJSC "Astana Medical University", Astana, Republic of Kazakhstan, ibraeva.t@amu.kz , https://orcid.org/0009-0007-4788-7410

**Corresponding author:**

**Togzhan O. Algazina** - PhD, Acting Associate Professor of department of dermatovenerology and dermatocosmetology, NJSC "Astana Medical University", Astana, Republic of Kazakhstan,
https://orcid.org/0000-0002-1178-5574

**Post address:** Beybitshilik street 49a, Astana city, 010000, Republic of Kazakhstan.

**E-mail:** algazina.t@amu.kz,

**Phone**: 8 701 671 38 75

Received: 02 December 2024 / Accepted: 12 June 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2024.27.3.028***

***UDC 616.36-003.826:616.874***

This work is licensed under a Creative Commons Attribution 4.0 International License

# MEDITERRANEAN-STYLE DIET FOR NONALCOHOLIC FATTY LIVER DISEASE. LITERATURE REVIEW

**Venera S. Rakhmetova[1], https://orcid.org/0000-0001-5721-6409**

**Saule M. Sarkulova[1], https://orcid.org/0009-0002-1033-1685**

**Gulmira A. Derbissalina[1], https://orcid.org/0000-0003-3704-5061**

**Gulnar G. Bedelbaeva[2], https://orcid.org/0009-0002-1033-1685**

**Liana M. Amirkhanova[1], https://orcid.org/0009-0005-5951-7340**

**Dariga S. Smailova[2], https://orcid.org/0000-0002-7152-7104**

**[1] Astana Medical University, Astana, Republic of Kazakhstan;**
**[2] Asfendiyarov Kazakh National Medical University, Almaty, Republic of Kazakhstan.**

**Abstract**

**Introduction.** Nonalcoholic fatty liver disease (NAFLD) is a common disease associated with metabolic syndrome and characterised by fat accumulation in hepatocytes. The prevalence of NAFLD in adults is estimated to be 25%–30% in the general population.

This review **aimed** to investigate the effect of the Mediterranean diet on non-alcoholic fatty liver disease and its metabolic complications.

**Search Strategy:** English-written articles in peer-reviewed journals were identified by searching PubMed from 2017 to 2024. The search strategy combined words from the following concepts: Mediterranean diet, metabolic syndrome, non-alcoholic fatty liver disease, lipid profile, and liver function. *Inclusion criteria:* Evidence level A, B publications: meta-analyses, systematic reviews, cohort and cross-sectional studies. *Exclusion criteria:* expert opinion in the form of short communications, promotional articles.

**The results** show that the Mediterranean diet has a positive effect on the lipid profile, helps in the regression of liver fibrosis and inflammation, and improves metabolic parameters such as insulin resistance. Moreover, the reported beneficial effects (antioxidant, anti-inflammatory) of Mediterranean-style diets provide high levels of phytochemicals, including dietary polyphenols.

**Conclusions.** The Mediterranean diet should be recommended for patients with nonalcoholic fatty liver disease. In case of updating the Kazakhstani clinical protocol for nonalcoholic fatty liver disease, the Mediterranean diet should be involved as a Public Health measure.

***Key words:*** *Mediterranean diet, metabolic syndrome, non-alcoholic fatty liver disease, lipid profile, liver function.*

***For citation:***

Rakhmetova V.S., Sarkulova S.M., Derbissalina G.A., Bedelbaeva G.G., Amirkhanova L.M., Smailova D.S. Mediterranean-style diet for nonalcoholic fatty liver disease. Literature review // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 267-274. *doi 10.34689/SH.2025.27.3.028*

**Резюме**

# СРЕДИЗЕМНОМОРСКАЯ ДИЕТА ПРИ НЕАЛКОГОЛЬНОЙ ЖИРОВОЙ БОЛЕЗНИ ПЕЧЕНИ. ОБЗОР ЛИТЕРАТУРЫ

**Венера С. Рахметова[1], https://orcid.org/0000-0001-5721-6409**

**Сауле М. Саркулова[1], https://orcid.org/0009-0002-1033-1685**

**Гульмира А. Дербисалина[1], https://orcid.org/0000-0003-3704-5061**

**Гульнар Г. Бедельбаева[2], https://orcid.org/0000-0002-4237-0478**

**Лиана М. Амирханова[1], https://orcid.org/0009-0005-5951-7340**

**Дарига С. Смаилова[2], http://orcid.org/0000-0002-7152-7104**

**[1] Медицинский университет Астана, г. Астана, Республика Казахстан;**
**[2] Казахский Национальный медицинский университет имени С.Д. Асфендиярова, г. Алматы, Республика Казахстан.**

**Актуальность.** Неалкогольная жировая болезнь печени (НАЖБП) - распространенное заболевание, связанное с метаболическим синдромом и характеризующееся накоплением жира в гепатоцитах. Распространенность НАЖБП среди взрослых оценивается в 25–30% в общей популяции.

**Цель данного обзора** — изучить влияние Средиземноморской диеты на течение неалкогольной жировой болезни печени и её метаболические осложнения.

**Стратегия поиска:** Статьи в рецензируемых журналах на английском языке были найдены в PubMed с 2017 по 2024 год. Стратегия поиска включала следующие ключевые слова: средиземноморская диета, метаболический синдром, неалкогольная жировая болезнь печени, липидный профиль, функция печени. *Критерии включения:* публикации уровня доказательности A, B: метаанализы, систематические обзоры, когортные и поперечные исследования. *Критерии исключения:* экспертное мнение в форме кратких сообщений, рекламных статей.

**Результаты исследования**. Результаты показывают, что средиземноморская диета оказывает положительное влияние на липидный профиль, помогает в регрессии фиброза печени и воспаления и улучшает метаболические параметры, такие как резистентность к инсулину. Более того, средиземноморские диеты обеспечивают высокий уровень фитохимических веществ, включая диетические полифенолы, которые, как сообщается, оказывают полезные эффекты, включая антиоксидантные, противовоспалительные.

**Выводы.** Средиземноморскую диету следует рекомендовать пациентам с неалкогольной жировой болезнью печени. В случае обновления казахстанского клинического протокола по неалкогольной жировой болезни печени средиземноморская диета должна быть включена в качестве меры общественного здравоохранения.

***Ключевые слова:*** *средиземноморская диета, метаболический синдром, неалкогольная жировая болезнь печени, липидный профиль, функция печени.*

***Для цитирования:***

*Рахметова В.С., Саркулова С.М., Дербисалина Г.А., Бедельбаева Г.Г., Амирханова Л.М., Смаилова Д.С.* Средиземноморская диета при неалкогольной жировой болезни печени. Обзор литературы // Наука и Здравоохранение. 2025. Vol.27 (3), С.267-274. *doi 10.34689/SH.2025.27.3.028*

**Түйіндеме**

# БАУЫРДЫҢ АЛКОГОЛЬДЫ ЕМЕС МАЙЛЫ АУРУЫ ЖЕРОРТА ТЕҢІЗДІК ДИЕТА. ӘДЕБИЕТТІК ШОЛУ

**Венера С. Рахметова[1], https://orcid.org/0000-0001-5721-6409**

**Сауле М. Саркулова[1], https://orcid.org/0009-0002-1033-1685**

**Гүлмира Ә. Дербісалина[1], https://orcid.org/0000-0003-3704-5061**

**Гульнар Г. Бедельбаева[2], https://orcid.org/0000-0002-4237-0478**

**Лиана М. Амирханова[1], https://orcid.org/0009-0005-5951-7340**

**Дарига С. Смаилова[2], http://orcid.org/0000-0002-7152-7104**

**[1] Астана медицина университеті, Астана қ., Қазақстан Республикасы**

**[2] С.Ж. Асфендияров атындағы Қазақ ұлттық медицина университеті, Алматы қ., Қазақстан Республикасы.**

**Кіріспе.** Алкогольсіз майлы бауыр ауруы (АМБА) - метаболикалық синдроммен байланысты және гепатоциттерде майдың жиналуымен сипатталатын кең таралған ауру. Ересектердегі АМБА-ның таралуы жалпы популяцияда 25% -30% құрайды.

**Бұл шолудың мақсаты -** жерорта теңізі диетасының алкогольсіз майлы бауыр ауруы және оның метаболикалық асқынуларының ағымына әсерін зерттеу болып табылады.

**Іздеу стратегиясы:**

Рецензияланған журналдардағы ағылшын тілінде жазылған мақалалар 2017-2024 жылдар аралығында PubMed дерекқорын іздеу арқылы анықталды. Іздеу стратегиясы келесі ұғымдардағы сөздерді біріктіруді қамтыды: Жерорта теңізі диетасы, метаболикалық синдром, алкогольсіз майлы бауыр ауруы, липидті профиль, бауыр функциясы. *Қосылу критерийлері:* Дәлелдер деңгейі A, B жарияланымдары: мета-талдаулар, жүйелі шолулар, когорттық және қималық зерттеулер. *Алып тастау критерийлері:* қысқаша хабарламалар, жарнамалық мақалалар түріндегі сараптамалық қорытынды.

**Нәтиже.** Жерорта теңізі диетасының липидті профильге оң әсер ететінін, бауыр фиброзының және қабынуының регрессиясына көмектесетінін және инсулинге төзімділік сияқты метаболикалық параметрлерді жақсартатынын көрсетеді. Сонымен қатар, жерорта теңізі үлгісіндегі диеталар антиоксидантты, қабынуға қарсы, пайдалы әсерлері туралы хабарланған диеталық полифенолдарды қоса, фитохимиялық заттардың жоғары деңгейін қамтамасыз етеді.

**Қорытынды.** Алкогольсіз майлы бауыр ауруы бар науқастарға Жерорта теңізі диетасы ұсынылуы керек. Алкогольсіз майлы бауыр ауруы бойынша қазақстандық клиникалық хаттаманы жаңарту жағдайында Қоғамдық денсаулық сақтау шарасы ретінде Жерорта теңізі диетасын қосу қажет.

***Түйінді сөздер:*** *Жерорта теңізі диетасы, метаболикалық синдром, алкогольсіз май бауыр ауруы, липидті профиль, бауыр қызметі.*

***Дәйексөз үшін:***

*Рахметова В.С., Саркулова С.М., Дербисалина Г.Ә., Бедельбаева Г.Г., Амирханова Л.М., Смаилова Д.С.* Бауырдың алкогольды емес майлы ауруы жерорта теңіздік диета. Әдебиеттік шолу // Ғылым және Денсаулық сақтау. 2025. Vol.27 (3), Б. 267-274. *doi 10.34689/SH.2025.27.3.028*

**Introduction**

Nonalcoholic fatty liver disease (NAFLD) is characterized by triacylglyceride accumulation in hepatocytes [32], it encompasses different abnormalities, ranging from a simple increase in intrahepatic lipid content (steatosis, nonalcoholic fatty liver, NAFL) to nonalcoholic steatohepatitis (NASH) with various degrees of necrotic inflammation, fibrosis, and ultimately, cirrhosis [29].

Males are more likely than females to have NAFLD, with an estimated 47 cases per 1,000 people worldwide [57]. Metabolic liver damage affects approximately 25% of the world population [24], among whom the proportion of liver disease caused by NAFLD was 45.8% [22]. Insulin resistance is a recognized mechanism that leads to fatty liver disease development [50]. Impairment of glucose and lipid metabolic pathways is most likely behind the increase in people with NAFLD [55], mainly due to obesity and diabetes [44].

Histopathological analysis remains the 'gold standard' to diagnose liver injury. However, invasiveness, risk, and cost are issues [3]. Moreover, NAFLD brings a heavy economic burden, increasing demand for liver transplantation in patients with liver cirrhosis and end-stage liver disease [69]. Severe liver fibrosis requires aggressive clinical management and efforts to reduce underlying obesity. For instance, it is centered on lifestyle, medications, surgical or endoscopic interventions, and metabolic derangements like prediabetes, type 2 diabetes, hypertension, hyperlipidemia, and others [9].

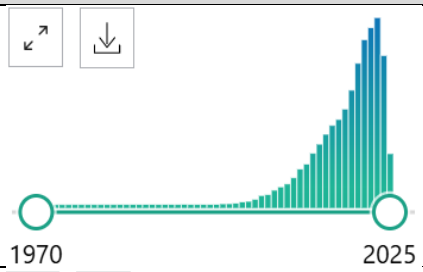
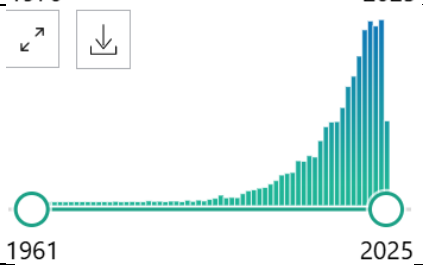
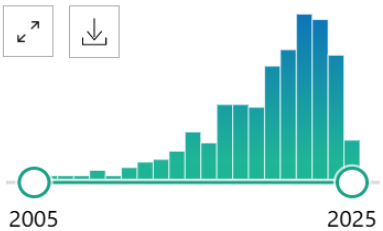
The most plausible factors contributing to NAFLD are genetic, epigenetic, and environmental [65]. Age, gender, ethnicity, and duration of fatty liver disease are epigenetic factors. Dietary habits, physical activity, and socioeconomic factors are environmental factors [12] that influence the development of metabolic syndrome [25]. Nowadays, the Mediterranean diet is recommended by researchers, which has been proven to affect the regression of inflammation and liver fibrosis [61] [14] due to the anti-inflammatory effects of the foods [54]. Despite short-term observation periods in studies, the Mediterranean diet shows potential to improve hepatic function and metabolic disorders in patients with NAFLD. Caloric restriction plays a pivotal role in weight loss and liver fat reduction, and the traditional reduced-calorie diet has a comparable effect to the Mediterranean diet [20].

**Objective.** This review aimed to investigate the effect of the Mediterranean diet on non-alcoholic fatty liver disease and its metabolic complications.

**Search Strategy.** English-written articles were identified by searching PubMed from 2017 to 2024 (Table 1). The search strategy combined words from the following concepts: Mediterranean diet, metabolic syndrome, non-alcoholic fatty liver disease, lipid profile, liver function.

*Table 1.*

**Search way in PubMed (included 60 articles).**

| Kew words | Publication date 2017-2025 | Text availability – free full-text | Publications related to the given keywords by years |
|---|---|---|---|
| Nonalcoholic fatty liver disease | 32,954 results | 20,812 results |   |
| Mediterranean diet | 8,466 results | 5,952 results |   |
| Nonalcoholic fatty liver disease and Mediterranean diet | 303 results | 223 results |   |

*Inclusion criteria:* Evidence level A, B publications: meta-analyses, systematic reviews, cohort and cross-sectional studies.

*Exclusion criteria:* expert opinion in the form of short communications, promotional articles.

**Research Results.**

**Public Health Policy for NAFLD and the Mediterranean diet**

With the increasing prevalence of obesity and type 2 diabetes mellitus and an aging population, the prevalence of NAFLD is increasing worldwide [64]. That is why NAFLD is becoming a growing challenge for public health [47].

Moreover, it is currently the fastest-growing indication for liver transplantation [10]. NAFLD causes ongoing medical expenses, financial losses, and a decline in the quality of life [48]. High-quality diets, physical activity, and socioeconomic status were associated with a lower risk of NAFLD [63].

NAFLD has received little attention from the global public health community. There is only a nascent global public health movement addressing NAFLD [30]. According to the global NAFLD policy review and preparedness index for 102 countries (Fig.1), no country has a national or sub-national strategy for NAFLD, about a third of countries (n = 32/102) are ready to address this silent public health challenge (preparedness index), only 32 countries had national NAFLD clinical guidelines; A comprehensive NAFLD public health response is lacking in all 102 countries [31].

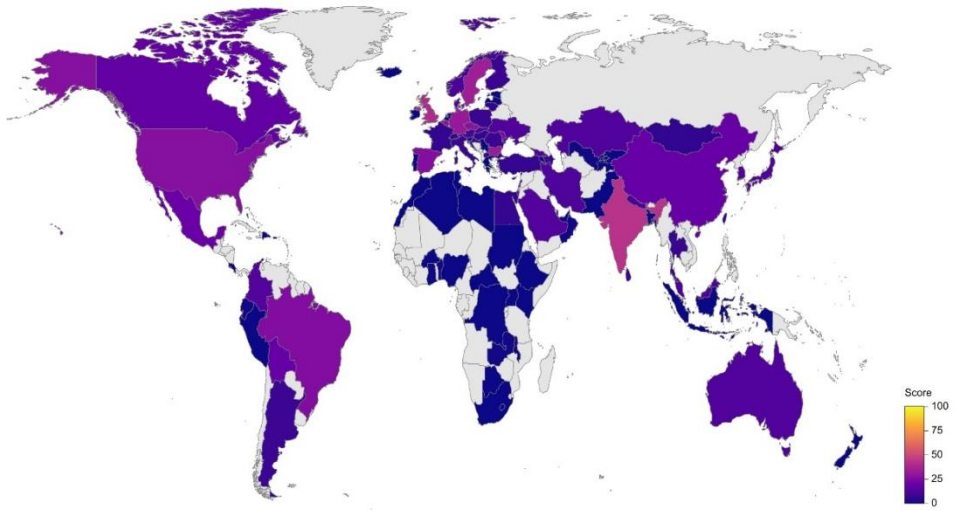



**Figure 1. NAFLD preparedness index scores for 102 countries** [31]**.**

In Table 2 current situation of NAFLD in Kazakhstan is shown for further steps in making decisions in the Public Health field.

It is important to follow strategies to improve adherence:

1. Web-based approach – a comprehensive, structured web-based program leads to increasing awareness.

2. Awareness – Mass media information is known to be associated with greater adoption of the Mediterranean lifestyle.

3. Public Health Policy – Environmental risk factors are modifiable; implementing public health policies can tackle a sedentary lifestyle and bad eating habits from early childhood [23].

**Mediterranean diet**

Since Ancel Keys established the Mediterranean diet in the 1960s [28], numerous epidemiological studies have examined the relationship between the Mediterranean diet and health [53]. Over the last few decades, MedStyle has been promoted worldwide as the healthiest dietary [37], adhering to the so-called food pyramid [43] with the following daily dietary intake: vegetables: 3–9 servings, fruits: 0.5–2 servings, cereals: 1–13 servings, olive oil: up to 8 servings [8]. Vegetables and fruits contain many nutrients, including vitamins A, C, K, E, B6, folic acid, copper, magnesium, iron, thiamine, niacin, and choline [70]. The low consumption of red meat and sweets and moderate consumption of wine at meals are included in the Mediterranean diet [7]. That is why the Mediterranean diet can be considered an easy-to-implement and safe lifestyle intervention to promote proper sleep hygiene [52].

The Med Diet 4.0 framework was developed between 2014 and 2015, assessed by following potential indicators of the sustainability of the Mediterranean diet: A. Nutrition and health, B. Environment, C. Economy, D. Society and culture [18].

*Table 2.*

**Public Health Policy for NAFLD in Kazakhstan.**

| Public Health Issues | Current situation |
|---|---|
| National or sub-national strategy for NAFLD in Kazakhstan | No |
| Disease management program for NAFLD in Kazakhstan | No |
| Clinical Guideline for NAFLD | Yes (2015) should be updated as soon as possible |
| Does Mediterranean diet recommend in Clinical Guideline for NAFLD | No |
| Screening program | No |

**Mediterranean diet for NAFLD.** According to a systematic review, the Mediterranean diet reduced liver stiffness and significantly reduced total cholesterol [1] [26]. However, the Mediterranean diet may reduce indirect and direct outcomes related to the severity of NAFLD, like liver fibrosis, total cholesterol, and body mass index [15].

In a prospective randomized study conducted in Spain among 155 patients aged 40-60 years with a BMI between 27-40 kg/m2, the effect of personalized nutrition based on the Mediterranean diet for 6-12 months was evaluated. The subjects were divided into 3 control groups in a 1:1:1 ratio: using a traditional diet with reduced calories, a Mediterranean diet, and a Mediterranean diet with physical activity. In all three intervention groups, after 6 months, some improvements were registered: BMI decreased, ALT, insulin levels, Hb1Ac, diastolic blood pressure and HDL cholesterol levels [45]. The reduced total caloric intake leads to the reduction of transaminase levels and insulin resistance in patients with obesity and fatty liver disease, regardless of the composition of the diet (low-carbohydrate, lean or balanced) [40].

In a randomized controlled trial registered in Australia-New Zealand involving 42 participants who were divided into 2 groups: using a traditional hypocaloric diet and a Mediterranean diet. As a result of the study, the group using the traditional hypocaloric diet showed a significant decrease in liver enzymes compared to the control group that used the Mediterranean diet [4] [35]. The weight reduction in the first group almost reached 5% (from 89.8 ± 24.5 kg to 85.8 ± 18.14 kg); whereas the group using the Mediterranean diet added 1.6 kg (from 87.7 ± 21.1 to 89.3 ± 22.8). The amount of visceral fat was significantly reduced in both groups [41]. The results of this randomized clinical trial showed that the Mediterranean diet had no significant effect on hepatic steatosis and did not outperform a traditional hypocaloric diet in an Australian cohort of patients with NAFLD [21].

A study conducted in Spain 2019 evaluated the effects of two personalised calorie-restricted dietary strategies differing in several dietary factors (macronutrients, fibre, meal frequency, total antioxidant capacity and adherence to the Mediterranean diet) on liver health and biochemical markers in patients with NAFLD after a 6-month follow-up. Both groups achieved comparable outcomes on the assessed measures, including weight loss as well as reductions in liver fat and liver volume. There were no significant differences in changes between the intervention groups [31].

Higher adherence to the Mediterranean diet correlated with a lower prevalence of hepatic steatosis. This suggests that adhering to the Mediterranean diet may reduce the risk of fatty liver disease [27].

According to the American and European associations for the study of the liver, Diet, weight loss, and physical activity are the cornerstone of every treatment for NAFLD [46]. A healthy diet and regular exercise could help people lose weight and control the progression of NAFLD [8]. Mediterranean diet can reduce liver fat even without weight loss and is the most recommended dietary pattern for NAFLD [49]. In recent years, a growing body of evidence has supported the idea that the Mediterranean diet could be a nutritional profile for the prevention and treatment of NAFLD patients [5].

In Table 3, we tried to highlight the main Health Benefits Mediterranean diet for patients with Nonalcoholic fatty liver disease based on studies.

*Table 3.*

**Benefits of the Mediterranean diet for patients with Nonalcoholic fatty liver disease based on studies.**

| Health Benefits | Study design of research/Sample Size | Evidence-based information |
|---|---|---|
| Weight loss | 88 Chinese females with NAFLD | Mild weight loss caused by a Mediterranean-style diet modified for Asians has numerous health benefits in females with NAFLD. Supplementing with pentadecanoic acid (C15:0) decreases LDL cholesterol and may promote positive alterations in the gut microbiota [17]. |
| Reducing total cholesterol | Ten randomized controlled trials | The review of RCTs confirmed the great potential of the Mediterranean diet on NAFLD severity due to a significant reduction in total cholesterol and liver stiffness [12]. |
| Antioxidant effect | Review | Numerous studies have shown that polyphenols are the most abundant antioxidants in the Mediterranean diet [42]. |
| Anti-inflammatory effect | Review | The increased intake of vegetables, whole grains, legumes, fish, fruits, and olive oil is included in the Mediterranean diet and the Dietary Approaches to Stop Hypertension (DASH) diet, which have anti-inflammatory effects [2]. |

The Mediterranean diet is a good choice for NAFLD treatment. Still, the evidence behind this recommendation is very low because lots of differences exist in the inclusion/exclusion criteria for a few patients [60] with comorbid conditions. NAFLD is associated with several comorbidities, which is still under investigation [33]. For instance, a growing number of studies indicate that NAFLD is strongly associated with an increased risk of major CVD events and other cardiac complications [56]. NAFLD increases the risk of incident chronic kidney disease [34], colon cancer, and precancerous lesions as well [67].

In Table 4, we demonstrated the efficiency of various types of diet for NAFLD.

*Table 4*

**Efficiency of varies types of diet for NAFLD.**

| Diet types | Food list | Recommend Yes/No |
|---|---|---|
| 1 | 2 | 3 |
| Mediterranean diet | The Mediterranean diet is characterized by a high percentage of fruits, vegetables, legumes, grains, white meat, and fish, with olive oil serving as the primary source of fat. At least 35% of the calories in this diet come from fats, 15% from proteins, and no more than 50% from carbohydrates [59]. | Yes<br>The Mediterranean diet is a safe and effective method for treating overweight, visceral obesity, and serum transaminase in patients with NAFLD, therefore establishing that it should be the first step in a treatment program for patient with NAFLD [13]. |
| Western diet | This diet includes an abundance of refined and processed meals, red meat, processed meat, sugary drinks, snacks, cakes, biscuits, eggs, and butter. It includes excessive calorie consumption, saturated fats, animal protein, sugar, cholesterol, and salt[11]. | No The Western diet is associated with weight gain, obesity, and, more recently, NAFLD [39]. Importantly, NAFLD-related liver failure is one of the major causes of liver transplantation in the Western world [6]. |

*Continuation of Table 4.*

| 1 | 2 | 3 |
|---|---|---|
| Vegan diet | Plant-based foods like fruit, vegetables, grains, legumes/beans, nuts, and seeds [36]. | There is no evidence on the possible benefit of vegan diets in NAFLD and/or nonalcoholic steatohepatitis (NASH) [16]. |
| Ketogenic diet | The ketogenic diet is based on a relatively low intake of dietary carbs, with varied proportions of protein and fat. The standard ketogenic diet consists of one gram of protein per kilogram of body weight, 10-15 grams of carbohydrates per day, with the remainder of calories coming from fat. The purpose of the diet is to cause ketosis [38].<br>The findings imply that ketosis may exert positive benefits independent of dietary content, and so necessitate studies aimed at determining the particular function played by ketone bodies in NAFLD pathogenesis, perhaps paving the way for new treatment targets and techniques [66]. | There is a shortage of well-designed studies in this area, so investigating this scientific topic should be a priority of research in the next few years. [19]. |
| DASH diet | Grains, low-fat dairy products, yogurt, olive oil, and chocolate [58] | Adherence to the DASH diet may be effective in managing the NAFLD [51].<br>It is proven that the DASH diet has a lower association with non-alcoholic fatty liver disease in middle-aged and elderly adults [68] |
| Low-fat diet | A general rule is that if a food provides 100 calories and 3 grams or less of fat, it is a low-fat food. Common examples include vegetables, fruits, whole grain cereals, egg whites, chicken and turkey breast without skin, beans, lentils, peas, seafood, and low-fat dairy, among others [12]. | All calorie-restricted dietary therapies are effective in lowering weight, liver fat content, and liver enzymes in people with NAFLD. Low-fat diets appear to be particularly effective in lowering transaminase levels. Additional research is required to investigate diet intensity, duration, and long-term outcomes [62]. |

**Conclusion**.

The Mediterranean diet should be recommended for patients with nonalcoholic fatty liver disease. In case of updating the Kazakhstani clinical protocol for nonalcoholic fatty liver disease, the Mediterranean diet should be involved as a Public Health measure.

***Funding Statement:*** *This research received no external funding.*

***Conflict of interest:*** *The authors declare no conflict of interest.*

***Authors' contributions:***

*Venera S. Rakhmetova -Guiding the process of writing a manuscript, quality assessment;*

*Saule M. Sarkulova - Searching articles, quality assessment;*

*Gulmira A. Derbissalina - Editing the manuscript;*

*Gulnar G. Bedelbaeva -Contributions to conceptualisation and methodology;*

*Liana M. Amirkhanova - Searching articles;*

*Dariga S. Smailova – Editing the manuscript, final corrections.*

*The final manuscript was approved by all the authors.*

***Literatura:***

1. *Abbate M. et al.* Energy Expenditure Improved Risk Factors Associated with Renal Function Loss in NAFLD and MetS Patients. Nutrients. 2021. № 2 (13). P. 1–24.

2. *Abdallah J. et al.* Effects of anti-inflammatory dietary patterns on non-alcoholic fatty liver disease: a systematic literature review. European Journal of Nutrition. 2023. № 4 (62). P. 1563.

3. *Abdelmalek M.F.* Nonalcoholic fatty liver disease: another leap forward. Nature Reviews. Gastroenterology & Hepatology. 2021. № 2 (18). P. 85.

4. *Abenavoli L. et al.* Effect of Mediterranean Diet and Antioxidant Formulation in Non-Alcoholic Fatty Liver Disease: A Randomized Study. Nutrients. 2017. № 8 (9). P.870.

5. *Abenavoli L. et al.* Health benefits of Mediterranean diet in nonalcoholic fatty liver disease. Expert review of gastroenterology & hepatology. 2018. № 9 (12). P. 873–881.

6. *Adam R., Karam V. et al.* Annual Report of the European Liver Transplant Registry (ELTR)—50-Year Evolution of Liver Transplantation. Transpl. Int. 2018. №31. P.1293–1317.

7. *Andreo-López M.C., Contreras-Bolívar V., et al.* Influence of the Mediterranean Diet on Healthy Aging. Int J Mol Sci. 2023. №24(5). P.4491.

8. *Barber T.M. et al.* The Effects of the Mediterranean Diet on Health and Gut Microbiota. Nutrients. 2023. № 9 (15). P. 2150.

9. *Basu R. et al.* Nonalcoholic Fatty Liver Disease: Review of Management for Primary Care Providers. Mayo Clinic Proceedings. 2022. № 9 (97). P. 1700–1716.

10. *Battistella S., D'Arcangelo F. et al.* Liver transplantation for non-alcoholic fatty liver disease: indications and post-transplant management. Clin Mol Hepatol. 2023. №29.P.S286-S301.

11. *Berná G. et al. T*he role of nutrition in non-alcoholic fatty liver disease: Pathophysiology and management. Liver International. 2020. № S1 (40). P. 102–108.

12. *Bhandari P., Sapra A.* Low Fat Diet. BMJ. 2023. № 7289 (322). P. 804.

13. *Biolato M. et al.* Intestinal permeability after Mediterranean diet and low-fat diet in non-alcoholic fatty liver disease. World Journal of Gastroenterology. 2019. № 4 (25). P. 509.

14. *Bo' C. Del et al.* Overview of Human Intervention Studies Evaluating the Impact of the Mediterranean Diet on Markers of DNA Damage. Nutrients. 2019. № 2 (11).P.391.

15. *Bo' C. Del et al.* Does the Mediterranean Diet Have Any Effect on Lipid Profile, Central Obesity and Liver Enzymes in Non-Alcoholic Fatty Liver Disease (NAFLD) Subjects? A Systematic Review and Meta-Analysis of Randomized Control Trials. Nutrients 2023, Vol. 15, Page 2250. 2023. № 10 (15). P. 2250.

16. *Chiarioni G. et al.* Vegan Diet Advice Might Benefit Liver Enzymes in Nonalcoholic Fatty Liver Disease: an Open Observational Pilot Study. Journal of Gastrointestinal and Liver Diseases. 2021. № 1 (30). P. 81–87.

17. *Chooi Y.C. et al*. Effect of an Asian-adapted Mediterranean diet and pentadecanoic acid on fatty liver disease: the TANGO randomized controlled trial. The American journal of clinical nutrition. 2024. № 3 (119). P. 788–799.

*18. Dernini S. et a*l. Med Diet 4.0: the Mediterranean diet with four sustainable benefits. Public Health Nutrition. 2016. № 7 (20). P. 1322.

19. *Dyńka D. et al.* Beneficial Effects of the Ketogenic Diet on Nonalcoholic Fatty Liver Disease (NAFLD/MAFLD). Journal of Clinical Medicine. 2024. № 16 (13). P. 4857.

20. *Eslamparast T., Tandon P., Raman M.* Dietary Composition Independent of Weight Loss in the Management of Non-Alcoholic Fatty Liver Disease. Nutrients. 2017. № 8 (9).P.800.

21. *George E.S. et al.* Impact of a Mediterranean diet on hepatic and metabolic outcomes in non-alcoholic fatty liver disease: The MEDINA randomised controlled trial. Liver international : official journal of the International Association for the Study of the Liver. 2022. № 6 (42). P. 1308–1322.

22. *Golabi P. et al.* Causes of death in patients with Non-alcoholic Fatty Liver Disease (NAFLD), alcoholic liver disease and chronic viral Hepatitis B and C. Annals of hepatology. 2022. № 1 (27).P.100556.

23. *Hadefi A., Arvanitakis M., Trépo E., Zelber-Sagi S.* Dietary strategies in non-alcoholic fatty liver disease patients: From evidence to daily clinical practice, a systematic review. United European Gastroenterol J. 2023 №11(7). P.663-689.

24. *He Q.J. et al.* Recent advances in age-related metabolic dysfunction-associated steatotic liver disease. World Journal of Gastroenterology. 2024. № 7 (30). P. 652.

25. *Iqbal U. et al.* The Epidemiology, Risk Profiling and Diagnostic Challenges of Nonalcoholic Fatty Liver Disease. Medicines (Basel, Switzerland). 2019. № 1 (6). P. 41.

26. *Katsagoni C.N. et al.* Improvements in clinical characteristics of patients with non-alcoholic fatty liver disease, after an intervention based on the Mediterranean lifestyle: a randomised controlled clinical trial. The British journal of nutrition. 2018. № 2 (120). P. 164–175.

27. *Khalatbari-Soltani S. et al.* The association between adherence to the Mediterranean diet and hepatic steatosis: cross-sectional analysis of two independent studies, the UK Fenland Study and the Swiss CoLaus Study. BMC medicine. 2019. № 1 (17).P.19.

28. *Kiani A.K. et al.* Modern vision of the Mediterranean diet. Journal of Preventive Medicine and Hygiene. 2022. № 2 Suppl 3 (63). P. E36.

29. *Kim H.Y.* Recent advances in nonalcoholic fatty liver disease metabolomics. Clinical and Molecular Hepatology. 2021. № 4 (27). P. 553.

30. *Lazarus J.V. et al.* Advancing the global public health agenda for NAFLD: a consensus statement. Nature Reviews Gastroenterology and Hepatology. 2022. № 1 (19). P. 60–78.

31. *Lazarus J.V. et al.* The global NAFLD policy review and preparedness index: Are countries ready to address this silent public health challenge? Journal of Hepatology. 2022. № 4 (76). P. 771–780.

32. *Loomba R. et al.* Expert Panel Review to Compare FDA and EMA Guidance on Drug Development and Endpoints in Nonalcoholic Steatohepatitis. Gastroenterology. 2021. № 3 (162). P. 680.

33. *Manikat R., Nguyen M.H.* Nonalcoholic fatty liver disease and non-liver comorbidities. Clinical and Molecular Hepatology. 2023. № Suppl (29). P. s86.

34. *Mantovani A. et al.* Nonalcoholic fatty liver disease increases risk of incident chronic kidney disease: A systematic review and meta-analysis. Metabolism: Clinical and Experimental. 2018. (79).P. 64–76.

35. *Marin-Alejandre B.A. et al.* The Metabolic and Hepatic Impact of Two Personalized Dietary Strategies in Subjects with Obesity and Nonalcoholic Fatty Liver Disease: The Fatty Liver in Obesity (FLiO) Randomized Controlled Trial. Nutrients. 2019. № 10 (11).

36. *Marrone G. et al.* Vegan Diet Health Benefits in Metabolic Syndrome. Nutrients. 2021. № 3 (13). C. 1–24.

37. *Mazza E., Ferro Y., et al.* Mediterranean Diet In Healthy Aging. J Nutr Health Aging. 2021. №25(9). C.1076-1083.

38. *McGaugh E., Barthel B.* A Review of Ketogenic Diet and Lifestyle. Missouri Medicine. 2022. № 1 (119). C. 84.

39. *Mirizzi A. et al.* Effects of Some Food Components on Non-Alcoholic Fatty Liver Disease Severity: Results from a Cross-Sectional Study. Nutrients. 2019. № 11 (11).P.2744

40. *Montemayor S. et al.* Effect of Dietary and Lifestyle Interventions on the Amelioration of NAFLD in Patients with Metabolic Syndrome: The FLIPAN Study. Nutrients. 2022. № 11 (14). P.2223

41.*Montemayor S., García S., et al.* Dietary Patterns, Foods, and Nutrients to Ameliorate Non-Alcoholic Fatty Liver Disease: A Scoping Review. Nutrients. 2023. №15(18). P. 3987.

42. *Nani A. et al.* Antioxidant and Anti-Inflammatory Potential of Polyphenols Contained in Mediterranean Diet in Obesity: Molecular Mechanisms. Molecules. 2021. № 4 (26). P. 985.

43. *Naureen Z. et al.* Foods of the Mediterranean diet: lacto-fermented food, the food pyramid and food combinations. Journal of Preventive Medicine and Hygiene. 2022. № 2 Suppl 3 (63). P. E28.

44. *Pafili K., Roden M.* Nonalcoholic fatty liver disease (NAFLD) from pathogenesis to treatment concepts in humans. Molecular Metabolism. 2020. (50). P. 101122.

45. *Pani A. et al.* Inositol and Non-Alcoholic Fatty Liver Disease: A Systematic Review on Deficiencies and Supplementation // Nutrients. 2020. № 11 (12). P. 1–13.

46. *Paternostro R., Trauner M.* Current treatment of non-alcoholic fatty liver disease. Journal of internal medicine. 2022. № 2 (292). P. 190–204.

47. *Pouwels S., Sakran N., et al.* Non-alcoholic fatty

liver disease (NAFLD): a review of pathophysiology, clinical management and effects of weight loss. BMC Endocr Disord. 2022. 22(1). P.63.

48. *Properzi C. et al.* Ad Libitum Mediterranean and Low-Fat Diets Both Significantly Reduce Hepatic Steatosis: A Randomized Controlled Trial. Hepatology (Baltimore, Md.). 2018. № 5 (68). P. 1741–1754.

49. *Romero-Gómez M., Zelber-Sagi S., Trenell M.* Treatment of NAFLD with diet, physical activity and exercise. Journal of Hepatology. 2017. № 4 (67). P. 829–846.

50. *Rong L. et al.* Advancements in the treatment of non-alcoholic fatty liver disease (NAFLD). Frontiers in Endocrinology. 2023. (13). P. 1087260.

51. *Sangouni A.A. et al.* Dietary approaches to stop hypertension (DASH) diet improves hepatic fibrosis, steatosis and liver enzymes in patients with non-alcoholic fatty liver disease: a randomized controlled trial. European journal of nutrition. 2024. № 1 (63). P. 95–105.

52. *Scoditti E., Tumolo M.R., Garbarino S.* Mediterranean Diet on Sleep: A Health Alliance. Nutrients. 2022. 14(14). P. 2998.

53. *Serra-Majem L. et al.* Benefits of the Mediterranean diet: Epidemiological and molecular aspects. Molecular Aspects of Medicine. 2019. (67). P. 1–55.

54. *Sotos-Prieto M. et al.* Association between the Mediterranean lifestyle, metabolic syndrome and mortality: a whole-country cohort in Spain. Cardiovascular Diabetology. 2021. № 1 (20). P. 5.

55. *Stefan N., et al.* global view of the interplay between non-alcoholic fatty liver disease and diabetes. The Lancet Diabetes and Endocrinology. 2022. № 4 (10). P. 284–296.

56. *Targher G., Byrne C.D., Tilg H.* NAFLD and increased risk of cardiovascular disease: Clinical associations, pathophysiological mechanisms and pharmacological implications. Gut. 2020. № 9 (69). P. 1691–1705.

57. T*eng M.L.P. et al.* Global incidence and prevalence of nonalcoholic fatty liver disease. Clinical and Molecular Hepatology. 2022. № Suppl (29). P. S32.

58. *Toi P.L. et al*. Preventive Role of Diet Interventions and Dietary Factors in Type 2 Diabetes Mellitus: An Umbrella Review. Nutrients. 2020. № 9 (12). P. 2722.

59. *Torres-Peña J.D. et al.* Different Dietary Approaches, Non-Alcoholic Fatty Liver Disease and Cardiovascular Disease: A Literature Review. Nutrients. 2023. № 6 (15).P.1483.

60. *Torres M.C.P. et al.* Mediterranean Diet and NAFLD: What We Know and Questions That Still Need to Be Answered. Nutrients. 2019. № 12 (11). P. 2971.

61. *Tsigalou C. et al.* Mediterranean Diet as a Tool to Combat Inflammation and Chronic Diseases. An Overview. Biomedicines. 2020. № 7 (8).P.201.

62. *Varkaneh H.K. et al.* Low fat diet versus low carbohydrate diet for management of non-alcohol fatty liver disease: A systematic review. Frontiers in Nutrition. 2022. (9).P. 987921.

63. *Vilar-Gomez E., Nephew L.D., Vuppalanchi R., Gawrieh S., et al.* High-quality diet, physical activity, and college education are associated with low risk of NAFLD among the US population. Hepatology. 2022. №75(6). P.1491-1506.

64. *Younossi Z.M.* Non-alcoholic fatty liver disease - A global public health perspective. J Hepatol. 2019. №70(3). P.531-544.

65. *Wajsbrot N.B. et al.* Non-alcoholic fatty liver disease and the impact of genetic, epigenetic and environmental factors in the offspring. World Journal of Gastroenterology. 2022. № 25 (28). P. 2890.

66. *Watanabe M. et al.* Beneficial effects of the ketogenic diet on nonalcoholic fatty liver disease: A comprehensive review of the literature. Obesity Reviews. 2020. № 8 (21).P.e13024

67. *Wong V.W.S. et al.* High prevalence of colorectal neoplasm in patients with non-alcoholic steatohepatitis. Gut. 2011. № 6 (60). P. 829–836.

68. *Xiao M.L. et al.* Adherence to the Dietary Approaches to Stop Hypertension (DASH) diet is associated with lower presence of non-alcoholic fatty liver disease in middle-aged and elderly adults. Public health nutrition. 2020. № 4 (23). P. 674–682.

69. *Zeng C., Chen M.* Progress in Nonalcoholic Fatty Liver Disease: SIRT Family Regulates Mitochondrial Biogenesis. Biomolecules. 2022. № 8 (12).P. 1079.

70. *Zielińska M. et al.* The Mediterranean Diet and the Western Diet in Adolescent Depression-Current Reports. Nutrients. 2022. № 20 (14). P. 4390.

**Information about the authors:**

**Venera S. Rakhmetova** – professor, Astana Medical University, Department of Internal Medicine, Kazakhstan phone: +7 701 185 5557, e-mail: venerarakhmetova@gmail.com, https://orcid.org/0000-0001-5721-6409

**Saule M. Sarkulova** – professor, Astana Medical University, Department of Internal Medicine, Kazakhstan, phone:87079333993, e-mail: saule_sark@mail.ru, https://orcid.org/0009-0002-1033-1685

**Gulmira A. Derbissalina** – associate professor, head, Astana Medical University, Department of General Medical Practice with a course in evidence-based medicine, Kazakhstan, phone: +77013469331, e-mail: derbissalina.g@amu.kz https://orcid.org/0000-0003-3704-5061

**Gulnar G. Bedelbaeva -** professor, head, Asfendiyarov Kazakh National Medical University, Department of Therapeutic Disciplines at the Institute of Continuing Education, Kazakhstan, phone:+7-777-228-1581, e-mail: bedelbaeva@mail.ru, https://orcid.org/0009-0002-1033-1685

**Liana M. Amirkhanova** - Resident gastroenterologist-hepatologist, Astana Medical University, Kazakhstan, phone: 87015552558, e-mail: miirbolovna@gmail.com, https://orcid.org/0009-0005-5951-7340

**Corresponding author:**

**Dariga S. Smailova** – PhD, associate professor, Asfendiyarov Kazakh National Medical University, Kazakhstan

**Mailing Address:** Kazakhstan, Almaty city, Tole bi str.94

**E-mail:** dari190490@gmail.com

**Tel.:** 8 705 555 84 68

Received: 10 March 2025 / Accepted: 16 June 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2025.27.3.029***

***UDC 616-002.5***

This work is licensed under a Creative Commons Attribution 4.0 International License

**Abstract**

# EXTRAPULMONARY TUBERCULOSIS IN A KAZAKH PATIENT WITH MIXED CONNECTIVE TISSUE DISEASE. CLINICAL CASE

**Maiya V. Goremykina*[1], https://orcid.org/0000-0002-5433-7771**

**Sandro Vento[2,3], https://orcid.org/0000-0003-0084-4062**

**[1] NCJSC «Semey Medical University», Semey, Republic of Kazakhstan;**
**[2] University of Puthisastra, Phnom Penh, Cambodia;**
**[3] Manash Kozybayev North Kazakhstan University, Petropavlovsk, Republic of Kazakhstan.**

Patients with systemic autoimmune diseases have increased susceptibility to infections, including tuberculosis, partly due to immunosuppressive treatment. We describe a case of extrapulmonary tuberculosis (tuberculous osteomyelitis of the right foot) occurring a few months after a diagnosis and apparently successful treatment of abdominal TB in a Kazakh patient with mixed connective tissue disease. Abdominal tuberculosis had occurred while the patient was on high doses of corticosteroids, whereas bone tuberculosis was diagnosed when glucocorticoid doses had been reduced. The diagnosis of tuberculous osteomyelitis was unfortunately made months after the disease manifested. Screening for latent tuberculosis should be mandatory before starting immunosuppressive treatment in patients with autoimmune diseases, especially in countries with a considerable tuberculosis burden, and tuberculosis should be high in the list of possible etiologies of multiple clinical manifestations in these patients.

***Key words:*** *Mycobacterium tuberculosis; Septic arthritis; Mixed connective tissue disease; Osteoarticular tuberculosis; Abdominal tuberculosis; Extrapulmonary tuberculosis.*

***For citation:***

*Goremykina M.V., Vento S.* Extrapulmonary tuberculosis in a kazakh patient with mixed connective tissue disease. Clinical case // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 275-279. *doi 10.34689/SH.2025.27.3.029*

**Резюме**

# ВНЕЛЕГОЧНЫЙ ТУБЕРКУЛЕЗ У КАЗАХСКОГО ПАЦИЕНТА СО СМЕШАННЫМ ЗАБОЛЕВАНИЕМ СОЕДИНИТЕЛЬНОЙ ТКАНИ. КЛИНИЧЕСКИЙ СЛУЧАЙ.

**Майя В. Горемыкина*[1], https://orcid.org/0000-0002-5433-7771**

**Сандро Венто[2,3], https://orcid.org/0000-0003-0084-4062**

**[1] НАО «Медицинский университет Семей», г. Семей, Республика Казахстан;**
**[2] Университет Путхисастра, г. Пномпень, Камбоджа;**
**[3]. Северо-Казахстанский университет имени Манаша Козыбаева, г. Петропавловск, Республика Казахстан.**

Пациенты с системными аутоиммунными заболеваниями имеют повышенную восприимчивость к инфекциям, включая туберкулез, отчасти из-за иммуносупрессивной терапии. Мы описываем случай внелегочного туберкулеза (туберкулезный остеомиелит правой стопы), возникший через несколько месяцев после постановки диагноза и, по-видимому, успешного лечения абдоминального туберкулеза у казахского пациента со смешанным заболеванием соединительной ткани. Абдоминальный туберкулез возник, когда пациент принимал высокие дозы кортикостероидов, тогда как костный туберкулез был диагностирован, когда дозы глюкокортикоидов были снижены. К сожалению, диагноз туберкулезного остеомиелита был поставлен через несколько месяцев после манифестации заболевания. Скрининг на латентный туберкулез должен быть обязательным перед началом иммуносупрессивной терапии у пациентов с аутоиммунными заболеваниями, особенно в странах со значительным бременем туберкулеза, и туберкулез должен быть одним из первых в списке возможных этиологий множественных клинических проявлений у этих пациентов.

***Ключевые слова:*** *Микобактерии туберкулеза; Септический артрит; Смешанное заболевание соединительной ткани; Костно-суставной туберкулез; Абдоминальный туберкулез; Внелегочный туберкулез.*

***Для цитирования:***

*Горемыкина М.В., Венто С.* Внелегочный туберкулез у казахского пациента со смешанным заболеванием соединительной ткани. Клинический случай // Наука и Здравоохранение. 2025. Т.27 (3), С. 275-279. doi: 10.34689/SH.2025.27.3.029

**Түйіндеме**

# АРАЛАС ДӘНЕКЕР ТІН АУРУЫ БАР ҚАЗАҚСТАНДЫҚ НАУҚАСТА ӨКПЕДЕН ТЫС ТУБЕРКУЛЕЗ. КЛИНИКАЛЫҚ ЖАҒДАЙ.

**Майя В. Горемыкина*[1], https://orcid.org/0000-0002-5433-7771**

**Сандро Венто[2,3], https://orcid.org/0000-0003-0084-4062**

**[1] «Семей медицина университеті» КеАҚ, Семей қ., Қазақстан Республикасы.**
**[2] Путисастра университеті, Пномпень, Камбоджа;**
**[3]. Манаш Қозыбаев атындағы Солтүстік Қазақстан университеті, Петропавл қ., Қазақстан Республикасы.**

Жүйелік аутоиммунды аурулары бар емделушілерде ішінара иммуносупрессивті емге байланысты туберкулезді қоса, жұқпалы аурулардың қаупі жоғары. Біз дәнекер тінінің аралас ауруымен ауыратын қазақстандық науқаста абдоминальды туберкулез диагнозы қойылған және сәтті емделгеннен кейін бірнеше айдан кейін пайда болған өкпеден тыс туберкулез (оң аяқтың туберкулездік остеомиелиті) жағдайын сипаттаймыз. Құрсақ қуысының туберкулезі науқас кортикостероидтардың жоғары дозаларын қабылдаған кезде дамыған, ал сүйек туберкулезі глюкокортикоидтардың дозасын азайтқанда анықталған. Өкінішке орай, туберкулезді остеомиелит диагнозы ауру басталғаннан кейін бірнеше айдан кейін қойылды. Аутоиммунды аурулары бар емделушілерде, әсіресе туберкулездің айтарлықтай ауыртпалығы бар елдерде иммуносупрессивті терапияны бастамас бұрын жасырын туберкулезге скрининг міндетті болуы керек, ал туберкулез осы науқастардағы көптеген клиникалық көріністер үшін ықтимал этиологиялар тізімінде жоғары болуы керек.

***Түйінді сөздер****: Туберкулез микобактериясы;Септикалық артрит; Аралас дәнекер тінінің ауруы; Сүйек және буын туберкулезі; Іштің туберкулезі; Өкпеден тыс туберкулез..*

***Дәйексөз үшін:***

*Горемыкина М.В., Венто С.* Аралас дәнекер тін ауруы бар қазақстандық науқаста өкпеден тыс туберкулез. Клиникалық жағдай // ғылым және Денсаулық. 2025. Т.27 (3), Б. 275-279. doi: 10.34689/SH.2025.27.3.029

**Introduction**

Susceptibility to infections in patients with systemic autoimmune diseases is increased, partly due to immunosuppressive treatment, and mixed connective tissue disease (MCTD) is no exception. One case of pulmonary and cutaneous tuberculosis (TB), and one case of pulmonary tuberculosis following steroid therapy for MCTD were reported from Japan [14] and Germany [6] respectively. Another case of pulmonary tuberculosis in a patient on immunosuppressives occurred in Senegal [7], and one case of pulmonary tuberculosis prior to the start of immunosuppressive therapy in a patient with MCTD was described from India [11]. One case of knee joint tuberculosis in a patient with a 9-year history of MCTD on long-term immunosuppressive treatment was reported from Germany [4]. Finally, a female patient in Germany who had been treated with immunosuppressive drugs for five years for mixed connective tissue disease and whose symptoms had changed (increasing joint pains and loss of weight) five years later, leading to higher doses of steroids, developed a tuberculous meningoencephalitis, and at that point *Mycobacterium tuberculosis* was detected in urine, sputum and secretions of different joints [9]. In this latter case, the misinterpretation of the change of symptoms as worsening of the MCTD ultimately led to the death of the patient [9].

We report a case of tuberculous osteomyelitis of the right foot occurring few months after a diagnosis of abdominal TB in a patient with mixed connective tissue disease in Kazakhstan, a country with a considerable TB burden and a high occurrence of multidrug-resistant tuberculosis [12].

**Case description**

A 48-year-old Kazakh female patient (who gave informed consent for publication of her clinical data) presented in mid-November 2024 at the Department of Internal Medicine and Rheumatology of Semey Medical University complaining of pain and swelling in the right ankle and foot (increasing with walking) and in the left wrist joint, and of an ulcer in the dorsal area of the right foot.

The patient had Raynaud's syndrome since 2019 and was diagnosed with mixed connective tissue disease in May 2021, after complaining of fever, weight loss, polyarthralgia, dysphagia, alopecia, xerostomia. Antinuclear antibodies were then positive (1:640), as well as anti-ribonucleoprotein (+++) and anti-SS-A/Ro52 antibodies (++). She was initially treated with hydroxychloroquine (400mg daily), mycophenolate mofetil (2g per day) and corticosteroids. The highest dose of methylprednisolone was 32 mg daily per os, while the average doses were 12–16mg per day. In May 2023, the patient was admitted to a hospital with a diagnosis of acute appendicitis and peritonitis. Appendectomy was performed; during the surgery, a large amount of fluid was noted in the abdominal cavity, and small light-yellow tubercles were seen in areas of the intestine, parietal peritoneum and omentum. Tuberculosis was suspected and subsequently confirmed histologically. Treatment started with rifampicin, pyrazinamide, isoniazid and ethambutol and continued for nine months. The patient had never had symptoms of, or had been treated for, pulmonary tuberculosis, but had fibro-focal changes at chest X-ray. Following the diagnosis of tuberculosis, methylprednisolone was reduced to 8 mg/day.

In February 2024, a marginal fracture of the base of the 5th metatarsal bone of the right foot was found and a plaster cast applied. In June the patient discontinued hydroxychloroquine and mycophenolate mofetil while methylprednisolone was further reduced to 4 mg daily. Because of the persistence of severe pain in the right ankle joint, in July of the same year a CT scan of the feet and ankle joints was performed and revealed fractures of the cuboid and talus bones of the right foot without displacement, and synovitis of the right ankle joint. In September 2024, a whitish lump and swelling at the base of the 1st toe of the right foot appeared. Two days after squeezing the swollen area, a "cheesy" content came out, and new foci with a whitish center appeared. These foci were also squeezed and the contents evacuated. After some time, an open wound of 3 cm in diameter developed on the back of the right foot, was interpreted as a trophic ulcer, and was periodically dressed.

In November 2024, in the absence of activity of mixed connective tissue disease, antibacterial therapy (ceftriaxone 2 mg/day intramuscularly for ten days, followed by azithromycin 250 mg twice daily for an additional ten days) was prescribed.

When the patient was seen for the first time at the Department of Internal Medicine and Rheumatology of Semey Medical University in January 2025, inflammatory arthritis of the left wrist joint with pain during palpation and movement was noted. The right ankle joint was severely deformed with edema, and pain was present at palpation and movement. A trophic ulcer of 3 cm in diameter with calloused edges was present in the 1st metatarsophalangeal and interdigital region on the dorsum of the right foot (Figure 1).

**Figure 1. Right foot of the patient: swelling of the ankle joint and metatarsus, fistula on the dorsum of the foot.**

Given the history of abdominal tuberculosis, a tuberculous abscess with ensuing fistula was suspected. An X-ray of the right ankle joint was done and showed destructive arthritis of the tarsal bones with predominant damage to the talonavicular and calcaneocuboid joints (Figure 2).

Gene-Xpert testing of the material from the ulcer on the right foot was positive and showed resistance to rifampicin. A diagnosis of tuberculous osteomyelitis with abscess formation was made in January 2025.

Treatment was prescribed with levofloxacin, cycloserine, bedaquiline, clofazimine and linezolid and is planned for twenty months. Methylprednisolone has been gradually reduced to 1 mg every other day. Three months after starting anti-tuberculosis treatment, the ulcer on the dorsum of the right foot healed and a fistula appeared on the medial and lateral sides of the right ankle joint (Figures 3 and 4).

**Figure 2. X-ray of the right foot (lateral projection): destructive arthritis of the tarsal bones with predominant damage to the talonavicular and calcaneocuboid joints.**

**Figure 3. Formation of new fistulas on the medial and lateral surface of the right ankle joint.**

**Figure 4. X-ray of the right and left foot (direct and lateral projections). Destructive arthritis of the tarsal bones with predominant damage to talonavicular and calcaneocuboid joints of the right foot. Osteoporosis of the right foot.**

**Discussion**

Our case reinforces the notion that patients with autoimmune diseases under immunosuppressive treatment are at risk for tuberculosis, which should always be considered in the differential diagnosis of compatible pulmonary and extrapulmonary lesions. In particular, our patient had two manifestations (abdominal and bone tuberculosis) of extrapulmonary TB (indicating the reactivation of past infection) in just 13 months, and, in spite of a recent diagnosis of abdominal TB, the subsequent fractures of bones of the right foot, synovitis of the right ankle joint, and swelling at the base of the first toe of the right foot were not suspected to be TB-related for months, and a quite large open wound on the back of the right foot was interpreted as a trophic ulcer. The delay in diagnosis of tuberculosis seems unfortunately not uncommon in patients with MCTD[6] or other systemic autoimmune diseases [5, 10]. Screening for latent tuberculosis should be mandatory clinical practice before starting immunosuppressive treatment in patients with autoimmune diseases. However, for patients already on corticosteroids, the risk of false negative results with both tuberculin skin test (TST) and interferon-gamma release assays (IGRA) increases [1]. Thus, a combination of IGRA and TST to increase sensitivity could be used in immunosuppressed patients, where these tests should be done sequentially, with the second test done only if the first test was negative [3].

An additional issue is the dosage of corticosteroids in patients with autoimmune diseases with a TB diagnosis, considering that other immunosuppressive drugs do not appear to be significantly associated with tuberculosis [2]. A systematic review and meta-analysis of tuberculosis disease and infection in patients with systemic lupus erythematosus (SLE) found that TB prevalence in SLE was quite high and associated with glucocorticoids, and lowering their dose was essential to reduce the risk [2]. The 1-year cumulative corticosteroid dose in patients with SLE contracting TB was significantly higher than in those without TB, with a mean difference of 2.56 (95% CI: 0.22-4.91) [2]. In another systematic review and meta-analysis, the incidence and of TB in SLE patients was 1.16 per 100 person-years (95% confidence interval 0.69-1.93) and the prevalence was 3.59% (95% CI: 2.57%-5.02%) [13]. The pooled prevalence of SLE-pulmonary TB and SLE-extrapulmonary was 2.46% (95% CI 1.73%-3.51%) and 1.42% (95% CI 0.98%-2.06%), respectively.[13] The incidence of SLE-TB was higher in countries with a high TB burden and the prevalence of SLE-TB was elevated in Asia and in patients taking a mean daily dose of corticosteroids ≥20 mg [13].

Hence, it is advisable to keep the dose of glucocorticoids as low as possible in patients with tuberculosis. In a study including 1,618 treatment episodes of prolonged (≥4 weeks), high-dose steroids (≥30mg/day of prednisone, approximately equivalent to ≥24mg methylprednisolone) in 1,160 patients with rheumatic diseases, a high-risk subgroup for TB was defined as patients with incomplete adherence to treatment of previous TB, positive interferon-γ release assay, and/or linear/reticular fibrotic lesions on chest radiographs [8]. To evaluate the preventive effect of isoniazid (INH), the drug was given in 152 (9.4%) treatment episodes [8]. During 1,579.8 person-years, there were 21 cases of TB, with a significantly higher TB incidence in the high-risk subgroup (incidence rate ratio 8.29). INH reduced the 1-year TB incidence in the high-risk subgroup [adjusted hazards ratio 0.37 (95% CI, 0.002-5.10)] [13]; there was an important risk of adverse drug reactions [8]. On the basis of this study, it seems that an eventual isoniazid prophylaxis should be carefully balanced in patients treated with high dose corticosteroids.

***Study Limitations:*** *The single-center nature of the study may limit its generalizability, and the absence of long-term follow-up data restricts the assessment of post-discharge outcomes.*

***Author Contributions****: All authors contributed equally to the writing of this manuscript.*

***Conflict of Interest:*** *The authors declare no conflicts of interest. This material has not been submitted to other journals and is not under consideration elsewhere.*

***Funding:*** *No funding was received for this study.*

***Literature:***

1. *Bartalesi F., Vicidomini S., Goletti D., Fiorelli C., Fiori G., Melchiorre D. et al.* QuantiFERON-TB Gold and the TST

are both useful for latent tuberculosis infection screening in autoimmune diseases. Eur Respir J. 2009. 33(3):586-93.

2. *Darmawan G., Liman L.M.S., Wibowo S.A.K., Hamijoyo L., Apriani L., Atik N. et al.* Global tuberculosis disease and infection in systemic lupus erythematosus patients: A systematic review and meta-analysis. Lupus 2024. 33(6):555-73.

3. *Dobler C.C.* Biological agents and tuberculosis: risk estimates and screening strategies. Int J Rheum Dis 2015. 18(3):264-67.

4. *Gaul C., Schmid A., Mohr W., Lohoff M., Heckmann J.G., Erbguth F., et al.* Cerebral tuberculosis in a patient with Sharp's syndrome. Dtsch Med Wochenschr. 2001. 126(25-26):750-3.

5. *Hou C.L., Tsai Y.C., Chen L.C., Huang J.L.* Tuberculosis infection in patients with systemic lupus erythematosus: pulmonary and extra-pulmonary infection compared. Clin Rheumatol. 2008. 27(5):557-63.

6. *Khot R.S., Patil A., Rathod B.D., Patidar M., Joshi P.P.* Uncovering the unusual: A case of mixed connective tissue disease with rare presentation, atypical complications, and therapeutic dilemmas. Cureus. 2023. 15(3):e36298.

7. *Ndiaye M., Hane A.A., Dieng M.T., Ndir M., Ba O., Cissokho S. et al.* Sharp syndrome complicating pulmonary tuberculosis: apropos of a case. Dakar Med. 1999. 44(2):236-9.

8. *Park J.W., Curtis J.R., Lee H., Lee J.K., Song Y.W., Lee E.B.* Risk-benefit analysis of isoniazid monotherapy to prevent tuberculosis in patients with rheumatic diseases exposed to prolonged, high-dose glucocorticoids. PLoS One 2020. 15(12):e0244239.

9. *Schmid K., Schoerner C., Drexler H.* Occupationally acquired tuberculosis in an administrative assistant: aspects of an expert report. Dtsch Med Wochenschr 2003. 128(9):432-4.

10. *Senarathna H., Deshapriya K.* Delayed diagnosis: Tuberculous arthritis of right knee joint in a patient with rheumatoid arthritis. Case Rep Rheumatol 2021. 2021:7751509.

11 *Strassburg A., Jafari C., Ernst M., Lotz W., Lange C.* Rapid diagnosis of pulmonary TB by BAL enzyme-linked immunospot assay in an immunocompromised host. Eur Respir J 2008. 31(5):1132-5.

12 World Health Organization. WHO global lists of high burden countries for tuberculosis (TB), TB/HIV and multidrug/rifampicin-resistant TB (MDR/RR-TB), 2021–2025: background document. 2021. Available at: https://iris.who.int/handle/10665/341980 (accessed on 21 May 2025).

13. *Wu Q., Liu Y., Wang W., Zhang Y., Liu K., Chen S.H. et al.* Incidence and prevalence of tuberculosis in systemic lupus erythematosus patients: A systematic review and meta-analysis. Front Immunol. 2022. 13:938406.

14 *Yagi T., Yamagishi F., Mizutani F., Sasaki Y., Saitou M., Tada Y. et al.* A case of cutaneous tuberculosis associated with steroid therapy for mixed connective tissue disease. Kekkaku 1998. 73(9):557-62.

**Information about the authors:**

**Goremykina Maiya Valentinovna** - Candidate of Medical Sciences, Associate Professor, Department of Internal Medicine and Rheumatology, NCJSC «Semey Medical University», 103 Abay street, Semey, 071400, Kazakhstan; Email: maya.goremykina@smu.edu.kz; phone number: +7 (777) 390 8234; https://orcid.org/0000-0002-5433-7771;

**Sandro Vento –** Adjunct Clinical Professor (Medicine), https://orcid.org/0000-0003-0084-4062; Faculty of Medicine, University of Puthisastra, Phnom Penh, Cambodia; Faculty of Medicine, Manash Kozybayev North Kazakhstan University, Petropavlovsk, Kazakhstan; Post address: #55, Street 180-184 Sangkat Boeung Raing, Khan Daun Penh, Phnom Penh, Cambodia; 150000, Kazakhstan Petropavlovsk, Pushkin street, 86; E-mail: ventosandro@yahoo.it; phone: + 971-556-621-955

***Correspondence author:**

**Goremykina Maiya Valentinovna** - Candidate of Medical Sciences, Associate Professor, Department of Internal Medicine and Rheumatology, NCJSC «Semey Medical University», Semey, Kazakhstan; https://orcid.org/0000-0002-5433-7771;

**Post address:** 103 Abay street, Semey, 071400, Kazakhstan;

**E-mail:** maya.goremykina@smu.edu.kz;

**Phone:** +7 (777) 390 8234.

Received: 28 February 2025 / Accepted: 02 June 2025 / Published online: 30 June 2025

***DOI 10.34689/SH.2025.27.3.030***

***UDC 616.72-002.77:611.018.4***

This work is licensed under a Creative Commons Attribution 4.0 International License

# THE EFFECT OF STEROID THERAPY ON BONE TISSUE IN RHEUMATIC DISEASES (DESCRIPTION OF A CLINICAL CASE)

**Tamara Kh. Rymbayeva[1], https://orcid.org/0000-0003-3769-6796**
**Gulnur B. Kanapiyanova[1], https://orcid.org/0000-0002-8102-5220**
**Madina R. Madiyeva[1], https://orcid.org/0000-0001-6431-9713**
**Alida Sh. Kaskabayeva[1], https://orcid.org/0000-0002-5184-214X**
**Gulzhan B. Bersimbekova[1], https://orcid.org/0000-0002-9416-5054**
**Maiya V. Goremykina[1], https://orcid.org/0000-0002-5433-7771**

**[1] NCJSC «Semey Medical University», Semey city, Republic of Kazakhstan.**

**Abstract**

Joint and bone pain is the most common symptom of most joint pathologies of inflammatory autoimmune nature. In patients with diagnosed rheumatic disease undergoing hormonal therapy, it can be regarded as an exacerbation of the underlying disease, and not as a symptom of secondary osteoporosis.

The article presents a clinical case of a patient with mixed connective tissue disease (systemic lupus erythematosus + juvenile idiopathic arthritis), who was referred for hospitalization due to deterioration of health in the form of severe arthralgia and myalgia against the background of glucocorticoid therapy.

***Keywords:*** *arthralgia, glucocorticosteroids, osteoporosis.*

***For citation:***

*Rymbayeva T.Kh., Kanapiyanova G.B., Madiyeva M.R., Kaskabayeva A.Sh., Bersimbekova G.B., Goremykina M.* The effect of steroid therapy on bone tissue in rheumatic diseases (description of a clinical case) // *Nauka i Zdravookhranenie* [Science & Healthcare]. 2025. Vol.27 (3), pp. 280-284. *doi 10.34689/SH.2025.27.3.030*

**Резюме**

# ВЛИЯНИЕ СТЕРОИДНОЙ ТЕРАПИИ РЕВМАТИЧЕСКИХ ЗАБОЛЕВАНИЙ НА СОСТОЯНИЕ КОСТНОЙ ТКАНИ (ОПИСАНИЕ КЛИНИЧЕСКОГО СЛУЧАЯ)

**Тамара Х. Рымбаева[1], https://orcid.org/0000-0003-3769-6796**
**Гульнур Б. Канапиянова[1], https://orcid.org/0000-0002-8102-5220**
**Мадина Р. Мадиева[1], https://orcid.org/0000-0001-6431-9713**
**Алида Ш. Каскабаева[1], https://orcid.org/0000-0002-5184-214X**
**Майя В. Горемыкина[1], https://orcid.org/0000-0002-5433-7771**
**Гульжан Б. Берсимбекова[1], https://orcid.org/0000-0002-9416-5054**

**[1] НАО «Медицинский университет Семей», г. Семей, Республика Казахстан**

Боли в суставах и костях – самый распространенный симптом большинства суставных патологий воспалительного аутоиммунного характера. У пациентов с диагностированным ревматическим заболеванием, находящихся на гормональной терапии, могут быть расценены как обострение основного заболевания, а не как симптом вторичного остеопороза.

В статье представлен клинический случай пациента со смешанным заболеванием соединительной ткани (Системная красная волчанка + Ювенильный идиопатический артрит), который был направлен на госпитализацию в связи с ухудшением самочувствия в виде появления выраженных артралгий и миалгий на фоне получаемой глюкокортикоидной терапии.

***Ключевые слова:*** *артралгии, глюкокортикостероиды, остеопороз.*

***Для цитирования:***

*Рымбаева Т.Х., Канапиянова Г.Б., Мадиева М.Р., Каскабаева А.Ш., Горемыкина М.В., Берсимбекова Г.Б.* Влияние стероидной терапии ревматических заболеваний на состояние костной ткани (описание клинического случая) // Наука и Здравоохранение. 2025. Т.27 (3), С. 280-284. doi: 10.34689/SH.2025.27.3.030

**Түйіндеме**

# РЕВМАТИКАЛЫҚ АУРУЛАР КЕЗІНДЕ СТЕРОИДТЫ ЕМНІҢ СҮЙЕК ТІНІНЕ ӘСЕРІ (КЛИНИКАЛЫҚ ЖАҒДАЙДЫ СИПАТТАУ)

**Тамара Х. Рымбаева[1], https://orcid.org/0000-0003-3769-6796**
**Гүльнұр Б. Канапиянова[1], https://orcid.org/0000-0002-8102-5220**
**Мадина Р. Мадиева[1], https://orcid.org/0000-0001-6431-9713**
**Алида Ш. Каскабаева[1], https://orcid.org/0000-0002-5184-214X**
**Гульжан Б. Берсимбекова[1], https://orcid.org/0000-0002-9416-5054**
**Майя В. Горемыкина[1], https://orcid.org/0000-0002-5433-7771**

**[1] «Семей медицина университеті» КеАҚ,**
**Семей қ., Қазақстан Республикасы.**

Буындар мен сүйектердегі ауырсыну – қабынулық аутоиммундық сипаттағы бірлескен патологиялардың көпшілігінің ең көп таралған симптомы. Ревматикалық ауру диагнозы қойылған гормональді ем қабылдайдын науқастарда екіншілік остеопороз емес негізгі аурудың өршуі ретінде бағалануы мүмкін.

Мақалада алынған глюкокортикоидты ем аясында айқын артралгия және миалгия түрінде жағдайының нашарлауына байланысты ауруханаға жатқызуға бағытталған дәнекер тінінің аралас ауруы бар науқастың клиникалық жағдайы (жүйелі қызыл жегі + ювенильді идиопатиялық артрит) ұсынылған.

**Түйінді *сөздер:*** *артралгиялар, глюкокортикостероидтар, остеопороз.*

***Дәйексөз үшін:***
*Рымбаева Т.Х., Канапиянова Г.Б., Мадиева М.Р., Каскабаева А.Ш., Горемыкина М.В., Берсимбекова Г.Б.* Ревматикалық аурулар кезінде стероидты емнің сүйек тініне әсері -(клиникалық жағдайды сипаттау) // Ғылым және Денсаулық. 2025. Т.27 (3), Б. 280–284. doi: 10.34689/SH.2025.27.3.030

**Introduction**

Joint and bone pain is one of the most common symptoms associated with autoimmune inflammatory joint pathologies. In patients diagnosed with rheumatic diseases who are undergoing corticosteroid therapy, these symptoms may be mistakenly interpreted as an exacerbation of the primary disease rather than a manifestation of osteoporosis.

This article presents a clinical case involving a patient with mixed connective tissue disease (Systemic Lupus Erythematosus and Juvenile Idiopathic Arthritis), who was hospitalized due to worsening symptoms, including pronounced arthralgia and myalgia, while receiving glucocorticoid therapy.

As is well known, this autoimmune pathology, characterized by clinical and immunological features of mixed connective tissue disease, presents with diverse manifestations occurring in various combinations; however, the predominant feature is the musculoskeletal syndrome due to the overlap of clinical signs with those of rheumatoid arthritis.

Osteoporosis (OP) is a metabolic skeletal disorder characterized by reduced bone mass, deterioration of bone microarchitecture, and, consequently, an increased risk of fractures from minimal trauma [5]. Osteoporosis can be classified as either primary or secondary. Primary osteoporosis develops independently, whereas secondary osteoporosis arises as a result of various diseases, conditions, or the use of certain medications.

The most frequent cause of secondary OP in children is the prolonged use of glucocorticosteroids, which, even in low doses, can lead to a significant reduction in bone mineral density (BMD). Glucocorticosteroids (GCS) suppress osteoblast activity and promote bone resorption. As a result, bone density and mass decrease, and bone architecture is altered. One of the key risk factors for steroid-induced osteoporosis is a high daily dose of GCS (more than 7.5 mg) and prolonged use.

**Relevance.** Patients of all ages and sexes undergoing long-term glucocorticoid therapy are considered at high risk for developing osteoporosis. The public health significance of osteoporosis is largely due to its consequences—namely, skeletal fractures. Bone is a metabolically active tissue in which continuous remodeling occurs, involving the resorption of old bone and the formation (ossification) of new bone tissue.

Prolonged use of GCS for the treatment of rheumatic diseases (RD) inhibits bone formation and increases resorption, reducing serum calcium concentrations. This can lead to secondary hyperparathyroidism, simultaneously stimulating osteoclasts and inhibiting osteoblasts. These effects, along with protein catabolism-induced reduction in protein matrix components, may result in impaired bone growth in children and adolescents and the development of osteoporosis in pediatric patients of all ages. In addition, GCS therapy decreases calcium absorption in the intestines, increases urinary calcium excretion, impairs ossification processes, and reduces endogenous estrogen synthesis—an important hormone for bone strength.

Maintaining stable plasma calcium levels is essential for proper physiological function and is tightly regulated by calcium homeostasis mechanisms. Vitamin D plays a crucial role in bone maintenance and growth by enhancing

calcium absorption in the intestines. Patients receiving GCS therapy should undergo regular monitoring of serum electrolyte and vitamin D levels. Additionally, bone mineral density (BMD) measurement is essential for diagnosing steroid-induced OP. In pediatric patients, BMD is assessed using the Z-score (the number of standard deviations above or below the mean for age-matched individuals). A normal Z-score in children ranges from +2.5 to -0.9 standard deviations. Values below -1 SD indicate decreased bone density (osteopenia), while scores below -2.5 SD are diagnostic for osteoporosis.

Epidemiological studies [9] have shown that the most rapid bone mass loss occurs within the first year of initiating corticosteroid therapy. Lumbar spine BMD may decrease by up to 30% within six months of treatment, and proximal femur BMD may decrease by 14% over 12 months. Although the rate of bone loss typically slows thereafter, it remains significantly higher than the rate of age-related physiological loss. Osteoporotic fractures occur in 30–50% of patients undergoing long-term systemic GCS therapy. The most common fracture sites include the ribs, vertebrae, and diaphyses of long tubular bones. At a daily GCS dose of 5 mg or more (in prednisone equivalents), the relative risk of fractures compared to the general population increases 1.9-fold overall, 2-fold for hip fractures, and nearly 2.9-fold for vertebral fractures. The greatest loss of bone mass occurs during the early stages of the disease, likely due to both high inflammatory activity and the use of high GCS doses. Thus, this patient category requires early screening for OP and timely initiation of anti-osteoporotic therapy.

In osteoporosis, clinical manifestations are often subtle and asymptomatic until the condition is advanced. Bone tissue serves as a reservoir and compensates for reductions in key parameters of phosphorus-calcium metabolism in the bloodstream by releasing essential components to maintain homeostasis [4].

**Objective**

To highlight the importance of a differential diagnostic approach in evaluating complaints of arthralgia in a patient with a rheumatic disease undergoing glucocorticoid therapy.

**Clinical Case Summary**

Patient B., 16 years old, was admitted to the Pediatric Department of the University Hospital at NAO "Semey Medical University" with complaints of bone pain; arthralgia in the elbow, knee, and ankle joints; muscle pain; morning stiffness lasting 20–30 minutes; general weakness; and recurrent oral ulcers.

**Medical history**: Since 2015, the patient has been followed for a diagnosis of Mixed Connective Tissue Disease, including Systemic Lupus Erythematosus (SLE) (manifesting as dermatitis, vasculitis, stomatitis, nephritis, lymphadenopathy, myositis, arthralgia, cheilitis) and Systemic Juvenile Idiopathic Arthritis, with a chronic relapsing course. For the past 10 years, the patient has been receiving Methylprednisolone (Meticor), initially at 8 mg/day and increased to 12 mg/day over the past 3 years, in combination with Hydroxychloroquine (Immard) 400 mg/day.

Over the last 6 months, symptoms worsened, prompting hospitalization for suspected disease exacerbation and administration of pulse therapy with methylprednisolone.

**Life history**: Second child in the family, with age-appropriate growth and development. No history of fractures. Positive family history: rheumatoid arthritis in older sister and maternal aunt; SLE in maternal grandmother.

**Physical examination**:

- Height: 150 cm; Weight: 78 kg; BMI: 34.67 (obesity class I).
- General condition: moderate severity due to musculoskeletal symptoms.
- Excess subcutaneous fat on abdomen and flanks; mild gynecomastia.
- Musculoskeletal: Tenderness over humeral and femoral bones and muscles. No joint deformities.
- No lymphadenopathy or peripheral edema.
- Cardiovascular: HR 98 bpm, rhythmic, muffled heart sounds.
- Respiratory: Vesicular breath sounds, no wheezing.
- Abdomen: Liver palpable +1 cm; spleen not palpable; no tenderness.
- Normal bowel and urinary habits.

**Laboratory and instrumental findings**:

1. CBC (21.05.2025): Hb – 152 g/L; WBC – 5.82 x$10^9$/L; RBC – 4.86 x$10^{12}$/L; PLT – 280 x$10^9$/L; ESR – 10 mm/h.
2. Urinalysis: Sp. gravity – 1025; RBCs – 2/μL; WBCs – 2/μL; protein – negative.
3. ECG (22.05.2025): Sinus arrhythmia (HR 85–92 bpm); signs of ventricular repolarization abnormalities.
4. Echocardiography: Normal heart chamber dimensions; valve structures intact; LVEF – 62%.
5. Ophthalmologic exam: Retinal angiopathy; ametropia.
6. Multislice computed tomography (MSCT) of the chest:The thoracic cage is of normal shape and symmetrical. The lungs are well-aerated and in full contact with the chest wall. No areas of pathological consolidation are detected. The major bronchi are patent and free of pathological inclusions. No pleural effusion is observed. The mediastinum is midline and of normal width. No pathological inclusions are identified in the anterior, central, or posterior compartments. The heart is of normal configuration with non-enlarged borders. The great vessels are unremarkable. The thoracic aorta is not dilated and is uniformly opacified with contrast. The pulmonary artery is not enlarged. Degenerative changes are noted in the thoracic spine.
7. Esophagogastroduodenoscopy (EGD) Findings:The esophageal mucosa is matte pink and glistening. The esophagogastric junction is visualized at 40 cm from the upper incisors; the cardiac rosette closes completely.The stomach is of normal shape and contains approximately 70.0 ml of gastric juice in the fasting state. The gastric body folds are tortuous, longitudinally oriented, and unfold uniformly upon insufflation. Antral peristalsis is active, rhythmic, and visible across all walls up to the pylorus. The gastric mucosa appears pink and glistening. In the antral region, it is edematous and focally hyperemic, with flat and linear erosions of round and polygonal shape, measuring 2–4 mm, covered with fibrin and surrounded by a rim of hyperemia. On palpation, the mucosa is soft, elastic, and mobile. The pylorus is not deformed, closes completely, and opens adequately. The duodenal bulb is not deformed, oval in shape, with a pink, velvety mucosa. The exit from the

bulb is unobstructed. The postbulbar segments are passable and show no abnormalities.

8.Bone densitometry: Total body Z-score = -0.3 SD – consistent with osteopenia for age.

9.Calcium-phosphate metabolism:

- Total calcium: 2.47 mmol/L (normal)
- Ionized calcium: 0.82 mmol/L (↓)
- Inorganic phosphate: 0.88 mmol/L (low-normal)
- Vitamin D: 12.0 ng/mL (deficiency, normal range: 30–100 ng/mL)

The patient with a known history of SLE and systemic JIA presents with symptom exacerbation and features of steroid-induced side effects, including obesity, osteopenia, vitamin D deficiency, and erosive gastritis. Current management involves re-evaluation of immunosuppressive therapy, pulse corticosteroid therapy, gastroprotection, vitamin D supplementation, and bone health monitoring.

**Discussion**

Due to the onset of pronounced pain in the bones, joints, and muscles, as well as the appearance of small ulcers in the mouth—interpreted as characteristic ulceration of the oral mucosa resulting from lupus activity—the boy was hospitalized in UG JSC "SMU" for adjustment of cytostatic therapy and an increase in the glucocorticoid component. However, the absence of fever, normal condition of the skin (i.e., no erythema), lack of articular syndrome or multi-organ involvement, and normal hematological parameters led to a decision to perform a differential diagnosis of arthralgia and myalgia. Moreover, intensive therapy is used in patients with autoimmune diseases, including mixed connective tissue disease, in the presence of severe immune complex pathology with nephrotic syndrome, severe cerebrovasculitis, cytopenias, systemic vasculitis. All of these listed complications were not present in this patient. In this regard, the development of secondary osteoporosis in this patient was suspected.

To this end, it was decided to conduct blood tests for calcium, phosphorus, and vitamin D levels, as well as to perform dual-energy X-ray absorptiometry (DEXA). The patient's total calcium and phosphorus levels were within the normal range—presumably due to compensatory leaching from the bones—while ionized calcium levels were found to be significantly decreased. There was also a noted deficiency in vitamin D, which may additionally be attributed to the fact that patients with systemic lupus erythematosus are contraindicated from ultraviolet exposure, i.e., being out in the sun.

Based on the onset of pronounced bone, joint, and muscle pain, along with the appearance of oral ulcers—regarded as characteristic ulceration of the oral mucosa due to systemic lupus erythematosus (SLE) activity—the patient was hospitalized at the University Hospital of the NJSC "Medical University of Semey" for adjustment of cytostatic therapy and intensification of glucocorticoid treatment. However, the absence of fever, the normal condition of the skin (no erythema), the absence of joint syndrome and multi-organ involvement, as well as normal hematological parameters, prompted a differential diagnosis of the musculoskeletal syndrome. This was particularly relevant given that intensive therapy is typically indicated in patients with autoimmune diseases, including mixed connective tissue disease, in the presence of severe immune complex pathology such as nephrotic syndrome, severe cerebrovascular involvement, cytopenias, or systemic vasculitis. None of these complications were present in this patient.

As a result, the development of secondary osteoporosis was suspected. Accordingly, laboratory tests were ordered to assess serum calcium, phosphorus, and vitamin D levels, and dual-energy X-ray absorptiometry (DEXA) was planned.

The coated tongue and presence of isolated ulcers were found to be a result of erosive gastritis, diagnosed through esophagogastroduodenoscopy and also associated with steroid therapy.

Based on the clinical, laboratory, and instrumental findings, it was decided not to change the treatment for the underlying disease. A concomitant diagnosis was made: *"Drug-induced osteoporosis without pathological fracture. Glucocorticoid-induced myopathy."*

A gradual reduction in glucocorticoid dosage was planned, along with recommendations to enhance the diet with calcium-rich foods or to prescribe calcium and vitamin D in pharmaceutical form, administered in age-appropriate dosages.

In accordance with the guidelines of the American College of Rheumatology (ACR), at discharge the patient will be recommended to undergo regular bone mineral density monitoring once every six months until stable bone density values are achieved [5].

**Conclusions**

To identify the cause of joint and muscle pain, it is essential—taking into account the nature of the therapy being administered—to distinguish a flare of the underlying disease from the likely development of secondary osteoporosis in such patients. Bone pain is a hallmark sign of osteoporosis, ranging in intensity from mild to severe, and can present in various localizations and degrees of expression.

Thus, a mandatory component of treatment for rheumatic diseases is careful monitoring of potential complications of glucocorticoid therapy and the application, whenever possible, of the minimum therapeutically effective glucocorticoid dose.

Prolonged glucocorticoid therapy necessitates the periodic administration of vitamin D and calcium supplements to enhance bone tissue mineralization, thereby serving as a preventive measure against hormone-induced osteoporosis and muscular dystrophy. Timely recognition of the clinical signs of osteoporosis is essential for the appropriate management and referral of the patient, as well as for the prevention of this complication as one of the possible outcomes of the underlying disease.

***Additional Information***

***Funding:*** *The work was carried out within the framework of a scientific grant on the topic IRN AP19680262 "Clinical and epidemiological characteristics of risk factors for the prevalence of osteoporosis in different age periods with assessment of the quantitative composition of bone tissue using dual-energy X-ray absorptiometry", funded by the Ministry of Education and Science of the Republic of Kazakhstan.*

***Publication status:*** *The material of this article has not been submitted for publication elsewhere.*

***Conflict of interest:*** *The authors declare no actual or potential conflicts of interest related to the publication of this article.*

***Author contributions:*** *All authors made a significant contribution to the research and preparation of the manuscript, and reviewed and approved the final version prior to publication.*

***Literature:***

1. *Belaya Zh.E., Belova K.Yu., Biryukova E.V., Dedov I.I., Dzeranova L.K., et al.* Federal clinical guidelines for the diagnosis, treatment, and prevention of osteoporosis. Osteoporosis and Osteopathy. 2021. 24(2):4–47.

2. *Lesnyak O.M., Baranova I.A., Toroptsova N.V.* Glucocorticoid-induced osteoporosis in adults. Yaroslavl: "Litera", 2021. 13 p.

3. *Pochkaylo A.S., Galashevskaya A.A., Vodyanova O.V.* Osteoporosis in pediatric practice: modern approaches to medical prevention, diagnosis, and treatment: educational-methodological manual. Minsk: BelMAPO, 2022. 94 p.

4. *Toroptsova N.V., Nasonov E.L.* Review of the 2022 American College of Rheumatology (ACR) guidelines for the prevention and treatment of glucocorticoid-induced osteoporosis: what's new? Scientific and Practical Rheumatology. 2024. 62(2):145–153.

5. *Chanakul A., Khunrattanaphon S., Deekajorndech T.* Low bone mineral density in Thai children with systemic lupus erythematosus: prevalence and risk factors. Asian Biomed (Res Rev News). 2021 Oct 29;15(5):245–250. doi:10.2478/abm-2021-0030. PMID: 37551322. PMCID: PMC10388791.

6. *Ciancia S., Högler W., Sakkers R.J.B., Appelman-Dijkstra N.M., Boot A.M., et al.* Osteoporosis in children and adolescents: how to treat and monitor? European Journal of Pediatrics. 2023 Feb. 182(2):501–511. doi:10.1007/s00431-022-04743-x. Epub 2022 Dec 6.

7. *Ciancia S., van Rijn R.R., Högler W., Appelman-Dijkstra N.M., Boot A.M., Sas T.C.J., Renes J.S.* Osteoporosis in children and adolescents: when to suspect and how to diagnose it. European Journal of Pediatrics. 2022 Jul;181(7):2549–2561. doi:10.1007/s00431-022-04455-2. Epub 2022 Apr 6. PMID: 35384509; PMCID: PMC9192469.

8. *Cipolla C., Sodero G., Cammisa I., Turriziani Colonna A., et al.* The impact of glucocorticoids on bone health and growth: endocrine and non-endocrine effects in children and young patients. Minerva Pediatrics (Torino). 2023 Dec;75(6):896–904. doi:10.23736/S2724-5276.22.07074-4. Epub 2022 Oct 31. PMID: 36315414.

9. *Cranney A., Welch V., Adachi J.D.,* et al. Calcitonin for the treatment and prevention of corticosteroid-induced osteoporosis. The Cochrane Library. 2004. Issue 1: CD001983.

10. *Galindo-Zavala R., Bou-Torrent R., Magallares-López B., et al.* Expert panel consensus recommendations for diagnosis and treatment of secondary osteoporosis in children. Pediatric Rheumatology Online Journal. 2020 Feb 24. 18(1):20. doi:10.1186/s12969-020-0411-9. PMID: 32093703; PMCID: PMC7041118.

11. *Hua J., Huang J., Li G., Lin S., Cui L.* Glucocorticoid-induced bone disorders in children: research progress in treatment mechanisms. Frontiers in Endocrinology (Lausanne). 2023 Apr 4. 14:1119427. doi:10.3389/fendo.2023.1119427. PMID: 37082116; PMCID: PMC10111257.

12. *Jin H.Y., Lee J.A.* Low bone mineral density in children and adolescents with cancer. Annals of Pediatric Endocrinology & Metabolism. 2020 Sep;25(3):137–144. doi:10.6065/apem.2040060.030. Epub 2020 Sep 30. PMID: 33017885; PMCID: PMC7538298.

13. *Sakka S.D.* Osteoporosis in children and young adults. Best Practice & Research Clinical Rheumatology. 2022 Sep;36(3):101776. doi:10.1016/j.berh.2022.101776. Epub 2022 Sep 13. PMID: 36109301.

14. *Soti Khiabani M., Tahghighi Sharabian F., Raeeskarami S.R., Ziaee V.* Evaluation of bone mineral density in juvenile systemic lupus erythematosus. *Archives of Bone and Joint Surgery.* 2023. 11(12):777–782. doi:10.22038/ABJS.2023.70697.3311. PMID: 38146515; PMCID: PMC10748809.

**Information about the authors:**

**Rymbaeva Tamara Khamitovna** – Candidate of Medical Sciences, Associate Professor of the Department of Internal Diseases and Rheumatology, NCJSC "Semey Medical University." Phone: +7 777 999 9159 Email: t_rymbaeva@mail.ru ORCID: 0000-0003-3769-6796

**Kanapiyanova Gulnur Bolatbekovna** – PhD Candidate, NCJSC "Semey Medical University." Phone: +7 775 177 9375 ORCID: 0000-0002-8102-5220

**Madiyeva Madina Rashidovna** – Doctor of Medical Sciences, Professor, Head of the Department of Radiology, NCJSC "Semey Medical University," Semey, Kazakhstan. Phone: +7 708 524 4745 ORCID: 0000-0001-6431-9713

**Kaskabayeva Alida Sharipovna** – Candidate of Medical Sciences, Professor, Head of the Department of Internal Diseases and Rheumatology, NCJSC "Semey Medical University," Semey, Kazakhstan. Phone: +7 777 267 5521 ORCID: 0000-0002-5184-214X

**Goremykina Maiya Valentinovna** – Candidate of Medical Sciences, Associate Professor of the Department of Internal Diseases and Rheumatology, NCJSC "Semey Medical University." Phone: +7 777 390 8234 ORCID: 0000-0002-5433-7771

**Bersimbekova Gulzhan Baltabekovna** – PhD Candidate, NCJSC "Semey Medical University." Phone: +7 702 372 8412 ORCID: 0000-0002-9416-5054

***Correspondence author:**

**Rymbaeva Tamara Khamitovna** – Candidate of Medical Sciences, Associate Professor of the Department of Internal Diseases and Rheumatology, NCJSC "Semey Medical University." Semey, Kazakhstan. ORCID: 0000-0003-3769-6796

**Post address:** Kazakhstan, Semey, Abaya st. 103.

**E-mail:** t_rymbaeva@mail.ru

**Phone:** +7 777 999 9159

## Содержание

### *ОРИГИНАЛЬНЫЕ ИССЛЕДОВАНИЯ*

**Bekbossynova M.S., Sailybaeva A.I., Kabduyeva G.A., Jetybayeva S.K., Tauekelova A.T., Novikova S.P., Myrzakhmetova G.Sh., Duisenbina Zh.S., Sakhipova A., Akzholova K.T., Kushugulova A.R.** **7-15**
Epidemiology, Resource Distribution, and Management Challenges of Chronic Heart Failure in Kazakhstan: A National Retrospective Analysis

**Murtazaliyeva A.V., Berezina G.M., Svyatova G.S., Yesset M.S. Burabayeva A.T.** **16-26**
Prevalence of polymorphisms in warfarin metabolism-related genes among the Kazakh population

**Antikeev D.A., Orazkhan A.A., Temirbulatova L.B., Beisimbayeva D.Zh., Abiltayev A.M., Tashtemirova O.G., Shukimbayeva A.M., Makhmutova A.M.** **27-35**
Neurological complications in extracorporeal membrane oxygenation: risk factors for the development of acute cerebrovascular events

**Zhautikova S.B., Urazalina N.M., Tolubayeva D.B.** **36-41**
The effect of repaglinide and metformin on external respiratory function in patients with diabetes and ischemic heart disease associated with obesity

**Uruzbayeva G.A., Bulegenov T.A., Mussakhanova A.K., Dzhusupov K., Ibekenov O.T., Smailova Zh.K., Baibussinova A.Zh., Imanbayev M.N., Zharykbassova F.Zh., Kussainova A.S., Armankyzy A.** **42-52**
Retrospective analysis of patients with obliterating atherosclerosis of the lower extremity arteries in the Abai region of the Republic of Kazakhstan

**Khangeldi A.Ye., Khamidullina Z.G., Shanazarov N.A., Afanasyev M.S., Grishache T.G., Akkazhieva N.N., Tanysheva G.A.** **53-63**
Эффективность фотодинамической терапии в лечении предраковых состояний шейки матки, вызванных вирусом папилломы человека

**Kyrykbayeva S.S., Oshibaeva A.E., Nuskabayeva G.O., Goremykina M.V., Urazalina N.M.** **64-69**
Domestic Violence as a Public Health Challenge: Results of a Mass Sociological Study in Turkistan Region

**Bayzullina A.O., Zhamaliyeva L.M., Ermagambetova A.P.** **70-78**
Assessment of depression, fatigue, and psychological well-being in patients after stroke: results of a cross-sectional study using the BECK, FAS, and MHC-SF scales

**Duisekova S., Gaisina M., Akhmetova K., Uazhanov M., Sekenova R.K., Dauletova G.Sh.** **79-87**
Social Determinants of Health Among Unemployed Youth in Kazakhstan: How Economic Disparity Affects Quality of Life

**Adilzhanov A.B., Adilgozhin M.S., Ibrayeva Zh.B., Urazalina N.M., Mukanova D.A., Zemlyanskaya N.S., Aitenova E.R., Shamshudinov T.M., Kassym L.T., Kussainova A.A.** **88-97**
Analysis of socio-demographic determinants and risk factors of tuberculosis in the Abai region during the period 2014–2022

## Мазмұны

### *БІРТУМА ЗЕРТТЕУЛЕР*

**Бекбосынова М.С., Сайлыбаева А.И., Кабдуева Г.А., Жетибаева С.К., Тауекелова А.Т., Новикова С.П., Мырзахметова Г.Ш., Дуйсенбина Ж.С., Сахипова А., Акжолова К.Т., Кушугулова А.Р.**
Қазақстандағы созылмалы жүрек жеткіліксіздігінің эпидемиологиясы, ресурстарын бөлу және басқару мәселелері: ұлттық ретроспективті талдау

**Муртазалиева А.В., Березина Г.М., Святова Г.С., Есет М.С., Бурабаева А.Т.**
Қазақ популяциясында варфарин алмасуымен байланысты гендік полиморфизмдердің таралуы

**Антикеев Д.А., Оразхан Ә.А., Темирбулатова Л.Б., Бейсимбаева Д.Ж., Абильтаев А.М., Таштемирова О.Г., Шукимбаева А.М., Махмутова А.М.**
Неврологические осложнения при экстракорпоральной мембранной оксигенации: факторы риска развития острого нарушения мозгового кровообращения

**Жаутикова С.Б., Уразалина Н.М., Толубаева Д.Б.**
Репаглинид пен метформиннің семіздікке байланысты қант диабеті және коронарлық артерия аурулары бар науқастарда тыныс алу функциясына әсері

**Урузбаева Г.А., Булегенов Т.А., Мусаханова А.К., Джусупов К., Ибекенов О.Т., Смаилова Ж.К., Байбусинова А.Ж., Иманбаев М.Н., Жарыкбасова Ф.Ж., Кусаинова А.С., Арманқызы А.**
Қазақстан Республикасы Абай облысында төменгі аяқ-атеросклерозы облитерациялық атеросклерозы бар науқастарға ретроспективалық талдау

**Хангелді А.Е., Хамидуллина З.Г., Шаназаров Н.А., Афанасьев М.С., Гришачева Т.Г., Аккажиева Н.Н., Танышева Г.А.**
HPV тудырған жатыр мойнының ісік алды жағдайларын емдеудегі фотодинамикалық терапияның тиімділігі

**Кырыкбаева С.С., Ошибаева А.Е., Нускабаева Г.О., Горемыкина М.В., Уразалина Н.М.**
Түркістан облысындағы жаппай социологиялық зерттеу нәтижелері: отбасылық зорлық-зомбылық – қоғамдық денсаулық сақтау жүйесі үшін маңызды шақыру

**Байзуллина А.О., Жамалиева Л.М., Ермагамбетова А.П.**
Инсульттан кейінгі науқастарда депрессияның, шаршаудың және психологиялық әл-ауқат деңгейін ауырлығын бағалау: BECK, FAS және MHC-SF шкалаларын қолдана отырып, көлденең зерттеу нәтижелері

**Дуйсекова С., Гайсина М., Ахметова К., Уажанов М., Секенова Р.К., Даулетова Г.Ш.**
Қазақстандағы жұмыссыз жастардың денсаулықтың әлеуметтік анықтауыштары: Экономикалық ерекшеліктердің өмір сапасына әсері

**Адилжанов А.Б., Адильгожин М.С., Ибраева Ж.Б., Уразалина Н.М., Муканова Д.А., Землянская Н.С., Айтенова Э.Р., Шамшудинов Т.М., Касым Л.Т., Кусаинова А.А.**
2014–2022 жылдар аралығындағы Абай облысындағы туберкулёздің әлеуметтік-демографиялық детерминанттары мен қауіп факторларын талдау

**Mukasheva G.D., Maukayeva S.B., Kudaibergenova N.K., Shabdarbayeva D.M., Smailova Zh.K., Tokayeva A.Z., Smail Y.M., Nuralinova G.I., Issabekova Zh.B., Karimova S.S., Kozubayeva D.B., Goremykina M.V., Urazalina N.M.**
Analysis of antibiotic susceptibility and resistance of Klebsiella pneumoniae in various biological materials

**Aldabekova G.U., Musina A.A., Kamalbekova G.M., Khamidullina Z.G, Danbayeva Zh.S. Abdrashidova S.B., Zhumabayeva E.M., Kokisheva G.A., Tanysheva G.A.**
Infection control in the maternity care system: assessment of resource availability, human capacity and professional development

**Furlan A.,Mukasheva G.D., Maukayeva S.B., Kudaibergenova N.K., Shabdarbayeva D.M., Smailova Zh.K., Turakhanova B.S., Kozubayeva D.B., Goremykina M.V., Issabekova Zh.B., Karimova S.S., Urazalina N.M.**
Clinical and immunological characteristics of bronchial asthma in children and adolescents in the Abay region

**Yerdalieva L.K., Gainutdin A.E., Nersesov A.V., Raisova A.M., Suleimenova D.S., Ashimova N.A., Madenova S.S., Shamshidinova M.A., Abdullaeva G.U., Zhakipova A.A., Seitkabilova Z.S., Baiduisenova G.A., Yerengaiyp B.S., Nurbekova F.N.**
Experience using capsule endoscopy

**Tuktiyeva N.A., Dossanov B.A., Zhunussov Ye.T. Abdulvakhabov G.M.**
Surgical treatment of Legg-Calve-Perthes disease in children

**Ibekenov O.T., Baymakhanov A.N.. Berkinbay A.B.. Zheldibaev Y.M., Duisebekov M.K.. Esenbekov N.B., Iskakov S.K., Abdykadyrov M.K., Tulebaev E.S., Myrzash D.D.**
Analysis of treatment outcomes for bleeding from esophageal and gastric varices

**Valiyeva S.R., Glushkova N.E., Buribayeva Zh.K., Izekenova A.K.**
Evaluation of the effectiveness of molecular allergy diagnostic methods in the personalized management of patients with allergic rhinitis

***АКТУАЛЬНАЯ ТЕМА - COVID-19***

**Janzakova A.K., Buribaeva J.K., Kamhen V.B., Janzakov B.B., Izekenova A.K., Doskojaeva S.T., Kurmanova G.K., Shin A.L.**
Analysis of Clinical and Epidemiological Features of Herpesvirus Reactivation in Individuals with a History of COVID-19

***ОБЗОР ЛИТЕРАТУРЫ***

**Dyussupov A., Chaizhunussova N., Baibussinova A., Massabayeva M., Abenova M., Pivina L., Orekhov A., Smailova Zh., Mukanova D., Lepesbayev M., Kissina R., Akhmadiyeva T., Alibayeva G., Apbassova S., Abdildinova G., Izdenov A., Dosmagambetova R., Shabdarbayeva D.**
Radiation Exposure in the Semipalatinsk Region: Transgenerational Risks and Dosimetry Approaches

**98-107 Мукашева Г.Д., Маукаева С.Б., Кудайбергенова Н.К., Шабдарбаева Д.М., Смаилова Ж.К., Токаева А.З., Смаил Е.М., Нуралинова Г.И., Исабекова Ж.Б., Каримова С.С., Козубаева Д.Б., Горемыкина М.В., Уразалина Н.М.**
Klebsiella pneumoniae-нің әртүрлі биологиялық материалдардағы антибиотиктерге сезімталдығы мен төзімділігін талдау

**108-116 Алдабекова Г.У., Мусина А.А., Камалбекова Г.М., Хамидуллина З.Г., Данбаева Ж.С., Абдрашидова С.Б., Жумабаева Э.М., Кокишева Г.А., Танышева Г.А.**
Босандыру ұйымдарындағы инфекциялық қауіпсіздік жүйесі: ресурстық қамтамасыз етілуі, кадрлық әлеуеті және кәсіби даму деңгейін бағалау

**117-124 Фурлан А., Мукашева Г.Д., Маукаева С.Б., Кудайбергенова Н.К., Шабдарбаева Д.М., Смаилова Ж.К., Тураханова Б.С., Козубаева Д.Б., Горемыкина М.В., Исабекова Ж.Б., Каримова С.С., Уразалина Н.М.**
Абай облысындағы балалар мен жасөспірімдердегі бронхиалды астманың клиникалық және иммунологиялық ерекшеліктері

**125-134 Ердалиева Л.К., Гайнутдин А.Е., Нерсесов А.В., Раисова А.М., Сулейменова Д.С., Ашимова Н.А., Маденова С.С., Шамшидинова М.А., Абдуллаева Г.У., Жакипова А.А., Сейткабилова З.С., Байдуйсенова Г.А., Еренгайып Б.С., Нурбекова Ф.Н.**
Капсулалық эндоскопияны қолдану тәжірибесі

**135-142 Tuktiyeva N.A., Dossanov B.A., Zhunussov Ye.T. Abdulvakhabov G.M.**
Surgical treatment of Legg-Calve-Perthes disease in children

**143-150 Ибекенов О.Т., Баймаханов А.Н., Беркинбай А.Б., Желдибаев Е.М., Дуйсебеков М.К., Есенбеко Н.Б., Искаков С.И., Абдыкадыров М.К., Тулебаев Е.С., Мырзаш Д.Д.**
Анализ результатов лечения кровотечений из варикозно-расширенных вен пищевода и желудка

**151-156 Сабина В.Р., Наталья Г.Е., Жанар Б.К., Изекенова А.К.**
Оценка эффективности методов молекулярной аллергодиагностики в персонализированном ведении пациентов с аллергическим ринитом

***COVID-19 - ӨЗЕКТІ ТАҚЫРЫП***

**157-164 Джанзакова А.К., Бурибаева Ж.К., Камхен В.Б., Джанзаков Б.Б., Изекенова А.К., Доскожаева С.Т., Курманова Г.М., Шин А.Л.,**
Анализ клинико-эпидемиологических признаков реактивации герпесвирусов у лиц, перенёсших COVID-19

***ӘДЕБИЕТТІК ШОЛУ***

**165-174 Дюсупов А., Чайжунусова Н., Байбусинова А., Масабаева М., Абенова М., Пивина Л., Орехов А., Смаилова Ж., Муканова Д., Лепесбаев М., Кисина Р., Ахмадиева Т., Алибаева Г., Апбасова С., Абдильдинова Г., Изденов А., Досмагамбетова Р., Шабдарбаева Д.**
Семей өңіріндегі радиациялық әсер: ұрпақаралық қауіптер және дозиметриялық тәсілдер

**Orazayeva B.B., Iskakova N.S., Serikova-Esengeldina D.S., Urazalina N.M., Atabayeva A.K., Khismetova Z.A.**
Trends and patterns of male reproductive system diseases in the context of medical and demographic indicators. Literature review

**Isakhanov R.B., Zhanbyrbekuly U., Akkaliev M.N., Nogayeva M.G., Novikova E.G.**
Infectious complications of urological interventions for urolithiasis. Literature review

**Samarova U.S., Kalbagaeva Zh.Ye., Zgotova N.S., Yegizbayeva G.S., Nogayeva M.G., Tazhibayeva K.N., Ibrayeva T.B., Iskakova A.M.,**
The prevalence of chronic obstructive pulmonary disease as a global health problem

**Kalbagayeva Zh.Ye., Khismetova Z.A., Iskakova N.S., Atabayeva A.K., Serikova-Esengeldina D.S. Razakova N.G., Zheksebergenova A.B.**
The quality of life of patients with COPD. Literature review

**Kozhabayeva A.D., Mansurova J.A., Zhunuspekova A.S., Orekhov A.Yu., Kassymova A.A., Ashirov B.A., Smailova Zh.K., Kapakova M.A., Urazalina N.M., Karazhanova L.K.**
The SST2 biomarker as a predictor of adverse clinical outcomes in heart failure. Literature review

**Petrova Y.V., Goremykina M.V., Ivanova R.L., Kozhakhmetova D.K., Botabayeva A.S., Razvodova A.A.**
Capabilities of Artificial Intelligence in Modern Rheumatology. Literature review

**Kapanova A.A., Alimbaeva A.R., Dairbekov Y.E., Abylgazinova A.Zh., Bektar Zh.S., Kovylina R.G., Masalov A.Ye., Terdykbayeva Z.S.**
Cognitive component in the rehabilitation of preschool children with congenital heart defects. Literature review

**Iskakova A.M., Algazina T.O., Touir G.Z., Batpenova G.R., Kotlyarova T.V., Samarova U.S., Bengu N.-A., Ibrayeva T.B.**
Advanced Approaches to Psoriasis Treatment. Literature review

**Rakhmetova V.S., Sarkulova S.M., Derbissalina G.A., Bedelbaeva G.G., Amirkhanova L.M., Smailova D.S.**
Mediterranean-style diet for nonalcoholic fatty liver disease. Literature review

## *КЛИНИЧЕСКИЙ СЛУЧАЙ*

**Goremykina M.V., Vento S.**
Extrapulmonary tuberculosis in a kazakh patient with mixed connective tissue disease. Clinical case

**Rymbayeva T.Kh., Kanapiyanova G.B., Madiyeva M.R., Kaskabayeva A.Sh., Bersimbekova G.B., Goremykina M.**
The effect of steroid therapy on bone tissue in rheumatic diseases (description of a clinical case)

175-188 **Оразаева Б.Б., Искакова Н.С., Серикова-Есенгелдина Д.С., Уразалина Н.М., Атабаева А.К., Хисметова З.А.**
Медициналық-демографиялық көрсеткіштер контекстісіндегі ерлердің репродуктивтік жүйесі ауруларының үрдістері мен заңдылықтары. Әдебиеттік шолу

189-199 **Исаханов Р.Б., Жаңбырбекұлы У., Аккалиев М.Н., Ногаева М.Г., Новикова Е.Г.**
Зәр тас ауруы кезіндегі урологиялық араласудың инфекциялық асқынулары. Әдебиеттік шолу

200-214 **Самарова У.С., Калбагаева Ж.Е., Зготова Н.С., Егизбаева Г.С., Ногаева М.Г., Тажибаева К.Н., Ибраева Т.Б., Искакова А.М.**
Жаһандық денсаулық проблемасы ретінде созылмалы обструктивті өкпе ауруларының таралуы

215-226 **Калбагаева Ж.Е., Хисметова З.А., Искакова Н.С., Атабаева А.К., Серикова-Есенгелдина Д.С., Разакова Н.Г., Жаксебергенова А.Б.**
СОӨА бар науқастардың өмір сапасы. Әдебиеттік шолу

227-235 **Кожабаева А.Д., Мансурова Ж.А., Жунуспекова А.С., Орехов А.Ю., Касымова А.А., Аширов Б.А., Смаилова Ж.К., Капакова М.А., Уразалина Н.М., Каражанова Л.К.**
SST2 биомаркері жүрек жеткіліксіздігі кезіндегі жағымсыз клиникалық нәтижелерді болжаушы көрсеткіш ретінде. Әдебиеттік шолу

236-244 **Петрова Ю.В., Горемыкина М.В., Иванова Р.Л., Кожахметова Д.К., Ботабаева А.С., Разводова А.А.**
Қазіргі ревматологиядағы жасанды интеллектінің мүмкіндіктері. Әдебиеттік шолу

245-254 **Қапанова А.А., Алимбаева А.Р., Даирбеков Е.Е., Абылгазинова А.Ж., Бектар Ж.С., Ковылина Р.Г., Масалов А.Е., Тердыкбаева З.С.**
Туа біткен жүрек ақаулары бар мектеп жасына дейінгі балаларды оңалтудың когнитивті компоненті. Әдебиетке шолу

255-266 **Искакова А.М., Алгазина Т.О., Туир Г.З., Батпенова Г.Р., Котлярова Т.В., Самарова У.С., Бенгу Н.-А., Ибраева Т.Б.**
Псориазды емдеудің заманауи тәсілдері. Әдебиеттік шолу

267-274 **Рахметова В.С., Саркулова С.М., Дербисалина Г.А., Бедельбаева Г.Г., Амирханова Л.М., Смаилова Д.С.**
Бауырдың алкогольды емес майлы ауруы жерорта теңіздік диета. Әдебиеттік шолу

## *КЛИНИКАЛЫҚ ЖАҒДАЙ*

275-279 **Горемыкина М.В., Венто С.**
Аралас дәнекер тін ауруы бар қазақстандық науқаста өкпеден тыс туберкулез. Клиникалық жағдай

280-284 **Рымбаева Т.Х., Канапиянова Г.Б., Мадиева М.Р., Каскабаева А.Ш., Берсимбекова Г.Б., Горемыкина М.В.**
Ревматикалық аурулар кезінде стероидты емнің сүйек тініне әсері (клиникалық жағдайды сипаттау)

**НАО «Медицинский университет Семей»**

**Министерство здравоохранения Республики Казахстан**

**Редакционно-издательский отдел.**

**071400, г. Семей, ул. Абая Кунанбаева, 103.**

**Подписано в печать 30.06.2025 г.**

**Формат 60х90/8. Печать цифровая.**

**Усл. п. л. 36. Заказ 187.**

**Тираж 500 экз.**