KJMPh

KAZAKHSTANIAN JOURNAL OF MEDICINE AND PHARMACY

ҚАЗАҚСТАН МЕДИЦИНА ЖӘНЕ ФАРМАЦИЯ ЖУРНАЛЫ

КАЗАХСТАНСКИЙ ЖУРНАЛ МЕДИЦИНЫ И ФАРМАЦИИ

eISSN: 3105-8035

ОҢТҮСТІК ҚАЗАҚСТАН МЕДИЦИНА АКАДЕМИЯСЫ

ҚАЗАҚСТАН МЕДИЦИНА ЖӘНЕ ФАРМАЦИЯ ЖУРНАЛЫ

ЮЖНО-КАЗАХСТАНСКАЯ МЕДИЦИНСКАЯ АКАДЕМИЯ

КАЗАХСТАНСКИЙ ЖУРНАЛ МЕДИЦИНЫ И ФАРМАЦИИ

SOUTH KAZAKHSTAN MEDICAL ACADEMY

JOURNAL OF MEDICINE AND PHARMACY OF KAZAKHSTAN

Основан с мая 1998 г.

Учредитель:
АО «Южно-Казахстанская медицинская академия»

Журнал перерегистрирован Министерством информации и коммуникаций Республики Казахстан
Регистрационное свидетельство №KZ89VPY00065454 от 24.02.2023 года.
ISSN 3105-8027

«Казахстанский журнал медицины и фармации» зарегистрирован в Международном центре по регистрации сериальных изданий ISSN(ЮНЕСКО, г.Париж,Франция), присвоен международный номер eISSN 3105-8035

Журнал индексируется в КазБЦ; в международной базе данных Information Service, for Physics, Electronics and Computing (InspecDirect)

Адрес редакции:
160019 Республика Казахстан,
г. Шымкент, пл. Аль-Фараби, 1
Тел.: 8(725-2) 39-57-57, (1095)
Факс: 40-82-19
www.skma.edu.kz
e-.mail: info@skma.kz

ӘОЖ 618.146-006.6-084:615.371

Жақсыбек Е.Ә., Жақсыбек Ж.Н., Тлеужан Р.Т.
«Оңтүстік Қазақстан медицина академиясы» АҚ, Шымкент, Қазақстан

HPV ВАКЦИНАЦИЯСЫНЫҢ ІРКІЛІСТІЛІГІ МЕН ҚАБЫЛДАНУЫ БОЙЫНША ЖАҺАНДЫҚ ЗЕРТТЕУ ТЕНДЕНЦИЯЛАРЫ: 10 ЖЫЛДЫҚ БИБЛИОМЕТРИЯЛЫҚ ТАЛДАУ (2015–2024)

Аңдатпа

Кіріспе. *Адам папилломавирусына (HPV) қарсы Вакцинация жатыр мойны обырының алдын алудың ең тиімді стратегияларының бірі болып қала береді. Алайда, вакцинацияға қатысты екіұштылық бүкіл әлем бойынша халықты жан-жақты қамтуға кедергі келтіруде. Бұл зерттеу HPV вакцинациясына қатысты жаһандық зерттеулердің шешімсіздік тенденцияларына библиометриялық талдау жасады. Онда жетекші елдер, институттар, журналдар, авторлар, ынтымақтастық және дәйексөз модельдері анықталды.*

Әдістер мен материалдар. *Деректер 2015-2024 жылдардағы Web of Science (WoS) дерекқорынан жиналды. "HPV вакцинациясы" және ("вакцинаға қатысты шешімсіздік" немесе "вакцинаны қабылдау") кілт сөздері қолданылды. Белгілі бір критерийлерді қолданғаннан кейін 443 басылым талданды. Бұл нәтижелер жыл сайынғы жарияланымдар санының айтарлықтай өсу тенденциясын көрсетеді.*

Нәтижелер. *Орташа мәні жылына 11,5 мақаланы құрады (p < 0,001, R2 = 0,926). Бұл өсіп келе жатқан сан Денсаулық сақтау жүйесі, әлеуметтік қызметтер және ұлттық денсаулық сақтау институттары тарапынан мақсатты қаржыландыру мен стратегиялық бастамалардың қажеттілігін көрсетеді. HPV вакцинациясына қатысты шешімсіздікті жою үшін шаралар қабылдау қажет. Америка Құрама Штаттары барлық басылымдардың жартысына жуығын құрайды (49,2%). Одан кейін Қытай (9,9%), Франция (5,6%), Канада (5,2%) және Англия (5,0%) болды. Ғылыми зерттеулерде табысы жоғары елдер басым болды. Алайда, Швеция мен Оңтүстік Африка халық пен жалпы ішкі өнімді (ЖІӨ) ескере отырып, пропорционалды емес үлес қосты. Басылымдардың көпшілігі түпнұсқа мақалалар болды (85,6%). Шолу мақалалары бастапқы зерттеулерге қарағанда (медиана = 11,5, диапазон: 1-279) айтарлықтай көп дәйексөз алды (медиана = 6, диапазон: 1-756) (p = 0,001). Жетекші журналдар Human Vaccines Immunotherapeutics (N = 51), Vaccine*

(N = 45), Vaccines (N = 39), BMC Public Health (N = 21) және PLOS ONE (n = 13) болды. Белгілі институттардың қатарына Техас университетінің жүйесі (N = 28) және Индиана университетінің жүйесі (N = 21) кіреді. Негізгі қаржыландыру ұйымдары АҚШ Денсаулық сақтау және халыққа қызмет көрсету департаменті (N = 71) және ұлттық денсаулық сақтау институты (N = 64) болды. Ең жемісті авторлар Демпси а.ф. (N = 10), Вергер п. (N = 9) және Зимет Г. (N = 9) болды. Халықаралық ынтымақтастық желілерін визуализациялау АҚШ пен Еуропа елдерінің басты орынға ие екендігін көрсетті. Табысы төмен және орташа елдер аз болды.

Қорытынды. *Біріктірілген бұл нәтижелер HPV вакцинациясына қатысты шешімсіздік артып келе жатқанын және табысы жоғары елдер көптеген басылымдарды ұсынып, олармен ынтымақтасатынын көрсетеді. Табысы төмен және орташа аймақтардағы ынтымақтастық пен зерттеу әлеуетін нығайту бүкіл әлемде HPV вакцинациясымен қамтуды арттыру жолындағы маңызды қадам болып қала береді.*

Түйін сөздер: *Библиометрия; дамыған елдер; адам папилломавирустары; Вакцинация; вакцинацияға қатысты шешімсіздік;*

Жақсыбек Е.Ә., Жақсыбек Ж.Н., Тлеужан Р.Т.

АО «Южно-Казахстанская медицинская академия», Шымкент, Казахстан

ГЛОБАЛЬНЫЕ ИССЛЕДОВАТЕЛЬСКИЕ ТЕНДЕНЦИИ В ОТНОШЕНИИ ПРЕРЫВИСТОСТИ И ПРИЕМЛЕМОСТИ ВАКЦИНАЦИИ ПРОТИВ ВПЧ: 10-ЛЕТНИЙ БИБЛИОМЕТРИЧЕСКИЙ АНАЛИЗ (2015-2024)

Аннотация

Введение. *Вакцинация против вируса папилломы человека (ВПЧ) остается одной из наиболее эффективных стратегий профилактики рака шейки матки. Однако нерешительность в отношении вакцинации по-прежнему препятствует всестороннему охвату населения во всем мире. В этом исследовании был проведен библиометрический анализ тенденций глобальных исследований в области нерешительности в отношении вакцинации против ВПЧ. В нем были определены ведущие страны, институты, журналы, авторы, а также модели сотрудничества и цитирования.*

Методы и материал. *Данные были собраны из базы данных Web of Science (WoS) за 2015-2024 годы. Использовались ключевые слова “Вакцинация против ВПЧ” И (“нерешительность в отношении вакцины” ИЛИ “принятие вакцины”). После применения*

определенных критериев было проанализировано 443 публикации. Эти результаты указывают на значительную тенденцию к увеличению количества ежегодных публикаций.

Результаты. *Среднее значение составило 11,5 статей в год (p < 0,001, R2 = 0,926). Это растущее число подчеркивает необходимость целевого финансирования и стратегических инициатив со стороны системы здравоохранения, социальных служб и Национальных институтов здравоохранения. Необходимо принять меры для устранения нерешительности в отношении вакцинации против ВПЧ. На Соединенные Штаты приходится почти половина всех публикаций (49,2%). За ними последовали Китай (9,9%), Франция (5,6%), Канада (5,2%) и Англия (5,0%). В научных исследованиях преобладали страны с высоким уровнем дохода. Однако Швеция и Южная Африка внесли непропорционально большой вклад с учетом численности населения и валового внутреннего продукта (ВВП). Большинство публикаций были оригинальными статьями (85,6%). Обзорные статьи получили значительно больше цитат (медиана = 11,5, диапазон: 1-279), чем оригинальные исследования (медиана = 6, диапазон: 1-756) (p = 0,001). Ведущими журналами стали Human Vaccines Immunotherapeutics (n = 51), Vaccine (n = 45), Vaccines (n = 39), BMC Public Health (n = 21) и PLOS ONE (n = 13). Среди известных институтов - система Техасского университета (n = 28) и система университета Индианы (n = 21). Основными финансирующими организациями были Министерство здравоохранения и социальных служб США (n = 71) и Национальный институт здравоохранения (n = 64). Самыми плодовитыми авторами были Демпси А.Ф. (n = 10), Верджер П. (n = 9) и Зимет Г. (n = 9). Визуализация международных сетей сотрудничества показала, что США и европейские страны занимают центральное место. Страны с низким и средним уровнем дохода были недопредставлены.*

Заключение. *В совокупности эти результаты подчеркивают, что нерешительность в отношении вакцинации против ВПЧ растет, и страны с высоким уровнем дохода предоставляют большинство публикаций и сотрудничают с ними. Укрепление сотрудничества и исследовательского потенциала в регионах с низким и средним уровнем дохода остается важным шагом на пути к повышению охвата вакцинацией против ВПЧ во всем мире.*

Ключевые слова: *Библиометрия; Развитые страны; Вирусы папилломы человека; Вакцинация; Нерешительность в отношении вакцинации;*

JSC «South Kazakhstan medical academy», Shymkent, Kazakhstan

GLOBAL RESEARCH TRENDS ON HPV VACCINATION HESITANCY AND ACCEPTANCE: A 10-YEAR BIBLIOMETRIC ANALYSIS (2015–2024)

Abstract

Introduction. *Vaccination against human papillomavirus (HPV) remains one of the most effective strategies for preventing cervical cancer. However, vaccine hesitancy continues to impede comprehensive population coverage globally. This study conducted a bibliometric analysis of global research trends in HPV vaccination hesitancy. It identified the leading countries, institutions, journals, authors, and patterns of collaboration and citation.*

Methods and materials. *Data were collected from the Web of Science (WoS) database for 2015–2024. The keywords used were "HPV vaccination" AND ("vaccine hesitancy" OR "vaccine acceptance"). After applying certain criteria, 443 publications were analyzed. These results indicate a significant upward trend in the number of annual publications.*

Results. *The average was 11.5 articles per year ($p < 0.001$, $R2 = 0.926$). This growing number underscores the need for targeted funding and strategic initiatives from the health system, social services, and the National Institutes of Health. Action is needed to address the hesitancy regarding HPV vaccination. The United States accounted for nearly half of all publications (49.2%). China (9.9%), France (5.6%), Canada (5.2%), and England (5.0%) followed. High-income countries dominated research output. However, Sweden and South Africa made disproportionately high contributions when adjusted for population and gross domestic product (GDP). Most publications were original articles (85.6%). Review articles received significantly more citations (median = 11.5, range: 1–279) than original studies (median = 6, range: 1–756) ($p = 0.001$). The leading journals were Human Vaccines Immunotherapeutics (n = 51), Vaccine (n = 45), Vaccines (n = 39), BMC Public Health (n = 21), and PLOS ONE (n = 13). Prominent institutions included the University of Texas System (n = 28) and Indiana University System (n = 21). The main funding bodies were the US Department of Health and Human Services (n = 71) and the NIH (n = 64). The most prolific authors were Dempsey AF (n = 10), Verger P (n = 9), and Zimet G (n = 9). Visualization of international collaboration networks showed the US and European countries in central positions. Low- and middle-income countries were underrepresented.*

Conclusion. *Together, these findings underscore that research on HPV vaccine hesitancy is rising, with high-income countries contributing the majority of publications and collaborations.*

Enhancing collaboration and research capacity in low- and middle-income regions remains a crucial step toward improving HPV vaccination uptake worldwide.

Keywords: *Bibliometrics; Developed Countries; Human Papillomavirus Viruses; Vaccination; Vaccination Hesitancy;*

Introduction

Human papillomavirus (HPV) is one of the most common infections worldwide, with a high global incidence. Malignancy prevention programs can also be carried out at the primary prevention level. This has become possible since the recent introduction of vaccines against this virus, which is estimated to cause 100% of cervical cancer cases [1]. Despite the clinical efficacy and safety of vaccines, many countries still have low population coverage. This is attributed to factors including a lack of awareness, misinformation, various cultural and religious barriers, and distrust of the healthcare system [2]

In 2019, the World Health Organization ranked hesitancy to vaccinate as one of the ten global threats to public health [3]

Bibliometric analysis offers a quantitative approach for evaluating global research trends and their impact across various disciplines. It helps identify the main structure of scientific cooperation, leading authors, top scientific organizations, journals, and general progress in this field. This is done by examining the citation structure. Bibliometric analysis is useful for evaluating academic results, analyzing the impact of specific studies, and determining research funding direction. The information obtained by bibliometric analysis can contribute to evidence-based policy development by identifying gaps and areas for further research. It also enables scientists and educational organizations to enhance their planning processes and increase recognition and influence in their research [4,5]

Previous bibliometric analyses have examined decision-making regarding HPV vaccination, with the most recent study covering the period from 2013 to 2022.6 The present study extends this scope by specifically aiming to identify global research trends related to HPV vaccination hesitancy through an analysis of authorship and citation structures over a longer period. The study seeks to clarify how research output, collaboration, and influence have evolved in this area.

The specific objectives of this study are to (1) assess the global distribution and impact of research outputs on HPV vaccination hesitancy, (2) evaluate the influence of countries and journals in this field, and (3) analyze scientific achievements to inform future research and policy directions.

Material and methods

Data source and search strategy

Data were collected from the Web of Science (WoS) database, which provides extensive citation resources and high-quality publications. The bibliometric analysis utilized Medical Subject Headings (MeSH) terms, specifically the phrase "HPV vaccination" AND ("vaccine hesitancy" OR "vaccine acceptance").

The study covered the time period from 2015 to 2024.

As a result of the analysis, 593 publications were found, and the methodology was applied using predefined inclusion and exclusion criteria. Publications not in English, early access materials, and other types of publications were excluded from the analysis. The exclusion of early access materials was based on the need to assess fully peer-reviewed and finalized studies, ensuring consistency and reliability in the data analysis process. This decision, along with language criteria, was made to enhance reproducibility and reduce the potential for bias. Recognizing the possibility of selection bias due to these criteria, efforts were made to ensure a clear and reproducible dataset, aligning with best practices in scientometric analysis. After applying the criteria, 443 publications were found suitable for bibliometric analysis. VOSviewer software was used to visualize the data. Detailed information is shown in Fig.1.

Data analysis

The total number of publications, the year of publication, the country of the journal/publisher, the number of citations, and the sources of publications were recorded. All publications were categorized according to the categories of the journal index (SSCI, SCIE, and ESCI) and their corresponding quartiles (Q1 to Q4). Данные о численности населения и внутреннего валового продукта стран были получены из общедоступных данных Всемирного банка (“https://www.cia.gov/the-world-factbook/field/population/country-comparison/”and“https://www.cia.gov/the-world-factbook/field/real-gdp-purchasing-power-parity/country-comparison/”). Based on these data, the top 20 countries were recognized as the most active countries. The total number of citations in each country and the average number of citations were calculated. According to the World Bank classification, all countries were divided into four income levels: low-income, lower-middle-income, upper-middle-income, and high-income countries (https://datatopics.worldbank.org/world-development-indicators/the-world-by-income-and-region.html).

The contribution of the most active countries was calculated based on the ratio of the number of publications from each country to the total number of publications.

The five leading journals and the five most active countries were identified. Additionally, the five leading journals from the five most active countries, the five leading funding organizations, and the five most prominent authors were identified. Frequently used keywords were extracted from the Web of Science and analyzed using VOSviewer (version 1.6.20). The graphic image was created based on data on co-authorship between countries, the number of co-authors among authors, and keyword matching networks. VOSviewer maps were performed by grouping countries, authors, and keywords based on the number of publications. The thickness of the line between the elements reflects the relative strength of the bond. The thicker the line, the stronger the bond. Individual links were highlighted by marking color schemes.

Statistical analysis

Descriptive statistics were applied. Results were presented as counts (n), percentages (%), medians, and minimum and maximum values. The Shapiro-Wilk test assessed data normality. Linear regression analysis was used to evaluate trends in annual publication counts, providing an overview of research growth. The average number of citations was also recorded.

Results:

Figure 2 illustrates that the number of publications is increasing annually, reaching a peak in 2024. A linear regression analysis was conducted to assess the publication trend over the years. The results demonstrated a consistent upward trajectory, with an average annual increase of 11.5 publications. The model showed statistical significance ($p < 0.001$) and explained approximately 92.6% of the variation in publication counts ($R^2 = 0.926$).

In total, the publications were published in 80 countries.

The 80 countries were classified into the following income categories according to the World Bank: 8 lower-income countries, 18 lower-middle-income countries, 15 upper-middle-income countries, and 38 high-income countries.

Figure 1 Selection process flowchart

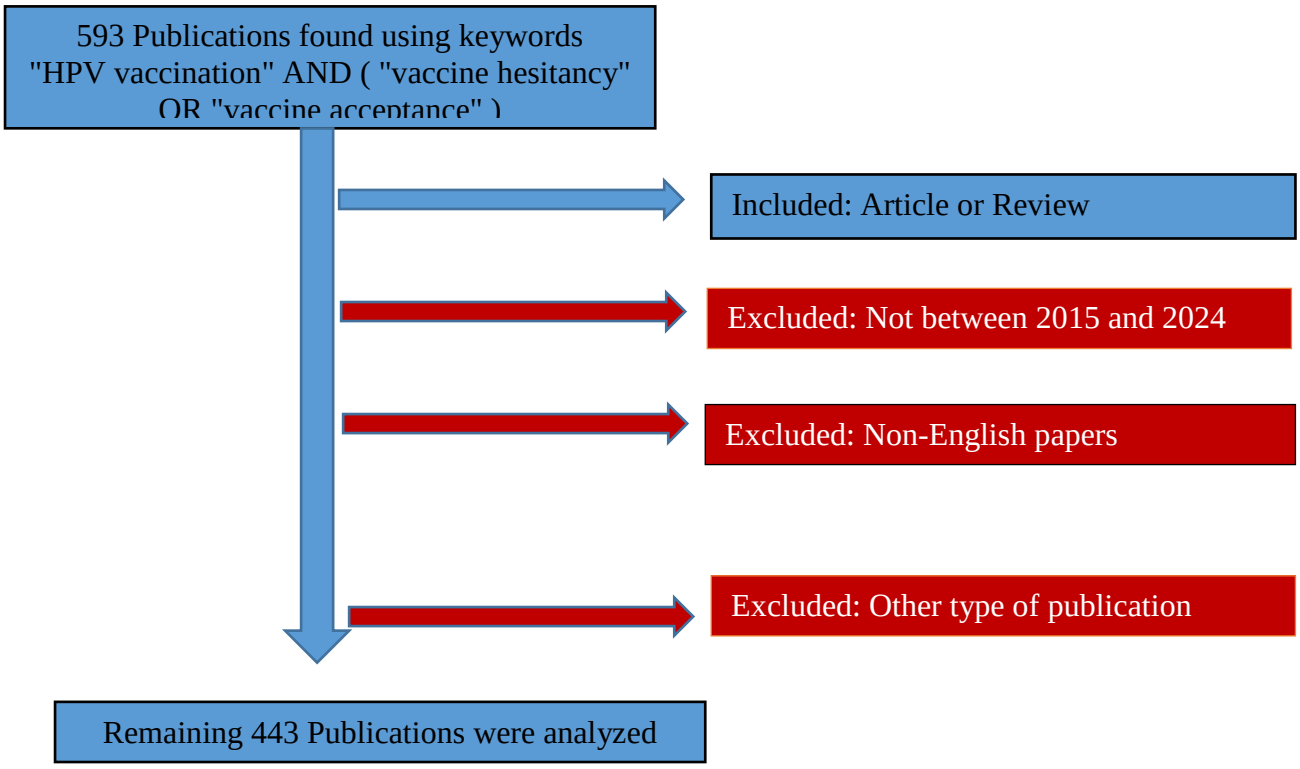
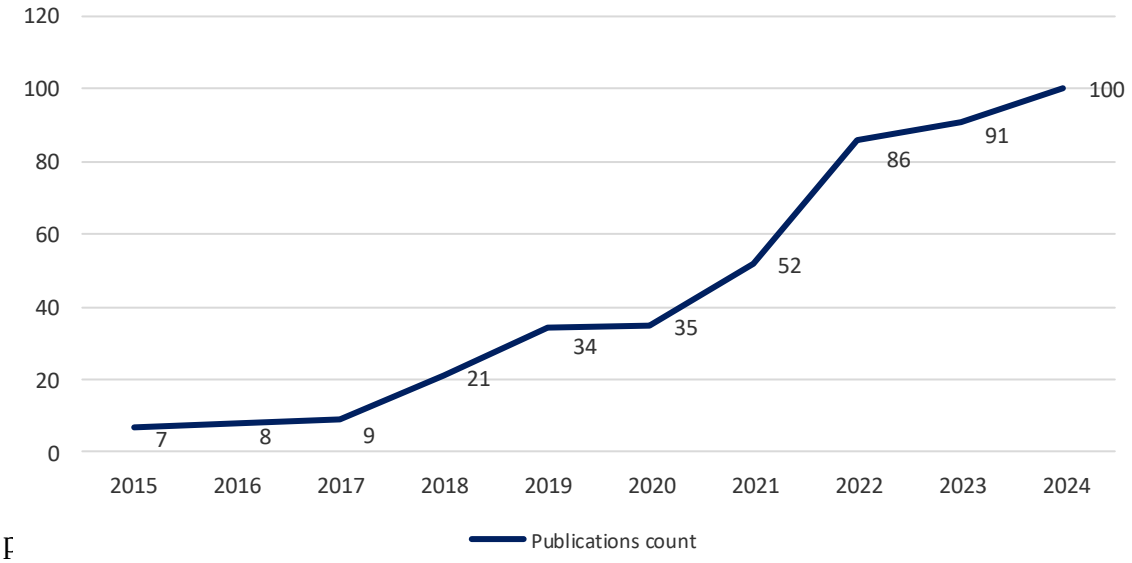
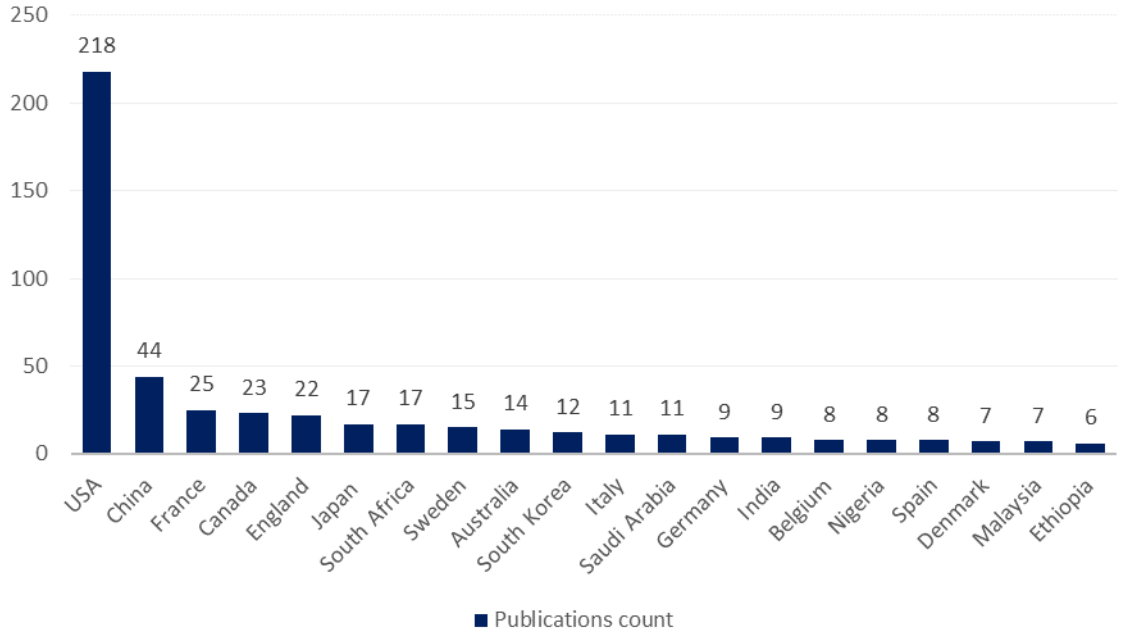


Figure 2 Publication count by year



Country-level [illegible] were a single article may be assigned to multiple countries based on author affiliations., While three main active countries were upper-middle-income, 14 had high-income countries, 2 countries fell into the lower-middle-income category, and 1 country had a low income (Fig. 3).

Figure 3 Publication counts of main active countries



Regarding document types, 379 (85.6%) publications were original articles. The average number of citations for articles and reviews was 6 (minimum = 1; maximum = 756) and 11,5 (minimum = 1; maximum = 279), respectively. Reviews were cited significantly more often than original articles (p = 0.001).

The median number of authors was 6 (1–46).

All 166 journals were indexed in SCIE and/or SSCI. Specifically, 51.2% (n = 85) of the journals were indexed solely in SSCI, 37.3% (n = 62) were indexed in both SSCI and SCIE, 69.9% (n = 116) were exclusively indexed in SCIE, and 15.7% (n = 26) were indexed in ESCI.

The quartile distribution of journals indexed in SCIE and/or SSCI and ESCI was as follows: 101 Q1 journals (60.8%), 38 Q2 journals (22,3%), 22 Q3 journals (13.3%), and 5 Q4 journals (3%).

The median number of citations for articles indexed in SCIE and/or SSCI was 8 (min = 1; max = 777), while for articles indexed in ESCI, it was 6 (min = 1; max = 69).

The contribution rate of the five most active countries has varied annually in recent years. The US share of contributions ranged from 41.0% to 87.7%, China's share ranged from 2.9% to 25%, France's share ranged from 3.0% to 12.5%, and England's share ranged from 2.9% to 28.6% (Table 1).

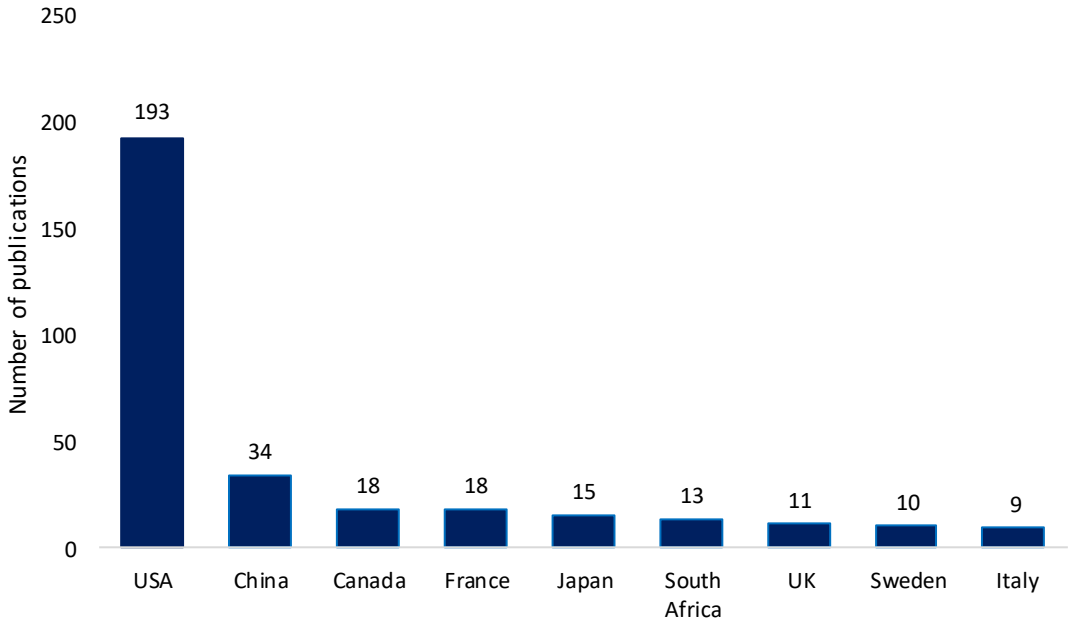
Table 1 Contribution rate of top five countries over the years

Top 5 countries					
Years	USA (%[a])	China (%[a])	France (%[a])	Canada (%[a])	England (%[a])
2015	(85.7)	(14.3)	n/a	1 (14.3)	2 (28.6)
2016	(50)	(25)	1 (12.5)	n/a	n/a
2017	(77.8)	n/a	1 (11.1)	n/a	1 (11.1)
2018	(57.1)	(4.8)	1 (4.8)	2 (9.5)	n/a
2019	(58.8)	(2.9)	4 (11.8)	2 (5.9)	1 (2.9)
2020	(42.9)	(5.7)	3 (8.6)	1 (2.9)	2 (5.7)
2021	(48.1)	3 (5.8)	5 (9.6)	2 (3.8)	5 (9.6)
2022	(46.5)	6 (7.0)	4 (4.7)	5 (5.8)	5 (5.8)
2023	(52.7)	9 (9.9)	3 (3.3)	5 (5.5)	3 (3.3)
2024	(41)	19 (19.0)	3 (3.0)	4 (4.0)	3 (3.0)

Notes: [a] Row Percentage

A map illustrating international cooperation has been created to visualize the countries involved in this effort. Publications with multiple co-authors from more than 25 countries were excluded, and the minimum number of publications and citations was 3 and 30, respectively. As a result, 35 countries met these criteria. The analysis was based on the number of publications. The size of the circles on the index corresponds to the number of publications (Fig. 4).

Figure 4 Corresponding countries



The United States accounted for 49.2% of the publications, followed by China (9.93%), France (5.64%), Canada (5.19%), and the United Kingdom (4.96%). The average number of citations per publication was highest in Canada (87.86), followed by France (36.12), Sweden (34.73), South Africa (32.76), and Australia (27.21)

The count of publications per million population and GDP was analyzed. Sweden (1.42), Belgium (0.68), and the USA (0.65) had the highest rates. According to the GDP analysis, the top three positions were held by Sweden (22.56%), South Africa (13.86%), and Belgium (10.57%), taking the top three spots (Table 2).

Table 2 Contribution of most active countries

	n (%)	n^a	n^b	Total citations	Average citations
US	218 (49.2)	0.65	8.73	4410	20.22
China	44 (9.93)	0.03	1.41	1003	22.79
France	25 (5.64)	0.37	6.6	903	36.12
Canada	23 (5.19)	0.57	10.26	2021	87.86
England	22(4.96)	0.32	5.9	1254	57
Japan	17 (3.83)	0.14	2.96	301	17.70
South Africa	17 (3.83)	0.27	13.86	557	32.76
Sweden	15 (3.38)	1.42	22.56	521	34.73
Australia	14 (3.16)	0.53	8.82	381	27.21
South Korea	12 (2.7)	0.23	4.59	152	12.66
Italy	11 (2.48)	0.19	3.5	263	23.90
Saudi Arabia	11 (2.48)	0.33	3.01	101	9.18
Germany	9 (2.03)	0.11	1.7	142	15.77
India	9 (2.03)	0.01	0.68	49	5.44
Belgium	8 (1.8)	0.68	10.57	158	19.75
Nigeria	8 (1.8)	0.04	6.27	122	15.25
Spain	8 (1.8)	0.17	3.51	112	14
Denmark	7 (1.58)	1.18	16.33	174	24.85
Malaysia	7 (1.58)	0.20	6.07	86	12.28

Ethiopia	6 (1.35)	0.05	16.92	67	11,16

Notes: n[a] number of articles per million population

n[b] number of articles per $ 100 billion gross domestic product

The US's highest contributions were to Human Vaccines Immunotherapeutics (28 publications), Vaccine (26), Vaccines (25), BMC Public Health (10), and PLOS ONE (8). China's highest contributions were to Human Vaccines Immunotherapeutics (11 publications) and BMC Public Health (5). France's contributions were to Vaccine (63 publications), Human Vaccines and Immunotherapeutics (4), and the European Journal of Health and the Frontiers of Public Health (each journal with two publications). Canada's highest contributions were to the Vaccine (each journal by two publications). England's contributions were to Human Vaccines Immunotherapeutics and Vaccine (by 5 publications), BMC Public Health, and Vaccines (2 publications each) (Table 3).

Table 3 Top five journals for the five most active countries

Rank	US (*n*)	China (*n*)	France (*n*)	Canada (*n*)	England (*n*)
1	*Human Vaccines Immunotherapeutics* (28)	*Human Vaccines Immunotherapeutics* (11)	*Vaccine* (6)	*Vaccine* (4)	*Human Vaccines Immunotherapeutics* (5)
2	*Vaccine* (26)	*Bmc Public Health* (5)	*Human Vaccines Immunotherapeutics* (4)	*Bmc Public Health* (2)	*Vaccine* (5)
3	*Vaccines* (25)	*Vaccines* (3)	*European Journal Of Public Health* (2)	*Human Vaccines Immunotherapeutics* (2)	*Bmc Public Health* (2)
4	*Bmc Public Health* (10)	*Cancer Control* (2)	*Frontiers In Public Health* (2)	*Annual Review Of Public Health* (1)	*Vaccines* (2)
5	*Plos One* (8)	*Frontiers In Public Health* (2)	*Annual Review Of Public Health* (1)	*Bmc Family Practice* (1)	Acta Psychologica (1)

Notes: n number of articles per million population

The top five journals, ranked by article count, were: Human Vaccines Immunotherapeutics (n = 51), Vaccine (n = 45), Vaccines (n = 39), BMC Public Health (n = 21), and PLOS ONE (n = 13). The US-led contributions in Human Vaccines Immunotherapeutics (28 publications). England had the highest number of publications in Vaccine (5). The top five leading countries and journals are shown in Table 4. The US published in 87 journals, China in 25, Canada in 19, France in 16, and England in 12.

Table 4 Top five active countries in the five most active journals

Rank	*Vaccines* (*n*)	*Human Vaccin Immunotherape s* (*n*)	*Vaccine* (*n*)	*Bmc Public Hec* (*n*)	*Plos One* (*n*)
1	US (25)	US (28)	US (26)	US (10)	US (8)
2	Australia (4)	China (11)	France (6)	China (5)	South Korea (2)
3	South Africa (4)	England (5)	England (5)	Canada (2)	Argentina (1)
4	Italy (3)	France(4)	Canada (4)	England (2)	Australia (1)
5	China (3)	Malaysia (3)	Denmark (4)	Sweden (2)	Brazil (1)

The institutions with the highest number of publications were the University of Texas System (n = 28), Indiana University System (n = 21), and the University of California System (n = 19) (Table 5).

Table 5 Top five institutions in terms of publication

Institution	Count
University Of Texas System	28
Indiana University System	21
University Of California System	19
University Of London	18
Institut National De La Sante Et De La Recherche Medicale Inserm	16

Among the funding organizations, the US Department of Health and Human Services (n = 71), National Institutes of Health (NIH) US (n = 64), and National Cancer Institute NIH (n = 37) were the leading organizations (Table 6).

Table 6 Top five funding organizations by number of articles

Funding Organization	Count
United States Department Of Health Human Services	71
National Institutes Of Health Nih Usa	64
Nih National Cancer Institute Nci	37
Centers For Disease Control Prevention Usa	11
Medical Research Council Uk Mrc	9

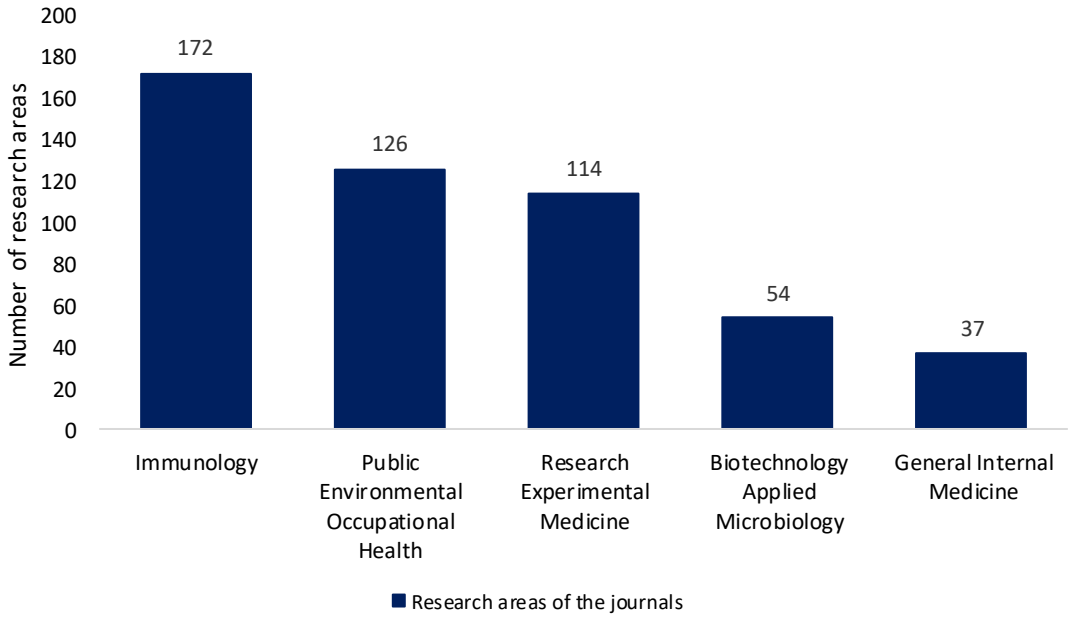
Prolific authors in this field included Dempsey AF (n = 10), Verger P (n = 9), and Zimet G (n = 9) (Table 7).

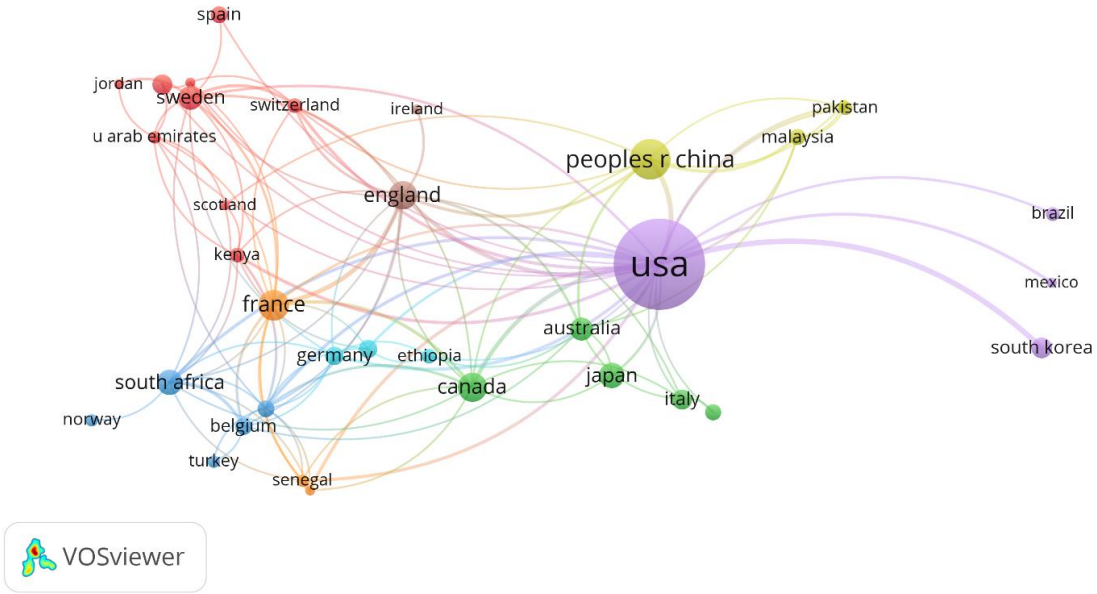
Table 7 Top ten prolific authors in the field

Author	Count
Dempsey AF	10
Verger P	9
Zimet G	9
Zimet GD	9
Peretti-watel P	8
Bednarczyk RA	7
Cooper S	7
Li J	6
Ueda Y	6
Wiysonge CS	6

In our research, the most common fields were Immunology (n = 172), Public Environmental and Occupational Health (n = 126), Research in Experimental Medicine (n = 114), Applied Microbiology (n = 54), and General Medicine (n = 37) (Fig.5): The co-authorship network and keyword visualization maps are shown in Figs. 6,7, and 8.

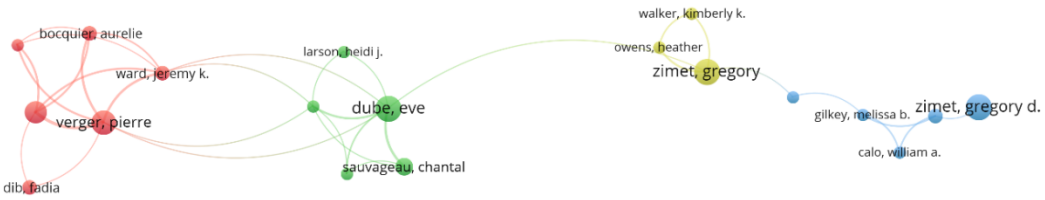
Figure 5 The top 5 research areas of the journals





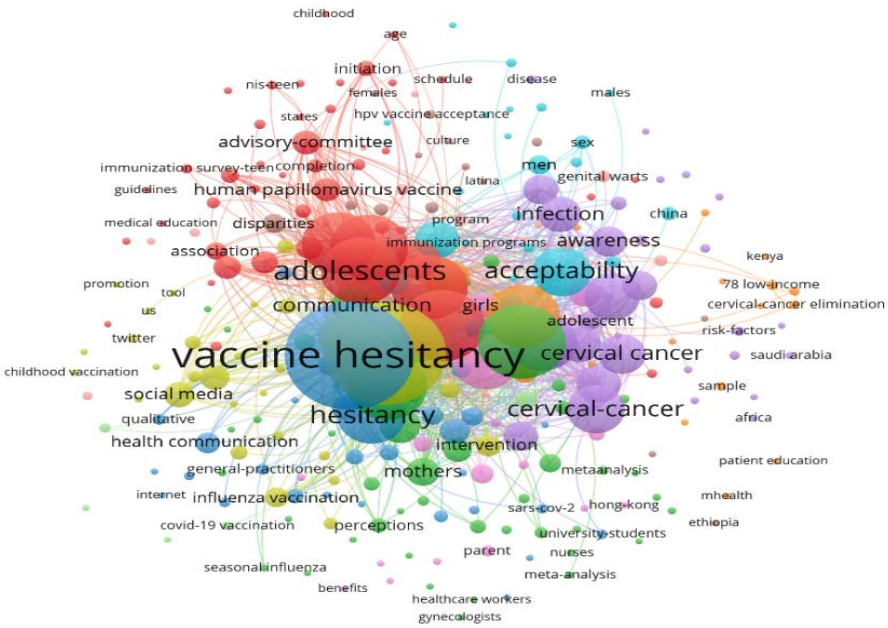
Cluster 1 (9 items): Hungary, Jordan, Kenya, Saudi Arabia, Spain, Sweden, Switzerland, United Arab Emirates, Scotland. Cluster 2 (5 items): Australia, Canada, Denmark, Italy, Japan. Cluster 3 (5 items): Belgium, Nigeria, Norway, South Africa, Turkey. Cluster 4 (4 items): Malaysia, Pakistan, China, Thailand. Cluster 5 (4 items): Brazil, Mexico, South Korea, USA. Cluster 6 (3 items): Ethiopia, Germany, India. Cluster 7 (3 items): France, Mali, Senegal, Cluster 8 (2 items): England, Ireland

Figure 7 Co-authorship network visualization map.



Before visualization, the minimum number of articles and citations for an author was set to 3 and 30, resulting in 53 authors. The visualization was conducted based on the number of articles produced.

Figure 8 Author keywords co-occurrence network visualization map.



Cluster 1 (46 items) – red. Cluster 2 (45 items) – blue. Cluster 3 (36 items) – green. Cluster 4 (35 items) – purple. Cluster 5 (30 items) – orange. Cluster 6 (24 items) – turquoise. Cluster 7 (19 items) – pink. Cluster 8 (18 items) – light green. Cluster 9 (16 items) – light purple. Cluster 10 (13 items) – yellow. Cluster 11 (5 items) – dark green

This study has certain limitations. It relied exclusively on the Web of Science database and covered a limited time period from 2015 to 2024.

This study is based on previous bibliometric analyses and demonstrates global trends at the intersection of vaccination and human papillomavirus over the past decade.

Discussion

This bibliometric study reveals rising global research activity on HPV vaccination hesitancy between 2015 and 2024, underscoring its critical importance to health policy and scientific inquiry. Serious measles outbreaks, such as in US in 2019, serve as warnings about vaccine hesitancy, highlighting the need for improved public understanding and response [7,8]. The development of the first HPV vaccine in 2006 marked a key milestone in fighting cervical cancer, yet global deaths remain high. A major driver of increased scholarly output is the WHO's systematic attention to the causes and prevalence of vaccine hesitancy [9]. This international focus has equipped researchers and policymakers with essential indicators, fostering more research. Comparing spikes in media coverage with peaks in citation counts further suggests that public health crises directly encourage academic interest, spotlighting the dynamic relationship between public awareness, media attention, and research priorities [10].

High-income countries dominate HPV vaccine hesitancy research, with the United States leading in volume, Sweden excelling in per capita and GDP-adjusted output, and Canada achieving the highest number of citations per publication. These trends reflect a growing global recognition of the importance of vaccine hesitancy. However, persistent barriers in low-income regions risk leaving important perspectives and expertise underrepresented, which could potentially limit the effectiveness of global responses. Setting a target for at least 20% of new publications to include co-authorship with LMIC researchers by 2025 strategically addresses imbalances and aims to foster more equitable and impactful global scientific collaboration [11].

Review articles received the highest number of citations compared to research articles. This trend correlates with bibliometric observations in various fields of medicine, as review articles often serve as a reference point for researchers and policymakers due to their comprehensive analysis of existing facts. Canada, Sweden, and South Africa ranked first in terms of citations per publication, demonstrating a significant contribution to science despite their low volume of publications. This

conclusion highlights not only the importance of measuring research productivity but also the necessity of evaluating its influence and impact [13].

The analysis identified the top five journals publishing on vaccine hesitancy as highly ranked according to the Journal Citation Reports. Human Vaccines & Immunotherapeutics, Vaccine, and Vaccines were the most influential, reflecting their specialization in immunization and vaccine research. These journals play a crucial role in disseminating evidence-based information to counter misinformation and mitigate the impact of anti-vaccine movements [14].

Healthcare professionals play a crucial role in countering vaccine hesitancy, most effectively by emphasizing the risks of infection. Evidence supports motivational interviewing as a strategy for increasing HPV vaccination rates, particularly among hesitant parents.[14] Social media's significant influence on public opinion and dissemination of misinformation calls for tailored, platform-specific engagement strategies. A deeper understanding of how TikTok and Facebook amplify or circulate misinformation enables more precise interventions, supporting the overall goal of reducing hesitancy and contributing to a unified public health response informed by this research [15, 16].

The University of Texas System and Indiana University System showed the greatest interest, which may be related to long-standing HPV vaccination programmes and adolescent health initiatives. Authors Dempsey, Verger, and Zimet contributed regularly to the discussion on the acceptability of HPV vaccines, highlighting the key role of a small group of experts in promoting this field. In our study, the most active countries were predominantly from Europe, which correlates with a study that found more than half of the publications were written by authors from North America and Europe, with no publications from Latin America or the Middle East [17,18]. This suggests the need for more inclusive research on geographical imbalances [19].

The results of this study, aligning with prior bibliometric research, further establish the central argument that global inequities and public trust are both key in shaping vaccine hesitancy research agendas. Developed countries act as innovation centers, but successes in countries like Sweden and South Africa indicate that productive engagement can occur beyond traditional hubs. However, structural barriers and trust issues, such as the Nigerian polio vaccine boycott, threaten progress. These findings reinforce the argument that sustainable solutions to vaccine hesitancy require both maintaining scientific momentum and addressing underlying social factors worldwide [20].

There was an important gap in previous studies, as they had insufficient attention to male vaccination and gender differences, with most studies focusing on female patients. Research shows that the inclusion of males in HPV vaccination programs significantly reduces HPV transmission, but there is still little in the existing literature in this area [21].

Visualization of the countries of origin of the authors showed that the United States and European countries are central, while low- and middle-income countries are underrepresented. To address this imbalance, it is recommended that international cooperation and partnerships with low- and middle-income countries be strengthened. High-income country institutions should lead initiatives to remove barriers caused by cultural biases, misinformation, and health system constraints. Additionally, continued support for global initiatives and improvement of WHO/UNICEF reporting systems are recommended to empower LMICs, where cultural barriers and misinformation remain key obstacles to HPV vaccination [22].

This study has several limitations. First, the analysis was limited to the Web of Science database, which may have excluded relevant publications indexed in other sources such as Scopus or PubMed. An estimate suggests that approximately 15-20% of papers on HPV vaccine hesitancy indexed in Scopus may not be present in WoS, highlighting potential gaps in our dataset. Second, only English-language publications were included, which may have introduced language bias and underrepresented research from non-English-speaking countries. Third, bibliometric indicators such as citation counts may not fully capture research quality, as they are influenced by factors including journal visibility and self-citation practices. Despite these limitations, the study provides valuable insights into the global landscape of HPV vaccine hesitancy research.

Conclusion

In summary, this bibliometric analysis highlights a substantial growth of research on HPV vaccine hesitancy over the past decade, dominated by high-income countries but with notable contributions from middle-income regions. While the evidence base continues to expand, it is crucial that stakeholders intensify their support for research in low-resource settings and proactively establish equitable international collaborations. Promptly addressing these disparities is essential for developing effective, globally relevant strategies to overcome vaccine hesitancy and improve HPV vaccination uptake.

Author contributions

Conceptualization: ZHE, ZHZN, and TRT.; **Investigation**: ZHE, ZHZN, TRT. Supervision: ZHE and TRT.; **Methodology**: ZHE, ZHZN and TRT.; **Writing** – review & editing: TRT,

Acknowledgments

The author(s) declare that they have no acknowledgments.

Disclosure

The author(s) report no conflicts of interest in this work.

References

1. World Health Organization. Human papillomavirus vaccines: WHO position paper. Wkly Epidemiol Rec. 2009;84(15):118-131

2. Kyei GK, Kyei EF, Ansong R. HPV Vaccine Hesitancy and Uptake: A Conceptual Analysis Using Rodgers' Evolutionary Approach. J Adv Nurs. 2025;81(5):2368-2381. doi:10.1111/jan.16653

3. World Health Organization. Ten threats to global health in 2019. World Health Organization. Published January 17, 2019. Accessed August 22, 2025. https://www.who.int/news-room/spotlight/ten-threats-to-global-health-in-2019

4. Kocyigit BF, Akyol A. Bibliometric analysis of publication activity in the field of familial Mediterranean fever in 2010-2019: a Scopus-based study. Rheumatol Int. 2021;41(11):2015-2023. doi:10.1007/s00296-021-04988-z

5. Kocyigit BF, Akyol A. Bibliometric and Altmetric Analyses of Publication Activity in the Field of Behcet's Disease in 2010-2019. J Korean Med Sci. 2021;36(32):e207. Published 2021 Aug 16. doi:10.3346/jkms.2021.36.e207

6. Deng D, Shen Y, Li W, Zeng N, Huang Y, Nie X. Challenges of hesitancy in human papillomavirus vaccination: Bibliometric and visual analysis. Int J Health Plann Manage. 2023;38(5):1161-1183. doi:10.1002/hpm.3665

7. Nelson R. US measles outbreak concentrated among unvaccinated children. Lancet Infect Dis. 2019;19(3):248. doi:10.1016/S1473-3099(19)30074-X

8. McDonald R, Ruppert PS, Souto M, et al. Notes from the Field: Measles Outbreaks from Imported Cases in Orthodox Jewish Communities - New York and New Jersey, 2018-2019. MMWR Morb Mortal Wkly Rep. 2019;68(19):444-445. doi:10.15585/mmwr.mm6819a4

9. World Health Organization. Human papillomavirus (HPV) and cervical cancer. World Health Organization. Updated July 24, 2023. Accessed August 22, 2025. https://www.who.int/news-room/fact-sheets/detail/human-papillomavirus-(hpv)-and-cervical-cancer

10. Centers for Disease Control and Prevention. 2009 H1N1 pandemic (H1N1pdm09 virus). Accessed August 22, 2025. https://www.cdc.gov/flu/pandemic-resources/2009-h1n1-pandemic.html

11. Bruni L, Diaz M, Barrionuevo-Rosas L, et al. Global estimates of human papillomavirus vaccination coverage by region and income level: a pooled analysis. Lancet Glob Health. 2016;4(7):e453-e463. doi:10.1016/S2214-109X(16)30099-7

12. Centers for Disease Control and Prevention (CDC):Talking to Parents about Vaccines [https://www.cdc.gov/vaccines/hcp/conversations/conv-materials.html].

13. Chen C, Yang Q, Tian H, et al. Bibliometric and visual analysis of vaccination hesitancy research from 2013 to 2022. Hum Vaccin Immunother. 2023;19(2):2226584. doi:10.1080/21645515.2023.2226584

14. Dempsey AF, Pyrznawoski J, Lockhart S, et al. Effect of a Health Care Professional Communication Training Intervention on Adolescent Human Papillomavirus Vaccination: A Cluster Randomized Clinical Trial. JAMA Pediatr. 2018;172(5):e180016. doi:10.1001/jamapediatrics.2018.0016

15. Ortiz RR, Smith A, Coyne-Beasley T. A systematic literature review to examine the potential for social media to impact HPV vaccine uptake and awareness, knowledge, and attitudes about HPV and HPV vaccination. Hum Vaccin Immunother. 2019;15(7-8):1465-1475. doi:10.1080/21645515.2019.1581543

16. Jessiman-Perreault G, Boucher JC, Kim SY, et al. The Role of Scientific Research in Human Papillomavirus Vaccine Discussions on Twitter: Social Network Analysis. JMIR Infodemiology. 2024;4:e50551. doi:10.2196/50551

17. Sweileh, WM. Global output of research on epidermal parasitic skin diseases from 1967 to 2017. Infect Dis Poverty 7, 74 (2018). https://doi.org/10.1186/s40249-018-0456-x

18. Sweileh, WM. Global research output on HIV/AIDS–related medication adherence from 1980 to 2017. BMC Health Serv Res 18, 765 (2018). https://doi.org/10.1186/s12913-018-3568-x

19. Perkins RB. HPV vaccination: Clinical potential, implementation challenges, and future directions. Hum Vaccin Immunother. 2016;12(6):1327-1331. doi:10.1080/21645515.2016.1177680

20. Cooper S, Betsch C, Sambala EZ, Mchiza N, Wiysonge CS. Vaccine hesitancy - a potential threat to the achievements of vaccination programmes in Africa. Hum Vaccin Immunother. 2018;14(10):2355-2357. doi:10.1080/21645515.2018.1460987

21. Rosado C, Fernandes ÂR, Rodrigues AG, Lisboa C. Impact of Human Papillomavirus Vaccination on Male Disease: A Systematic Review. Vaccines (Basel). 2023;11(6):1083. Published 2023 Jun 9. doi:10.3390/vaccines11061083

22. Lane S, MacDonald NE, Marti M, Dumolard L. Vaccine hesitancy around the globe: Analysis of three years of WHO/UNICEF Joint Reporting Form data-2015-2017. Vaccine. 2018;36(26):3861-3867. doi:10.1016/j.vaccine.2018.03.063

УДК 616.381:616.12

Кумаров М.К., Джолдасов О.К.,Жапбархан Т.Ж., Ағабек А.Т., Әмзеханов М.Қ.,Алдешев А.А.

АО «Южно-Казахстанская медицинская академия», Шымкент, Казахстан

ПСЕВДОПЕРИТОНИТ У ПАЦИЕНТА С ТЕРМИНАЛЬНОЙ СТАДИЕЙ ХРОНИЧЕСКОЙ БОЛЕЗНИ ПОЧЕК: КЛИНИЧЕСКИЙ СЛУЧАЙ

Аннотация

Введение*. Острый панкреатит варьирует от легкой самоограниченной формы до тяжелого некротизирующего панкреатита с полиорганной недостаточностью. При тяжелом панкреатите реактивное раздражение брюшины может имитировать клиническую картину перитонита, формируя так называемый псевдоперитонит. У пациентов с терминальной хронической болезнью почек клинические симптомы, лабораторные показатели и иммунный ответ могут изменяться под влиянием уремии и заместительной почечной терапии, что затрудняет своевременную диагностику и выбор лечебной тактики.*

Описание случая*. В работе представлен клинический случай 49-летнего пациента с хронической болезнью почек 5 стадии, получающего программный гемодиализ, который был госпитализирован с клиникой острого живота. У пациента отмечались интенсивная диффузная боль в животе, напряжение мышц передней брюшной стенки, положительный симптом Щеткина–Блюмберга, отсутствие кишечной перистальтики, а также выраженная системная воспалительная реакция. Основные клинические проявления, выявленные при поступлении, представлены на рисунке 1. На основании совокупности клинических, лабораторных и инструментальных данных был заподозрен тяжелый панкреатит с псевдоперитонеальным синдромом и вероятным инфицированным внутрибрюшным процессом. В экстренном порядке была выполнена лапаротомия с вскрытием и дренированием сальниковой сумки, марсупиализацией и санацией брюшной полости. В послеоперационном периоде проводились интенсивная терапия, программный гемодиализ, коррекция коагулопатии, нутритивная поддержка, трансфузия компонентов крови и антибактериальная терапия с учетом результатов микробиологического исследования. На фоне лечения достигнута положительная клиническая динамика, и пациент был выписан в удовлетворительном состоянии.*

***Заключение**. Псевдоперитонит при тяжелом панкреатите может полностью имитировать хирургический перитонит, особенно у пациентов с терминальной хронической болезнью почек. Представленный случай подчеркивает необходимость ранней междисциплинарной оценки, своевременного решения вопроса о хирургической санации при подозрении на инфекционный процесс и адаптации терапии к режиму гемодиализа.*

***Ключевые слова**: псевдоперитонит; панкреонекроз; перитонит; хроническая болезнь почек; гемодиализ; Pseudomonas aeruginosa.*

Кумаров М.К., Джолдасов О.К.,Жапбархан Т.Ж., Ағабек А.Т., Әмзеханов М.Қ.,Алдешев А.А.

«Оңтүстік Қазақстан медицина академиясы» АҚ, Шымкент, Қазақстан

БҮЙРЕКТІҢ СОҢҒЫ САТЫДАҒЫ СОЗЫЛМАЛЫ АУРУЫ БАР НАУҚАСТАҒЫ ПСЕВДОПЕРИТОНИТ: КЛИНИКАЛЫҚ ЖАҒДАЙ

Аңдатпа

***Кіріспе.** Жедел панкреатит жеңіл, өздігінен шектелетін түрден бастап, көпағзалық жеткіліксіздікпен жүретін ауыр некроздаушы панкреатитке дейін әртүрлі ағымда көрінуі мүмкін. Ауыр панкреатит кезінде ішперденің реактивті тітіркенуі перитониттің клиникалық көрінісіне ұқсап, псевдоперитонит деп аталатын жағдайды қалыптастыруы мүмкін. Бүйректің терминальді сатыдағы созылмалы ауруы бар пациенттерде уремия мен бүйрек орнын басушы терапияның әсерінен клиникалық симптомдар, зертханалық көрсеткіштер және иммундық жауап өзгеруі мүмкін, бұл дер кезінде диагноз қоюды және ем тактикасын таңдауды қиындатады.*

***Жағдай сипаттамасы.** Мақалада бағдарламалық гемодиализ қабылдайтын, созылмалы бүйрек ауруының 5 сатысы бар 49 жастағы пациенттің клиникалық жағдайы ұсынылған. Науқас жедел іш клиникасымен ауруханаға жатқызылған. Пациентте іштің диффузды қатты ауыруы, алдыңғы құрсақ қабырғасы бұлшықеттерінің кернеуі, Щеткин–Блюмберг симптомы оң болуы, ішек перистальтикасының болмауы, сондай-ақ айқын жүйелік қабыну реакциясы анықталды. Қабылдау кезіндегі негізгі клиникалық көріністер 1-суретте көрсетілген. Клиникалық, зертханалық және аспаптық деректердің жиынтығы негізінде псевдоперитонеальді синдроммен және ықтимал инфицирленген құрсақішілік үрдіспен қатар жүретін ауыр панкреатитке күдік тудырылды. Шұғыл түрде лапаротомия жасалып, шарбы қапшығы ашылып дренаждалды, марсупиализация және құрсақ қуысына*

санация жүргізілді. Операциядан кейінгі кезеңде қарқынды терапия, бағдарламалық гемодиализ, коагулопатияны түзету, нутритивтік қолдау, қан компоненттерін трансфузиялау және микробиологиялық зерттеу нәтижелерін ескере отырып антибактериялық терапия жүргізілді. Ем аясында оң клиникалық динамикаға қол жеткізіліп, пациент қанағаттанарлық жағдайда шығарылды.

***Қорытынды**. Ауыр панкреатит кезіндегі псевдоперитонит, әсіресе бүйректің терминальді сатыдағы созылмалы ауруы бар пациенттерде, хирургиялық перитонитті толық имитациялауы мүмкін. Ұсынылған клиникалық жағдай ерте пәнаралық бағалаудың, инфекциялық үдеріс күдігінде хирургиялық санация мәселесін дер кезінде шешудің және емді гемодиализ режиміне бейімдеудің маңыздылығын көрсетеді.*

***Түйін сөздер:** псевдоперитонит; панкреонекроз; перитонит; созылмалы бүйрек ауруы; гемодиализ; Pseudomonas aeruginosa.*

Kumarov M.K., Dzholdasov O.K., Zhapbarhan T.Zh., Agabek A.T., Amzekhanov M.K., Aldeshev A.A.

JSC «South Kazakhstan medical academy», Shymkent, Kazakhstan

PSEUDOPERITONITIS IN A PATIENT WITH END-STAGE CHRONIC KIDNEY DISEASE: A CLINICAL CASE

Abstract

***Introduction:** Acute pancreatitis ranges from mild self-limited form to severe necrotizing pancreatitis with multiple organ failure. In severe pancreatitis, reactive irritation of the peritoneum can mimic the clinical picture of peritonitis, forming the so-called pseudoperitonitis. In patients with terminal chronic kidney disease, clinical symptoms, laboratory parameters, and immune response may be altered due to uremia and renal replacement therapy, which makes timely diagnosis and choice of treatment tactics difficult.*

***Description of the case.** The paper presents a clinical case of a 49-year-old patient with stage 5 chronic kidney disease undergoing programmed hemodialysis, who was hospitalized with an acute abdominal clinic. The patient had intense diffuse abdominal pain, muscle tension of the anterior abdominal wall, positive Shchetkin–Blumberg symptom, absence of intestinal motility, as well as a pronounced systemic inflammatory reaction. The main clinical manifestation observed at admission are presented in Figure 1. According to the combination of clinical, laboratory and instrumental data, severe pancreatitis with pseudoperitoneal syndrome and a probable infected*

intra-abdominal process is suspected. Laparotomy with opening and drainage of the omentum, marsupialization and sanitation of the abdominal cavity was urgently performed. In the postoperative period, intensive therapy, programmed hemodialysis, correction of coagulopathy, nutritional support, transfusion of blood components and antibacterial therapy were performed, taking into account the results of microbiological examination. Positive clinical dynamics was achieved during the treatment, and the patient was discharged in a satisfactory condition.

Conclusion. *Pseudoperitonitis in severe pancreatitis can completely mimic surgical peritonitis, especially in patients with terminal chronic kidney disease. The presented case highlights the need for an early interdisciplinary assessment, timely resolution of the issue of surgical rehabilitation in case of suspected infection, and adaptation of therapy to the hemodialysis regimen.*

Key words: *pseudoperitonitis; pancreatic necrosis; peritonitis; chronic kidney disease; hemodialysis; Pseudomonas aeruginosa.*

Introduction

Acute pancreatitis is one of the most clinically variable acute diseases of the abdominal cavity. Its course may be limited to a mild interstitial form, but in some cases a severe necrotic process develops with a pronounced systemic inflammatory reaction, multiple organ failure and high mortality. The current stratification of severity and complications of acute pancreatitis is based on the revised 2012 Atlanta Classification, which is crucial for choosing optimal treatment tactics [1-3].

In severe pancreatitis, reactive irritation of the peritoneum often occurs, clinically mimicking the picture of common peritonitis. In such situations, pseudoperitonitis may form, when the severity of peritoneal symptoms does not always reflect the presence of true surgical peritonitis, but requires urgent differential diagnosis [4, 5]. Additional difficulties arise in patients with terminal chronic kidney disease, since uremia, anuria, hemostasis disorders, chronic inflammation, and programmed hemodialysis can distort both the clinical and laboratory picture of the acute disease [6, 7].

The purpose of this work is to present a clinical case of pseudoperitonitis in a patient with total pancreatic necrosis and end—stage chronic kidney disease, as well as to analyze the diagnostic difficulties, surgical tactics and features of antimicrobial treatment in this clinical situation.

Patient Information

Patient R., 49 years old, was hospitalized on an emergency basis with complaints of sudden intense abdominal pain, mainly in the epigastric region, with rapid spread throughout the abdomen,

nausea, repeated vomiting and progressive deterioration of the general condition. According to the medical history, the onset of the disease was noted approximately 12 hours before admission to the hospital.

It is known from the concomitant pathology that the patient had been suffering from stage 5 chronic kidney disease for a long time and had been receiving programmed hemodialysis since 11/08/2012. He also had a history of stage III hypertension. The basic therapy included treatment related to programmed hemodialysis and blood pressure control. According to available data, the medical history and ongoing drug therapy are not reflected in detail in the presented materials. The allergological history did not contain any clinically significant features. Information about bad habits, family history, and other social risk factors in medical records was limited.

Clinical data

Upon admission on 02/18/2025, the patient's condition was assessed as severe. There were signs of pronounced endogenous intoxication. Consciousness was preserved, the situation was forced. The skin is pale. The blood pressure was 120/70 mmHg, the heart rate was about 100 beats per minute, and the body temperature was 36.9 °C.

Examination of the abdomen revealed moderate bloating, severe pain on palpation in all parts, pronounced tension of the muscles of the anterior abdominal wall and a positive Shchetkin–Blumberg symptom throughout the abdomen. Peristalsis was not listened to, stool and gas retention were noted, and clinical signs of intestinal paresis were noted. There was no diuresis, which corresponded to a combination of an acute process with the initial terminal stage of CKD and anuria.

Thus, already at the stage of the initial examination, the clinical picture corresponded to acute abdominal syndrome with pronounced peritoneal symptoms and a systemic inflammatory reaction.

Chronology of the clinical case

11/08/2012 — the beginning of programmed hemodialysis for stage 5 chronic kidney disease.

12 hours before hospitalization — sudden onset of intense abdominal pain, nausea, vomiting, deterioration of general condition.

02/18/2025 — admission to the hospital, examination, detection of peritoneal syndrome and signs of severe acute abdominal disease.

On the night of 02/19/2025— an emergency laparotomy was performed with opening and drainage of the omentum, marsupialization and sanitation of the abdominal cavity.

The postoperative period includes treatment in the Department of anesthesiology, intensive care and intensive care, hemodialysis, correction of coagulopathy, electrolyte disorders, antibacterial and nutritional therapy.

03/12/2025 — the patient is discharged in a satisfactory condition with recommendations for outpatient follow-up and continued dialysis.

Diagnostic assessment

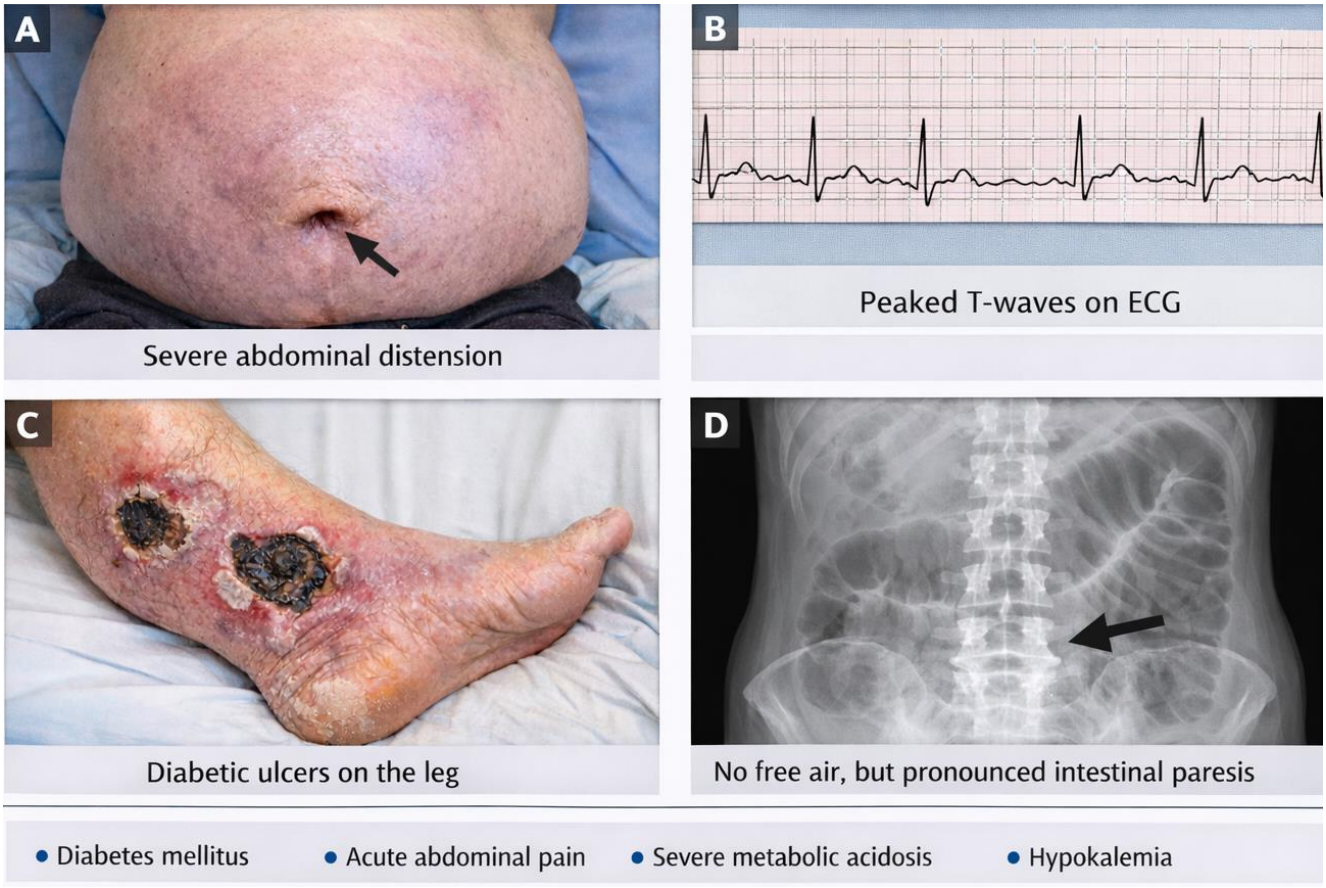
According to the laboratory study, the patient showed pronounced signs of an inflammatory process and metabolic disorders. Leukocytosis reached 19.5×109/l, the level of C-reactive protein increased to 206.8 mg/l. Hypoalbuminemia was detected in the range of 21-27 g/l. The activity of amylase varied and reached about 160 U/l. The indicators of nitrogen metabolism were significantly increased: creatinine on different days increased to about 1002 mmol / l, urea — to about 35 mmol/ l, which was interpreted taking into account the initial terminal stage of chronic kidney disease. A sharp increase in the D-dimer to about 39,586 ng/ml was also detected. The coagulogram showed an increase in INR to 2.4 and an increase in fibrinogen to 4.5–6.17 g/l. Anemia and the need for transfusion therapy were observed.

Instrumental diagnostics included ultrasound examination of the abdominal organs, which revealed diffuse changes in the pancreatic parenchyma and signs of fluid accumulations. Ultrasound examination of the kidneys showed signs of secondary wrinkling and the presence of cysts. Chest X-ray revealed focal changes corresponding to pneumonia of the lower lobe of the right lung, as well as fractures of the ribs on the right.

From a clinical point of view, the most difficult was the differential diagnosis between true surgical peritonitis and pseudoperitonitis on the background of severe pancreatitis. The patient had typical signs of peritoneal syndrome: diffuse intense abdominal pain, abdominal muscle tension, positive Shchetkin–Blumberg symptom, lack of peristalsis, intestinal paresis and flatulence. However, the presence of ultrasound changes in the pancreas, a moderate increase in amylase, and a pronounced systemic inflammatory reaction indicated severe pancreatitis. At the same time, the patient had a focus of intra-abdominal infection, described as an abscess of the omentum sac, which actually combined the features of reactive pseudoperitonitis and a true infected intra-abdominal process.

An additional diagnostic problem was caused by the presence of terminal CKD and hemodialysis, since uremia, anuria, chronic hemostasis disorders and features of the immune response could mask or distort the severity of the acute process. In the presented situation, the

diagnosis was based on a comprehensive assessment of the clinical picture, laboratory parameters, instrumental examination data and intraoperative findings.



On the night of 02/19/2025, the patient underwent emergency surgery — laparotomy with opening and drainage of the omentum, marsupialization and sanitation of the abdominal cavity. The choice of open surgical tactics was determined by the severity of the condition, expressed by the clinic of peritoneal syndrome, increasing intoxication and a high probability of an infected intra-abdominal process.

After the operation, the patient was transferred to the Department of Anesthesiology, intensive care and intensive care. In conditions of acute respiratory viral infection, complex treatment was carried out, including intensive infusion therapy taking into account the water balance, programmed hemodialysis, correction of electrolyte disorders, parenteral nutrition, transfusion of blood components according to indications and round-the-clock monitoring of vital functions. This made it possible to monitor the patient's condition, prevent the development of multiple organ failure and maintain the functions of vital organs in the critical postoperative period.

Taking into account the severity of the condition and the risk of infectious complications, broad-spectrum antibacterial therapy was performed, followed by correction based on the results of a microbiological study. After Pseudomonas aeruginosa was isolated, the treatment regimen was adapted according to the sensitivity of the pathogen and the pharmacokinetic characteristics of the hemodialysis patient. Special attention was paid to the correction of doses and intervals of administration of antibacterial drugs against the background of severe renal insufficiency and dialysis dependence.

Observation and outcomes

In the postoperative period, comprehensive management in the ICAR played a key role in stabilizing the condition. Hemodialysis, maintenance of water and electrolyte balance, correction of coagulopathy, nutritional support, antibacterial therapy and dynamic monitoring of the functions of the cardiovascular and respiratory systems were performed. During treatment, there was a positive clinical trend with a decrease in the severity of the inflammatory response and an improvement in the general condition.

By the time of her discharge on 12.03.2025, the patient's condition was considered satisfactory. Intestinal motility was restored, pain decreased, the temperature profile returned to normal, the postoperative wound was clean, without signs of active inflammation. The patient was given recommendations for further outpatient follow-up and continuation of programmed hemodialysis according to the established schedule.

Discussion

The presented case demonstrates the high complexity of the diagnosis of pseudoperitonitis in a patient with severe pancreatitis on the background of terminal chronic kidney disease. The clinical picture of an acute abdomen with pronounced symptoms of peritoneal irritation in such cases may be due to both sterile reactive inflammation and an infected intra-abdominal process requiring emergency surgery [8].

As rightly noted in the source material, when the patient's condition is stabilized, computed tomography of the abdominal organs with contrast is the optimal imaging method, which allows detecting necrosis, fluid accumulations, abscesses and signs of infection. However, in conditions of decompensation, severe intoxication and suspicion of a progressive intra-abdominal process, surgical intervention remains a justified and sometimes life-saving solution [9]. In this case, the presence of an abscess of the omentum sac, severe peritoneal syndrome and severe general condition led to the choice of emergency laparotomy [10].

Modern approaches to the treatment of infected pancreatic necrosis are often focused on a minimally invasive step-up strategy. Nevertheless, open surgical rehabilitation remains important in the case of widespread fibrinous-purulent process, severe intoxication and the inability to postpone the intervention. The presented clinical case confirms that an individualized approach, taking into account the real clinical status of the patient, is of fundamental importance [11].

Of particular interest is the combination of severe pancreatitis with terminal CKD. Patients in this category have an increased risk of severe acute pancreatitis, infectious complications, and nosocomial mortality. In addition, the initial uremia, anuria, tendency to coagulopathy, and features of the immune response make it difficult to interpret laboratory data and clinical dynamics. This requires the participation of a multidisciplinary team, including surgeons, intensive care physicians, nephrologists, and antimicrobial therapists [12].

The isolation of Pseudomonas aeruginosa in this case highlights the problem of hospital flora in severe patients, especially in intensive care and invasive interventions. In patients on hemodialysis, the choice of antibacterial therapy should take into account not only the sensitivity profile of the pathogen, but also the dialyzability of drugs, the need for dose adjustment and administration intervals, as well as the risk of accumulation of toxic metabolites. Therefore, targeted antibacterial therapy with further de-escalation is an important component of successful treatment [13].

Thus, the clinical case reflects not only the diagnostic dilemma between pseudoperitonitis and true peritonitis, but also the need to adapt standard approaches to the management of acute pancreatitis in a patient with severe concomitant nephrological pathology [14, 15].

The patient's perspective

According to the patient, the disease started suddenly and was accompanied by severe abdominal pain, pronounced weakness and a feeling of fear due to the severity of the condition. After the surgical treatment and intensive therapy, she noted a gradual decrease in pain and improved well-being. By the time of discharge, the patient reported significant improvement in her condition and readiness to continue further treatment and hemodialysis under the supervision of specialists.

Conclusion

Pseudoperitonitis is an important option for differential diagnosis in severe pancreatitis, since the clinical picture can completely mimic surgical peritonitis. In patients with end-stage chronic kidney disease, the diagnostic search is particularly difficult due to uremia, anuria, hemostasis

disorders and the effect of programmed hemodialysis on laboratory parameters and clinical reactivity of the body.

The presented case shows that timely clinical assessment, early decision-making on surgical rehabilitation in case of suspected infection, intensive therapy and adaptation of antibacterial treatment to the hemodialysis regimen can ensure a favorable outcome even in extremely severe patients.

Informed consent

Informed consent was obtained from the patient to use anonymized clinical data for scientific purposes and to publish the clinical case.

Author contribution

Conceptualization: MKK and AAA. **Investigation:** MKK, TZhZh, and MKA. **Supervision:** AAA and AAT. **Methodology:** MKK and AAA. **Writing – original draft:** MKK, TZhZh, and MKA. **Writing – review & editing:** AAA, DOK and TZhZh.

Funding: None.

Declarations

Conflict of interest: The authors declare no conflicts of interest.

Disclaimer: The authors state that no part of this report has been copied from or published elsewhere, either in whole or in part.

References

1. Banks PA, Bollen TL, Dervenis C, et al. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013;62(1):102-111. doi:10.1136/gutjnl-2012-302779.

2. Thoeni RF. The revised Atlanta classification of acute pancreatitis: its importance for the radiologist and its effect on treatment. Radiology. 2012;262(3):751-764. doi:10.1148/radiol.11110947.

3. Sheu Y, Furlan A, Almusa O, Papachristou GI, Bae KT. The revised Atlanta classification for acute pancreatitis: a CT imaging guide for radiologists. Emerg Radiol. 2012;19(3):237-243. doi:10.1007/s10140-011-1001-4.

4. Zaheer A, Singh VK, Qureshi RO, Fishman EK. The revised Atlanta classification for acute pancreatitis: updates in imaging terminology and guidelines. Abdom Imaging. 2013;38(1):125-136. doi:10.1007/s00261-012-9908-0.

5. Foster BR, Jensen KK, Bakis G, Shaaban AM, Coakley FV. Revised Atlanta Classification for Acute Pancreatitis: a pictorial essay. Radiographics. 2016;36(3):675-687. doi:10.1148/rg.2016150097.

6. Chen HJ, Wang JJ, Tsay WI, et al. Epidemiology and outcome of acute pancreatitis in end-stage renal disease dialysis patients: a 10-year national cohort study. Nephrol Dial Transplant. 2017;32(10):1731-1736. doi:10.1093/ndt/gfw335.

7. Barbara M, Tsen A, Rosenkranz L. Acute pancreatitis in chronic dialysis patients. Pancreas. 2018;47(8):946-951. doi:10.1097/MPA.0000000000001119.

8. Leppäniemi A, Tolonen M, Tarasconi A, et al. 2019 WSES guidelines for the management of severe acute pancreatitis. World J Emerg Surg. 2019;14:27. doi:10.1186/s13017-019-0247-0.

9. van Santvoort HC, Besselink MG, Bakker OJ, et al. A step-up approach or open necrosectomy for necrotizing pancreatitis. N Engl J Med. 2010;362(16):1491-1502. doi:10.1056/NEJMoa0908821.

10. van Brunschot S, van Grinsven J, van Santvoort HC, et al. Endoscopic or surgical step-up approach for infected necrotising pancreatitis: a multicentre randomised trial. Lancet. 2018;391(10115):51-58. doi:10.1016/S0140-6736(17)32404-2.

11. Besselink MGH. The step-up approach to infected necrotizing pancreatitis: delay, drain, debride. Dig Liver Dis. 2011;43(6):421-422. doi:10.1016/j.dld.2011.04.001.

12. Garg PK, Singh VP. Organ failure due to systemic injury in acute pancreatitis. Gastroenterology. 2019;156(7):2008-2023. doi:10.1053/j.gastro.2018.12.041.

13. Mowbray NG, Ben-Ismaeil B, Hammoda M, Shingler G, Al-Sarireh B. The microbiology of infected pancreatic necrosis. Hepatobiliary Pancreat Dis Int. 2018;17(5):456-460. doi:10.1016/j.hbpd.2018.08.006.

14. Schepers NJ, Bakker OJ, Besselink MG, et al. Impact of characteristics of organ failure and infected necrosis on mortality in necrotising pancreatitis. Gut. 2019;68(6):1044-1051. doi:10.1136/gutjnl-2017-314657.

15. Guo Q, Li A, Xia Q, et al. The role of organ failure and infection in necrotizing pancreatitis: a prospective study. Ann Surg. 2014;259(6):1201-1207. doi:10.1097/SLA.0000000000000264.

UDC 616.379-008.64

Asankulova M.[1]; Kamitbekova Zh.[2]; Pavlova N.[3]; Bazarova A.[4]

[1] NJSC "Astana Medical University", endocrinologist, Astana, Kazakhstan.
asankulovam97@gmail.com ORCID: https://orcid.org/0009-0003-9715-7062

[2] Head of the Department of Endocrinology No. 1 of the Multidisciplinary City Hospital, doctor of the highest category, endocrinologist, Astana, Kazakhstan.
zhanarkamitbekova@gmail.com ORCID: https://orcid.org/0009-0006-3918-9703

[3] Head of the Department of Internal Expertise and Patient Support service , doctor of the highest category, therapist, GKP at the Municipal Hospital No. 1 of the Akimat of Astana
nata2829@mail.ru ORCID: https://orcid.org/0009-0000-0193-5092

[4] Candidate of Medical Sciences, Professor of the Department of NJSC "Astana Medical University", doctor of the highest category, endocrinologist, Astana, Kazakhstan.
bazarova.a@gmail.com ORCID: https://orcid.org/0000-0002-6518-7174

NEW-ONSET DIABETES AFTER COVID-19: EMERGING CONCEPTS AND OPEN QUESTIONS

Abstract

Following the COVID-19 pandemic, accumulating evidence has demonstrated the development of disturbances in glucose metabolism among individuals without a prior diagnosis of diabetes. The term "new-onset diabetes after COVID-19" has been introduced to describe this phenomenon. Despite the growing body of literature, substantial inconsistencies remain regarding the incidence, underlying mechanisms, and clinical significance of new-onset diabetes after COVID-19. The objective of this review was to synthesize current evidence on the epidemiology, risk factors, pathogenesis, and diagnostic challenges of this condition, and to identify unresolved issues and clinical implications. A narrative review of the literature was conducted, focusing on studies investigating glucose metabolism disturbances following SARS-CoV-2 infection. The incidence of new-onset diabetes after COVID-19 is estimated at approximately 1.3-1.5% among individuals with prior COVID-19. The risk of developing diabetes after infection is increased by 1.4-1.7 times compared with non-infected populations. Major risk factors include severe COVID-19, older age, male sex, obesity, and prediabetes. Evidence suggests that, in many cases, new-onset diabetes after COVID-19 represents an accelerated manifestation of previously subclinical metabolic dysfunction. The pathogenesis is multifactorial and involves systemic inflammation and insulin resistance, as well as potential β-cell dysfunction and autoimmune processes. Significant

diagnostic challenges arise from the lack of a unified definition, variability in diagnostic criteria, and the difficulty in distinguishing true diabetes from stress-induced hyperglycemia. Identification of high-risk groups and longitudinal monitoring of glycemic parameters in patients after COVID-19 are essential. Further research is needed to standardize diagnostic criteria and to clarify long-term outcomes.

Keywords: *COVID-19; SARS-CoV-2; Diabetes Mellitus, Type 2; Hyperglycemia; Insulin Resistance; Prediabetic State; Risk Factors; Disease Progression*

Асанқұлова М.[1]; Камитбекова Ж.[2]; Павлова Н.[3]; Базарова А.[4]

[1] НАО «Медицинский университет Астана», врач-эндокринолог, г. Астана, Казахстан. asankulovam97@gmail.com *ORCID:* https://orcid.org/0009-0003-9715-7062

[2] Заведующая отделением эндокринологии №1 Многопрофильной городской больницы, врач высшей категории, эндокринолог, г. Астана, Казахстан. zhanarkamitbekova@gmail.com *ORCID:* https://orcid.org/0009-0006-3918-9703

[3] Начальник отдела внутренней экспертизы и службы поддержки пациентов , врач высшей категории, терапевт, ГКП на ПХВ «Городская больница №1» акимата города Астана nata2829@mail.ru *ORCID:* https://orcid.org/0009-0000-0193-5092

[4] Кандидат медицинских наук, профессор кафедры НАО «Медицинский университет Астана», врач высшей категории, эндокринолог, г. Астана, Казахстан. bazarova.a@gmail.com *ORCID:* https://orcid.org/0000-0002-6518-7174

ВПЕРВЫЕ ВОЗНИКШИЙ ДИАБЕТ ПОСЛЕ COVID-19: НОВЫЕ КОНЦЕПЦИИ И ОТКРЫТЫЕ ВОПРОСЫ

Аннотация

После пандемии COVID-19 накопились данные о развитии нарушений углеводного обмена у пациентов без ранее диагностированного диабета. Для описания данного феномена используется термин «впервые возникший диабет после COVID-19». Несмотря на растущее число исследований, остаются значительные противоречия в оценке частоты, механизмов и клинического значения этого состояния. Целью настоящего обзора являлось обобщение современных данных об эпидемиологии, факторах риска, патогенезе и диагностических трудностях данного состояния, а также выявление нерешённых вопросов и практических импликаций. Проведен нарративный обзор публикаций, посвящённых развитию нарушений углеводного обмена после инфекции SARS-CoV-2. Частота впервые

возникшего диабета после COVID-19 составляет около 1,3-1,5% среди перенёсших инфекцию. Риск развития диабета после инфекции повышен в 1,4-1,7 раза по сравнению с неинфицированной популяцией. Наиболее значимыми факторами риска являются тяжёлое течение COVID-19, пожилой возраст, мужской пол, ожирение и наличие предиабета. Показано, что во многих случаях впервые возникший диабет после COVID-19 отражает ускоренную манифестацию ранее субклинических метаболических нарушений. Патогенез носит мультифакторный характер и включает системное воспаление и инсулинорезистентность, а также потенциальное поражение β-клеток и аутоиммунные процессы. Существенные диагностические сложности связаны с отсутствием единого определения, вариабельностью критериев и трудностью дифференциации между истинным диабетом и стресс-индуцированной гипергликемией. Важное значение имеет выделение групп высокого риска и проведение динамического наблюдения пациентов после COVID-19 с контролем гликемических показателей. Необходимы дальнейшие исследования для стандартизации диагностических критериев и уточнения долгосрочных исходов.

***Ключевые слова**: COVID-19; SARS-CoV-2; сахарный диабет 2 типа; гипергликемия; инсулинорезистентность; предиабет; факторы риска.*

Асанқұлова М.[1]; Камитбекова Ж.[2]; Павлова Н.[3]; Базарова А.[4]

[1] «Астана медицина университеті» КЕАҚ, дәрігер-эндокринолог, Астана , Қазақстан. asankulovam97@gmail.com ORCID: https://orcid.org/0009-0003-9715-7062

[2] №1 көпсалалы қалалық ауруханаңың Эндокринология бөлімшесінің меңгерушісі, жоғары санатты дәрігер, эндокринолог, Астана қ., Қазақстан. zhanarkamitbekova@gmail.com ORCID: https://orcid.org/0009-0006-3918-9703

[3] Ішкі сараптама және пациенттерді қолдау қызметі бөлімінің бастығы , Жоғары санатты дәрігер, терапевт, Астана қаласы әкімдігінің "№1 қалалық аурухана" ШЖҚ МКК nata2829@mail.ru ORCID: https://orcid.org/0009-0000-0193-5092

[4] Медицина ғылымдарының кандидаты, "Астана медицина университеті" КЕАҚ кафедрасының профессоры, Жоғары санатты дәрігер, эндокринолог, Астана қ., Қазақстан. bazarova.a@gmail.com ORCID: https://orcid.org/0000-0002-6518-7174

COVID-19-ДАН КЕЙІН АЛҒАШ РЕТ ПАЙДА БОЛҒАН ДИАБЕТ: ЖАҢА ТҰЖЫРЫМДАМАЛАР ЖӘНЕ АШЫҚ СҰРАҚТАР

Аңдатпа

COVID-19 пандемиясынан кейін бұрын қант диабеті диагнозы қойылмаған пациенттерде көмірсу алмасуының бұзылыстарының дамуы туралы деректер жинақталды. Бұл құбылысты сипаттау үшін «COVID-19-дан кейін алғаш рет пайда болған диабет» термині енгізілді. Зерттеулер санының артуына қарамастан, бұл жағдайдың жиілігі, патогенезі және клиникалық маңыздылығы бойынша айтарлықтай қайшылықтар сақталуда. Осы шолудың мақсаты - аталған жағдайдың эпидемиологиясы, қауіп факторлары, патогенезі және диагностикалық қиындықтары жөніндегі қазіргі деректерді жүйелеу, сондай-ақ шешілмеген мәселелер мен клиникалық маңызын анықтау. Әдебиетке нарративті шолу жүргізілді, онда SARS-CoV-2 инфекциясынан кейінгі көмірсу алмасуының бұзылыстарына арналған зерттеулер талданды. COVID-19-дан кейін алғаш рет пайда болған диабеттің жиілігі инфекцияны өткерген адамдар арасында шамамен 1,3-1,5% құрайды. Инфекциядан кейін диабеттің даму қаупі жұқтырмаған популяциямен салыстырғанда 1,4-1,7 есе жоғары. Негізгі қауіп факторларына COVID-19-дың ауыр ағымы, егде жас, ер жынысы, семіздік және предиабет жатады. Қолда бар деректер көптеген жағдайларда бұл диабет бұрын байқалмаған (субклиникалық) метаболикалық бұзылыстардың жедел көрініс беруін көрсететінін айғақтайды. Патогенезі көпфакторлы сипатқа ие және жүйелік қабыну мен инсулинге төзімділікті, сондай-ақ β-жасушалардың ықтимал зақымдануын және аутоиммундық үдерістерді қамтиды. Маңызды диагностикалық қиындықтар бірыңғай анықтаманың болмауымен, диагностикалық критерийлердің әртүрлілігімен және шынайы диабетті стресс-индуцирленген гипергликемиядан ажыратудың күрделілігімен байланысты. COVID-19-дан кейін пациенттерді динамикалық бақылау және гликемиялық көрсеткіштерді мониторингтеу, әсіресе қауіп тобына жататын адамдарда, аса маңызды. Диагностикалық критерийлерді стандарттау және ұзақ мерзімді нәтижелерді нақтылау үшін қосымша зерттеулер қажет.

Түйін сөздер: *COVID-19; SARS-CoV-2; 2 типті қант диабеті; гипергликемия; инсулинге төзімділік; предиабет; қауіп факторлар*

Введение

Пандемия COVID-19, вызванная вирусом SARS-CoV-2, стала одним из крупнейших глобальных вызовов для системы здравоохранения 21-го века и оказала значительное влияние не только на респираторную, но и на эндокринную систему человека [1,2]. В последние годы внимание клиницистов и исследователей всё чаще привлекает рост числа случаев впервые возникшего диабета у пациентов после COVID-19 (NODAC). Согласно данным систематического обзора и метаанализа Lai et al. (2022), включившего 11 ретроспективных когортных исследований с общей численностью более 47,1 млн человек, риск развития диабета после перенесённой инфекции COVID-19 был на 64 % выше по сравнению с лицами без данной инфекции [3].

Накопленные данные свидетельствуют о том, что COVID-19 может сопровождаться нарушениями углеводного обмена, включая гипергликемию, ухудшение гликемического контроля и развитие острых метаболических осложнений [4]. При этом у части пациентов без ранее диагностированных нарушений углеводного обмена наблюдается стойкая гипергликемия и манифестация диабета после перенесённой инфекции, что и формирует основу концепции NODAC. Важно отметить, что термин NODAC используется как рабочее понятие и не отражает единого патогенетического механизма: в его рамках могут сосуществовать различные клинические состояния, включая ранее недиагностированный сахарный диабет, стресс-индуцированную гипергликемию, последствия терапии глюкокортикоидами, а также потенциальные аутоиммунные процессы [5]. В связи с этим NODAC следует рассматривать как гетерогенное состояние, требующее осторожной клинической интерпретации.

Среди предложенных механизмов развития NODAC, объясняющих наблюдаемые нарушения углеводного обмена, особое внимание уделяется возможному поражению β-клеток поджелудочной железы. Экспериментальные и клинические данные свидетельствуют о способности SARS-CoV-2 инфицировать клетки панкреатической ткани, что может сопровождаться нарушением секреции инсулина и развитием гипергликемии [6,7]. Однако, несмотря на рост числа публикаций, механизмы формирования NODAC, его клинические особенности и факторы риска остаются до конца не изученными. Это определяет высокую актуальность систематизации имеющихся данных и дальнейшего углублённого изучения NODAC, как сложного и гетерогенного клинического феномена

Целью настоящего обзора является систематизация и критический анализ современных данных о NODAC, включая его эпидемиологию, факторы риска заболевания, механизмы патогенеза и диагностические трудности.

Методы и материалы

Настоящее исследование представляет собой нарративный обзор литературы с элементами структурированного поиска. Поиск научных публикаций осуществлялся в базах данных PubMed (n = 317), Web of Science (n = 1486) и Scopus (n = 2432). Дополнительно для расширения поиска и выявления потенциально релевантных публикаций использовались Google Scholar, eLibrary и ResearchGate. Указанные источники рассматривались как вспомогательные, тогда как основные выводы обзора базировались преимущественно на рецензируемых публикациях, индексируемых в PubMed, Scopus и Web of Science.

В анализ были включены статьи, опубликованные в период с января 2020 по ноябрь 2025 года, представленные в рецензируемых медицинских журналах и посвящённые изучению клинических, патогенетических и эпидемиологических аспектов NODAC. Дополнительно учитывались систематические обзоры, метаанализы, когортные и ретроспективные клинические исследования, а также публикации, описывающие молекулярные механизмы поражения β-клеток поджелудочной железы при инфекции SARS-CoV-2. Критериями исключения являлись: нерецензированные источники, дублирующиеся публикации, статьи с неполными данными или посвящённые экспериментальным моделям на животных без клинического подтверждения. Использовались комбинации ключевых слов и MeSH-терминов, связанных с COVID-19 и нарушениями углеводного обмена, объединённые с помощью логических операторов AND/OR.

Детальная стратегия поиска, включая используемые поисковые запросы, комбинации ключевых слов и логические операторы для каждой базы данных, представлена в Приложении 1, что обеспечивает прозрачность и воспроизводимость проведённого поиска.

Результаты

В результате поиска было выявлено 4235 публикаций. После удаления дубликатов осталось 2760 записей. На этапе скрининга заголовков и аннотаций было исключено 2480 публикаций по следующим причинам: отсутствие связи с диабетом или COVID-19, публикации на животных моделях, а также обзорные статьи без релевантного анализа. Для полнотекстового анализа было отобрано 280 статей. По результатам оценки полнотекстовых публикаций было исключено 243 статьи в связи с отсутствием чёткой связи с феноменом

NODAC, недостаточной методологической строгостью, отсутствием клинических данных, или несоответствием цели обзора. В итоговый анализ включено 37 публикаций.

Эпидемиология и факторы риска развития NODAC

Накопленные эпидемиологические данные свидетельствуют о том, что развитие NODAC представляет собой клинически значимое и распространённое явление. По данным метааналитических исследований, доля пациентов с NODAC составляет около 1,3-1,5% среди перенёсших инфекцию [8]. При этом при включении всех случаев гипергликемии, включая транзиторные нарушения углеводного обмена, совокупная частота может достигать около 5% [9].

Относительный риск развития диабета у пациентов, перенёсших COVID-19, остаётся значительно повышенным по сравнению с неинфицированной популяцией. Согласно данным различных метаанализов, риск увеличивается в 1,4-1,7 раза [3,9,10], а в отдельных исследованиях показано, что он примерно в 1,5 раза выше по сравнению с пациентами, перенёсшими другие респираторные вирусные инфекции, включая грипп [11,12]. В группах высокого риска, в частности среди госпитализированных пациентов, частота развития NODAC может достигать 20-25% [13,14].

Риск развития NODAC имеет выраженную временную динамику: наибольшая вероятность его возникновения наблюдается в первые 3 месяца после перенесённой инфекции, что соответствует постострой фазе заболевания. В дальнейшем риск снижается, однако остаётся повышенным в течение как минимум 6–12 месяцев наблюдения [15,16]. Отмечена также вариабельность риска в зависимости от циркулирующих вариантов SARS-CoV-2: более высокие показатели наблюдались в периоды доминирования исходного штамма и варианта Delta по сравнению с Omicron [11].

Существенное значение имеют демографические и клинические факторы риска. Выявлена чёткая градиентная зависимость между тяжестью течения COVID-19 и вероятностью развития NODAC: наибольший риск наблюдается у пациентов, перенёсших тяжёлое течение заболевания и требовавших госпитализации или лечения в условиях отделения интенсивной терапии [12,15,16]. У лиц с лёгким течением инфекции избыточный риск выражен значительно слабее или может отсутствовать [17].

Среди демографических факторов более высокая частота NODAC отмечается у мужчин и у лиц старших возрастных групп, особенно старше 65 лет [9,12,15]. В то же время, несмотря на более низкую абсолютную частоту у детей и подростков, относительный риск у них также повышен по сравнению с неинфицированной популяцией [3,15]. Выраженные

различия выявлены и в зависимости от расово-этнической принадлежности: более высокий риск наблюдается среди представителей афроамериканских, латиноамериканских, а также азиатских популяций, что, вероятно, отражает сочетание генетических и социально-экономических факторов [8,16,18].

Ключевую роль также играют метаболические факторы риска. Наличие ожирения, артериальной гипертензии, дислипидемии и предиабета значительно повышает вероятность развития NODAC [19,20]. Ожирение рассматривается как один из центральных факторов, определяющих как тяжесть течения COVID-19, так и последующий риск нарушения углеводного обмена. Показано, что у пациентов с индексом массы тела ≥30 риск развития диабета после инфекции может увеличиваться более чем в 3 раза, что может быть связано с особенностями жировой ткани и хроническим воспалением, усиливающим инсулинорезистентность [12,16,21]. На этом фоне COVID-19 может выступать в роли триггера, ускоряющего манифестацию ранее субклинических метаболических нарушений [22,23].

С точки зрения клинических фенотипов, большинство случаев NODAC соответствует сахарному диабету 2 типа [11]. В то же время описаны случаи аутоиммунного диабета, включая LADA-подобные состояния и дебют с диабетического кетоацидоза, что подтверждает гетерогенность данного феномена [24–26]. Также важным аспектом является естественное течение NODAC. У значительной части пациентов нарушения углеводного обмена носят транзиторный характер и регрессируют до нормогликемии или предиабета после восстановления, что предполагает вклад транзиторной стресс-индуцированной гипергликемии, обусловленной системным воспалением или применением глюкокортикоидов [15,26,27]. В то же время у значительной доли пациентов нарушения сохраняются в течение длительного времени, что указывает на необходимость динамического мониторинга таких пациентов [27,28].

Таким образом, развитие NODAC вероятно является результатом сложного взаимодействия исходных метаболических нарушений и факторов, связанных с тяжестью инфекции. Именно сочетание этих механизмов может определять гетерогенность и клиническую вариабельность данного состояния.

Патогенез NODAC: мультифакторная и гетерогенная модель

С учётом представленной гетерогенности NODAC, развитие нарушений углеводного обмена после перенесённой инфекции SARS-CoV-2 следует рассматривать как результат взаимодействия нескольких взаимосвязанных патогенетических процессов. В отличие от

классических форм сахарного диабета, при NODAC предполагается, что данные механизмы могут реализовываться параллельно и потенциально усиливать друг друга, формируя широкий спектр клинических фенотипов. Следует отметить, что степень доказанности указанных механизмов различается: в то время как системное воспаление и инсулинорезистентность хорошо подтверждены клиническими и эпидемиологическими данными, прямое поражение β-клеток и аутоиммунные процессы в значительной степени основаны на экспериментальных и ограниченных клинических наблюдениях.

Прямое поражение β-клеток и нарушение их функции

Одним из предполагаемых и активно обсуждаемых механизмов NODAC является нарушение функции β-клеток поджелудочной железы. Показано, что β-клетки экспрессируют рецепторы и кофакторы, обеспечивающие проникновение SARS-CoV-2, включая ACE2 [1,14], TMPRSS2 [24,29] и нейропилин-1[1,23], что делает их потенциальной мишенью для вируса . После инфицирования β-клеток наблюдается снижение глюкозо-стимулированной секреции инсулина (GSIS), уменьшение числа секреторных гранул и развитие эндоплазматического стресса, что отражает нарушение внутриклеточного метаболизма [6].

Также важную роль, по-видимому, играет нарушение работы ренин-ангиотензиновой системы: снижение экспрессии ACE2 может приводить к накоплению ангиотензина II, активации оксидативного стресса и усилению воспаления, что потенциально способствует угнетению секреторной функции β-клеток [8,12]. Кроме того, описан феномен дедифференцировки β-клеток - состояния, при котором клетки утрачивают способность нормально вырабатывать инсулин и функционируют менее эффективно [30].

Инсулинорезистентность как центральный системный компонент

Среди предложенных механизмов NODAC системная инсулинорезистентность является одним из наиболее хорошо подтверждённых и, вероятно, клинически значимых компонентов. Воспалительная реакция, индуцированная SARS-CoV-2, сопровождается повышением уровней провоспалительных цитокинов (IL-6, IL-1β, TNF-α), которые способны активировать стресс-ассоциированные сигнальные пути, включая JNK и MAPK, тем самым нарушая инсулиновую сигнализацию и способствуя развитию инсулинорезистентности [22,31,32]. Дополнительный вклад вносит оксидативный стресс, усиливающий воспалительный ответ через активацию NF-κB и формирующий замкнутый “воспалительно-метаболический” цикл [22].

Жировая ткань играет особую роль в поддержании этих процессов: высокая экспрессия ACE2 делает её потенциальным резервуаром вируса, а продукция адипокинов и хемокинов (включая CXCL10) способствует развитию хронического мета-воспаления и усугублению инсулинорезистентности [22,33]. Таким образом, формируется состояние выраженной метаболической нагрузки, при котором даже умеренное снижение функции β-клеток может приводить к клинически значимой гипергликемии.

Роль стресса и транзиторной гипергликемии

Острая инфекция сопровождается активацией контринсулярных механизмов, включая повышение уровня кортизола и катехоламинов, что усиливает глюконеогенез и снижает периферическую утилизацию глюкозы. На этом фоне у части пациентов развивается транзиторная гипергликемия, не отражающая стойкого нарушения углеводного обмена [16,21]. Это позволяет предположить, что значительная часть наблюдаемых случаев представляет собой стресс-индуцированную гипергликемию, обусловленную системным воспалением или применением глюкокортикоидов. Именно данный механизм может объяснять значительную долю обратимых форм NODAC, наблюдаемых в клинических исследованиях.

Ятрогенные факторы: вклад глюкокортикоидной терапии

Также важным компонентом патогенеза NODAC является влияние терапии, в первую очередь глюкокортикоидов. Их применение сопровождается снижением чувствительности тканей к инсулину, усилением глюконеогенеза и нарушением GLUT-4-зависимого транспорта глюкозы [13] . В клиническом контексте это создаёт эффект “дополнительного удара”, при котором вирус-индуцированные изменения сочетаются с медикаментозно обусловленной инсулинорезистентностью. При этом глюкокортикоиды нередко выступают не как единственная причина гипергликемии, а как фактор, ускоряющий манифестацию ранее существующих метаболических нарушений [16].

Аутоиммунные механизмы как отдельный фенотип NODAC

У части пациентов NODAC может реализовываться через аутоиммунные механизмы, что подтверждается выявлением антител к островковым антигенам (GAD65, IA-2) после перенесённой инфекции [25,34]. Предполагается, что SARS-CoV-2 может инициировать аутоиммунные реакции через механизмы молекулярной мимикрии или неспецифической активации иммунных клеток (bystander activation) в условиях выраженного воспаления [23]. Данный путь, вероятно, лежит в основе развития LADA-подобных состояний и некоторых случаев дебюта диабета 1 типа после COVID-19, хотя имеющиеся данные ограничены и

основаны преимущественно на отдельных клинических наблюдениях [24,25]. Предполагаемые иммунные механизмы повреждения β-клеток представлены на **Рисунке 1 (**воспроизведено из [35]**).**

Интегративная модель патогенеза NODAC

Представленные механизмы не являются альтернативными и, по-видимому, могут реализовываться одновременно и взаимно потенцировать друг друга. В результате NODAC может формироваться как следствие сочетания:

- умеренного или выраженного нарушения функции β-клеток
- системной инсулинорезистентности
- стресс- и терапевтически обусловленных метаболических сдвигов
- индивидуальной предрасположенности.

Обобщённая схема предполагаемого патогенеза NODAC представлена на **Рисунке 2 (**адаптировано из [12]**).**

Важным является то, что в значительной части случаев NODAC отражает не истинное возникновение диабета, а ускоренную манифестацию ранее субклинических нарушений углеводного обмена. Таким образом, NODAC следует рассматривать как динамический спектр состояний с различными механизмами и исходами, что имеет принципиальное значение для клинической интерпретации и последующего наблюдения пациентов.

Диагностические особенности и сложности выявления NODAC

Поскольку на сегодняшний день не существует специфических диагностических критериев для NODAC, его выявление основывается на общепринятых критериях диагностики сахарного диабета. В клинической практике NODAC обычно рассматривается как состояние, при котором у пациента без ранее известного диабета после подтверждённой инфекции SARS-CoV-2 впервые выявляются показатели, соответствующие диагностическим порогам диабета. В качестве одного из наиболее используемых рабочих определений предлагается сочетание трёх критериев: подтверждённый диагноз диабета, отсутствие признаков предшествующего нарушения углеводного обмена и документированная инфекция COVID-19 в течение предшествующих 6 месяцев [15].

Согласно стандартам Американской диабетической ассоциации, диагноз сахарного диабета устанавливается при наличии одного из следующих показателей: уровень глюкозы натощак ≥ 126 мг/дл (7.0 ммоль/л); случайная глюкоза ≥ 200 мг/дл (11.1 ммоль/л) при наличии симптомов гипергликемии; HbA1c ≥ 6,5%, или уровень глюкозы через 2 часа при

ПГТТ ≥ 200 мг/дл. При этом требование повторного подтверждающего теста остаётся обязательным [36].

Однако в контексте COVID-19 многие исследования нарушали эти стандарты, не проводя повторное тестирование, что снижает точность диагностики и может приводить к гипердиагностике. Ряд стационарных работ использовали альтернативные, упрощённые критерии, адаптированные под острую фазу болезни: глюкоза натощак ≥ 140 мг/дл [31]; случайная глюкоза ≥ 200 мг/дл на протяжении двух суток [15], или необходимость инсулинотерапии в течение ≥ 48 часов у ранее недиабетических пациентов [15]. Такие подходы позволяют выявлять пациентов с нарушениями гликемии в острой фазе заболевания, однако они также увеличивают вероятность включения случаев транзиторной стресс-индуцированной гипергликемии, не отражающей стойкое нарушение углеводного обмена [16,23,37].

Подтверждение факта перенесённой инфекции SARS-CoV-2 также является важным компонентом диагностики и в исследованиях может основываться на положительных результатах ПЦР или антигенных тестов, наличии соответствующих кодов МКБ-10 (например, U07.1), а также на документации специфической терапии (например, применение противовирусных препаратов). В то же время отсутствие документированных данных о перенесённой инфекции, особенно при бессимптомном или лёгком течении COVID-19, может затруднять установление временной связи между инфекцией и последующим развитием гипергликемии [15,18].

Одной из ключевых проблем является невозможность достоверного исключения ранее существовавшего, но нераспознанного диабета. По данным допандемического периода, значительная доля пациентов с диабетом (до 23–50%) оставалась недиагностированной. В условиях COVID-19, сопровождающихся более частыми медицинскими обследованиями, происходит так называемое “раскрытие” ранее скрытого диабета, что может приводить к его ошибочной классификации как NODAC [15,37].

Сложности возникают и при классификации диабета. Во многих исследованиях она основывается на кодах МКБ-10 без учёта функции β-клеток или иммунологических маркеров, что может приводить к смешению различных клинических фенотипов, включая сахарный диабет 1 типа, сахарный диабет 2 типа, LADA и стероид-индуцированный диабет. Кроме того, повышенная частота контактов пациентов с системой здравоохранения в период COVID-19 создаёт эффект наблюдательного смещения (surveillance bias), увеличивая вероятность выявления диабета по сравнению с неинфицированной популяцией [17,18].

Таким образом, диагностика NODAC остаётся сложной междисциплинарной задачей, требующей осторожной интерпретации клинических и лабораторных данных. Гетерогенность клинических сценариев, отсутствие унифицированных критериев и наличие множества потенциальных смешивающих факторов подчёркивают необходимость стандартизации подходов и проведения проспективных исследований с чётким определением исходного метаболического статуса пациентов. В этом контексте NODAC следует рассматривать не как самостоятельную нозологическую единицу, а как гетерогенный клинический феномен, что имеет принципиальное значение для его диагностики и интерпретации.

Обсуждение результатов

Настоящий обзор обобщает современные данные о впервые выявленном диабете после перенесённой инфекции SARS-CoV-2 (NODAC) и подтверждает, что данное состояние представляет собой клинически значимое, но гетерогенное явление. Полученные данные свидетельствуют о статистически значимом увеличении риска развития диабета после COVID-19, однако интерпретация этого риска требует осторожности с учётом методологических ограничений доступных исследований.

Полученные результаты указывают на то, что NODAC не следует рассматривать как самостоятельную нозологическую единицу с единым патогенезом. Напротив, его развитие, вероятно, отражает взаимодействие нескольких взаимосвязанных процессов, включая системную инсулинорезистентность, нарушение функции β-клеток, воспалительный ответ и влияние терапевтических факторов. При этом наиболее убедительные доказательства накоплены в отношении роли воспаления и инсулинорезистентности, тогда как гипотезы прямого повреждения β-клеток и аутоиммунных механизмов остаются менее определёнными и требуют дальнейшего изучения.

Особое значение имеет выявленная зависимость риска NODAC от тяжести течения COVID-19. Более высокая частота нарушений углеводного обмена у госпитализированных пациентов, особенно в условиях интенсивной терапии, вероятно, отражает совокупное влияние гипоксии, выраженного воспалительного ответа и применения глюкокортикоидов. Это позволяет предположить, что инфекция SARS-CoV-2 в ряде случаев выступает не столько как первичная причина диабета, сколько как фактор, ускоряющий клиническую манифестацию ранее субклинических метаболических нарушений.

Важным наблюдением является также наличие транзиторных форм гипергликемии. У части пациентов нормализация гликемии после выздоровления свидетельствует о

значительном вкладе стресс-индуцированных механизмов, включая активацию контринсулярных гормонов и системное воспаление. Это подчёркивает, что не все случаи, диагностируемые в острой фазе COVID-19, отражают истинный дебют диабета, и требует подтверждения стойкости нарушений углеводного обмена в динамике.

Существенным ограничением современной доказательной базы является отсутствие единых диагностических подходов. Использование различных гликемических критериев, отсутствие повторного подтверждения диагноза и ограниченные возможности исключения ранее недиагностированного диабета снижают сопоставимость результатов исследований. Дополнительное влияние оказывает использование административных данных и кодов МКБ-10 без уточнения клинического фенотипа, что может приводить к гипердиагностике и смешению различных форм диабета.

Полученные результаты также позволяют выделить ряд методологических ограничений, характерных для большинства исследований в данной области. К ним относятся анализ уже имеющихся данных, отсутствие информации о состоянии углеводного обмена до COVID-19, различия между группами пациентов, а также возможные ошибки, связанные с особенностями наблюдения. В совокупности это не позволяет однозначно установить, вызывает ли COVID-19 развитие диабета.

Практические клинические выводы

С практической точки зрения результаты обзора подчёркивают необходимость более структурированного подхода к наблюдению пациентов после COVID-19. Наиболее обоснованным представляется проведение скрининга нарушений углеводного обмена у групп повышенного риска, к которым относятся:

• пациенты с тяжёлым течением COVID-19, требовавшие госпитализации или интенсивной терапии;

• лица с ожирением, предиабетом и другими компонентами метаболического синдрома;

• пациенты, получавшие системную глюкокортикоидную терапию.

В качестве основных показателей целесообразно использовать уровень глюкозы натощак и HbA1c с повторной оценкой в динамике. Оптимальные сроки наблюдения включают ранний постострый период (до 3 месяцев), а также последующий контроль в течение 6–12 месяцев для дифференциации транзиторной гипергликемии и стойкого диабета.

Таким образом, результаты настоящего обзора подтверждают, что NODAC следует рассматривать как гетерогенный клинический феномен, возникающий на пересечении инфекционных и метаболических процессов. Дальнейшие исследования должны быть

направлены на стандартизацию диагностических критериев, уточнение патогенетических механизмов и разработку клинических алгоритмов ведения пациентов. Это имеет ключевое значение для повышения точности диагностики и оптимизации долгосрочного наблюдения пациентов после перенесённой инфекции COVID-19.

Источники финансирования

Работа выполнена по инициативе авторов без привлечения финансирования.

Конфликт интересов

Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с содержанием настоящей статьи.

Вклад авторов

Концептуализация – Асанқұлова М.А., Павлова Н.П.**; Методология** – Асанқұлова М.А., Камитбекова Ж.У., Павлова Н.П.**;Проверка** – Базарова А.В., Камитбекова Ж.У., Павлова Н.П.**; Формальный анализ** – Асанқұлова М.А., Базарова А.В., Павлова Н.П.**;Написание (оригинальная черновая подготовка)** – Асанқұлова М.А.;**Написание (обзор и редактирование)** – Базарова А.В., Камитбекова Ж.У., Павлова Н.П**.**

Все авторы одобрили финальную версию статьи перед публикацией, выразили согласие нести ответственность за все аспекты работы, подразумевающую надлежащее изучение и решение вопросов, связанных с точностью или добросовестностью любой части работы.

Список литературы

1. Steenblock C, Toepfner N, Beuschlein F, Perakakis N, Mohan Anjana R, Mohan V, Mahapatra NR, Bornstein SR. SARS-CoV-2 infection and its effects on the endocrine system. Best Pract Res Clin Endocrinol Metab. 2023 Jul;37(4):101761. https://doi.org/10.1016/j.beem.2023.101761

2. Singh AK, Khunti K. COVID-19 and Diabetes. Annu Rev Med. 2022 Jan 27;73(1):129–47. https://doi.org/10.1146/annurev-med-042220-011857

3. Lai H, Yang M, Sun M, Pan B, Wang Q, Wang J, Tian J, Ding G, Yang K, Song X, Ge L. Risk of incident diabetes after COVID-19 infection: A systematic review and meta-analysis. Metabolism. 2022 Dec;137:155330. https://doi.org/10.1016/j.metabol.2022.155330

4. Pal R, Banerjee M. COVID-19 and the endocrine system: exploring the unexplored. J Endocrinol Invest. 2020 Jul;43(7):1027–31. https://doi.org/10.1007/s40618-020-01276-8

5. Khunti K, Del Prato S, Mathieu C, Kahn SE, Gabbay RA, Buse JB. COVID-19, Hyperglycemia, and New-Onset Diabetes. Diabetes Care. 2021 Dec;44(12):2645–55. https://doi.org/10.2337/dc21-1318

6. Müller JA, Groß R, Conzelmann C, Krüger J, Merle U, Steinhart J, Weil T, Koepke L, Bozzo CP, Read C, Fois G, Eiseler T, Gehrmann J, Van Vuuren J, Wessbecher IM, Frick M, Costa IG, Breunig M, Grüner B, Peters L, Schuster M, Liebau S, Seufferlein T, Stenger S, Stenzinger A, MacDonald PE, Kirchhoff F, Sparrer KMJ, Walther P, Lickert H, Barth TFE, Wagner M, Münch J, Heller S, Kleger A. SARS-CoV-2 infects and replicates in cells of the human endocrine and exocrine pancreas. Nat Metab. 2021 Feb 3;3(2):149–65. https://doi.org/10.1038/s42255-021-00347-1

7. Wu CT, Lidsky PV, Xiao Y, Lee IT, Cheng R, Nakayama T, Jiang S, Demeter J, Bevacqua RJ, Chang CA, Whitener RL, Stalder AK, Zhu B, Chen H, Goltsev Y, Tzankov A, Nayak JV, Nolan GP, Matter MS, Andino R, Jackson PK. SARS-CoV-2 infects human pancreatic β cells and elicits β cell impairment. Cell Metab. 2021 Aug;33(8):1565-1576.e5. https://doi.org/10.1016/j.cmet.2021.05.013

8. El-Naas A, Hamad O, Nair S, Alfakhri B, Mahmoud S, Haji A, Ahmed L, Lebbe A, Aboulwafa A, Shaikh F, Bouhali I, Zakaria D. New onset of type 1 and type 2 diabetes post-COVID-19 infection: a systematic review. Emerg Microbes Infect. 2025 Dec;14(1):2492211. https://doi.org/10.1080/22221751.2025.2492211

9. Li J, Li Y, Wang Z, Liu N, He L, Zhang H. Increased risk of new-onset diabetes in patients with COVID-19: a systematic review and meta-analysis. Front Public Health. 2023;11:1170156. https://doi.org/10.3389/fpubh.2023.1170156

10. Cocking E, Daher J, Alabbood M. New-onset diabetes mellitus post COVID-19 infection: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2025 Sep;227:112417. https://doi.org/10.1016/j.diabres.2025.112417

11. Matsumoto A, Kodera S, Matsuura T, Takayama Y, Yamada Y, Hirata A. Differential impact of SARS-CoV-2 infection during different outbreak periods on incident diabetes in Japan: a matched cohort study utilizing health insurance claims. Environ Health Prev Med. 2024;29:52. https://doi.org/10.1265/ehpm.24-00191

12. Pantea Stoian A, Bica IC, Salmen T, Al Mahmeed W, Al-Rasadi K, Al-Alawi K, Banach M, Banerjee Y, Ceriello A, Cesur M, Cosentino F, Firenze A, Galia M, Goh SY, Janez A, Kalra S, Kapoor N, Kempler P, Lessan N, Lotufo P, Mikhailidis DP, Nibali L, Papanas N, Powell-Wiley T, Rizvi AA, Sahebkar A, Santos RD, Toth PP, Viswanathan V, Rizzo M, The

Cardiometabolic Panel of International Experts on Syndemic COVID-19 (CAPISCO). New-Onset Diabetes Mellitus in COVID-19: A Scoping Review. Diabetes Ther. 2024 Jan;15(1):33–60. https://doi.org/10.1007/s13300-023-01465-7

13. Făgărășan I, Rusu A, Cristea M, Bala CG, Vulturar DM, Cristea C, Todea DA. Predictors of New-Onset Diabetes in Hospitalized Patients with SARS-CoV-2 Infection. Int J Environ Res Public Health. 2022 Oct 14;19(20). https://doi.org/10.3390/ijerph192013230

14. Fadini GP, Morieri ML, Boscari F, Fioretto P, Maran A, Busetto L, Bonora BM, Selmin E, Arcidiacono G, Pinelli S, Farnia F, Falaguasta D, Russo L, Voltan G, Mazzocut S, Costantini G, Ghirardini F, Tresso S, Cattelan AM, Vianello A, Avogaro A, Vettor R. Newly-diagnosed diabetes and admission hyperglycemia predict COVID-19 severity by aggravating respiratory deterioration. Diabetes Res Clin Pract. 2020 Oct;168:108374. https://doi.org/10.1016/j.diabres.2020.108374

15. Kim SH, Arora I, Hsia DS, Knowler WC, LeBlanc E, Mylonakis E, Pratley R, Pittas AG. New-Onset Diabetes After COVID-19. J Clin Endocrinol Metab. 2023 Oct 18;108(11):e1164–74. https://doi.org/10.1210/clinem/dgad284

16. Chourasia P, Goyal L, Kansal D, Roy S, Singh R, Mahata I, Sheikh AB, Shekhar R. Risk of New-Onset Diabetes Mellitus as a Post-COVID-19 Condition and Possible Mechanisms: A Scoping Review. J Clin Med. 2023 Feb 1;12(3). https://doi.org/10.3390/jcm12031159

17. Reges O, Test T, Hoshen M, Cicurel A, Saliba W, Greenland P, Dicker D, Lavie G. Time-varying association of acute and post-acute COVID-19 with new-onset diabetes mellitus among hospitalized and non-hospitalized patients. BMJ Open Diabetes Res Care. 2023 Jan;11(1). https://doi.org/10.1136/bmjdrc-2022-003052

18. Keck JW, Lacy ME, Bressler S, Blake I, Chukwuma U, Bruce MG. COVID-19 infection and incident diabetes in American Indian and Alaska Native people: a retrospective cohort study. Lancet Reg Health Am. 2024 May;33:100727. https://doi.org/10.1016/j.lana.2024.100727

19. Demidova TYu, Volkova EI, Gritskevich EYu. Peculiarities of the COVID-19 course and consequences in overweight and obese patients. Lessons from the current pandemic. Obes Metab. 2020 Dec 25;17(4):375–84. https://doi.org/10.14341/omet12663

20. Xu AY, Wang SH, Duong TQ. Patients with prediabetes are at greater risk of developing diabetes 5 months postacute SARS-CoV-2 infection: a retrospective cohort study. BMJ Open Diabetes Res Care. 2023 Jun;11(3). https://doi.org/10.1136/bmjdrc-2022-003257

21. Landstra CP, De Koning EJP. COVID-19 and Diabetes: Understanding the Interrelationship and Risks for a Severe Course. Front Endocrinol. 2021 Jun 17;12:649525. https://doi.org/10.3389/fendo.2021.649525

22. Hayden MR. An Immediate and Long-Term Complication of COVID-19 May Be Type 2 Diabetes Mellitus: The Central Role of β-Cell Dysfunction, Apoptosis and Exploration of Possible Mechanisms. Cells. 2020 Nov 13;9(11):2475. https://doi.org/10.3389/fcdhc.2022.826006

23. Gerganova A, Assyov Y, Kamenov Z. Stress Hyperglycemia, Diabetes Mellitus and COVID-19 Infection: Risk Factors, Clinical Outcomes and Post-Discharge Implications. Front Clin Diabetes Healthc. 2022;3:826006. https://doi.org/10.3389/fcdhc.2022.826006

24. Lee N, Prabhu P, Swaminath S, Amini SS. Development of Islet Antigen 2 (IA2) Antibodies Post-COVID-19 Infection: A Sign of Autoimmunity or Latent Autoimmune Diabetes Mellitus in Adults (LADA)? Cureus. 2023 Jun 26. https://doi.org/10.7759/cureus.40971

25. Milic G, Ristic M, Milosevic M, Mitovic N, Dimitrijevic L, Jesic Petrovic T, Salovic B. Post-COVID-19 Syndrome Associated With Multiple Autoimmune Diseases (DM I—LADA, Chronic Autoimmune Thyroiditis and Pernicious Anemia): Case Report. Clin Med Insights Endocrinol Diabetes. 2024 Jan;17:11795514241267185. https://doi.org/10.1177/11795514241267185

26. Doğan EE, Rasulova N, Bayramova F, Hacisahinoğulları H, Yalın GY, Selçukbiricik ÖS, Gül N, Üzüm AK, Karşıdağ K, Satman İ. The effect of COVID-19 pandemic on new-onset adult diabetes and its one-year follow-up. Prim Care Diabetes. 2025 Feb;19(1):74–81. https://doi.org/10.1016/j.pcd.2024.11.004

27. Rizvi AA, Kathuria A, Al Mahmeed W, Al-Rasadi K, Al-Alawi K, Banach M, Banerjee Y, Ceriello A, Cesur M, Cosentino F, Galia M, Goh SY, Janez A, Kalra S, Kempler P, Lessan N, Lotufo P, Papanas N, Santos RD, Stoian AP, Toth PP, Viswanathan V, Rizzo M. Post-COVID syndrome, inflammation, and diabetes. J Diabetes Complications. 2022 Nov;36(11):108336. https://doi.org/10.1016/j.jdiacomp.2022.108336

28. Sathish T, Anton MC. Persistence of new-onset diabetes in the post-acute phase of COVID-19. Int J Diabetes Dev Ctries. 2023 Feb;43(1):118–9. https://doi.org/10.1007/s13410-022-01119-7

29. Bornstein SR, Dalan R, Hopkins D, Mingrone G, Boehm BO. Endocrine and metabolic link to coronavirus infection. Nat Rev Endocrinol. 2020 Jun;16(6):297–8. https://doi.org/10.1038/s41574-020-0353-9

30. Tang X, Uhl S, Zhang T, Xue D, Li B, Vandana JJ, Acklin JA, Bonnycastle LL, Narisu N, Erdos MR, Bram Y, Chandar V, Chong ACN, Lacko LA, Min Z, Lim JK, Borczuk AC, Xiang J, Naji A, Collins FS, Evans T, Liu C, tenOever BR, Schwartz RE, Chen S. SARS-CoV-2 infection induces beta cell transdifferentiation. Cell Metab. 2021 Aug;33(8):1577-1591.e7. https://doi.org/10.1016/j.cmet.2021.05.015

31. Chen M, Zhu B, Chen D, Hu X, Xu X, Shen WJ, Hu C, Li J, Qu S. COVID-19 May Increase the Risk of Insulin Resistance in Adult Patients Without Diabetes: A 6-Month Prospective Study. Endocr Pract Off J Am Coll Endocrinol Am Assoc Clin Endocrinol. 2021 Aug;27(8):834–41. https://doi.org/10.1016/j.eprac.2021.04.004

32. Pal R, Bhadada SK. COVID-19 and diabetes mellitus: An unholy interaction of two pandemics. Diabetes Metab Syndr Clin Res Rev. 2020 Jul;14(4):513–7. https://doi.org/10.1016/j.dsx.2020.04.049

33. Da Porto A, Tascini C, Colussi G, Peghin M, Graziano E, De Carlo C, Bulfone L, Antonello M, Sozio E, Fabris M, Curcio F, Pucillo C, Catena C, Sechi LA. Relationship between cytokine release and stress hyperglycemia in patients hospitalized with COVID-19 infection. Front Med. 2022;9:988686. https://doi.org/10.3389/fmed.2022.988686

34. Kayhan S, Hepsen S, Kalkisim HK, Sendur IN, Altay FA, Yalcindag A. The evaluation of pancreas β-cell autoantibodies in non-diabetic COVID-19 patients. Arch Endocrinol Metab. 2022 Jun 3. https://doi.org/10.20945/2359-3997000000498

35. Batista-Roche JL, Mirabent-Casals M, Manzanares D, Lund G, García-Gasca A. New-Onset Diabetes Mellitus after COVID-19: Combined Effects of SARS-CoV-2 Variants, Molecular Mimicry, and m6A RNA Methylation. COVID. 2024;4(4):481–94. https://doi.org/10.3390/covid4040032

36. American Diabetes Association Professional Practice Committee. 7. Diabetes Technology: *Standards of Medical Care in Diabetes—2022*. Diabetes Care. 2022 Jan 1;45(Supplement_1):S97–112. https://doi.org/10.2337/dc22-S007

37. Sathish T, Anton MC, Sivakumar T. New-onset diabetes in “long COVID ”. J Diabetes. 2021 Aug;13(8):693–4. https://doi.org/10.1111/1753-0407.13187

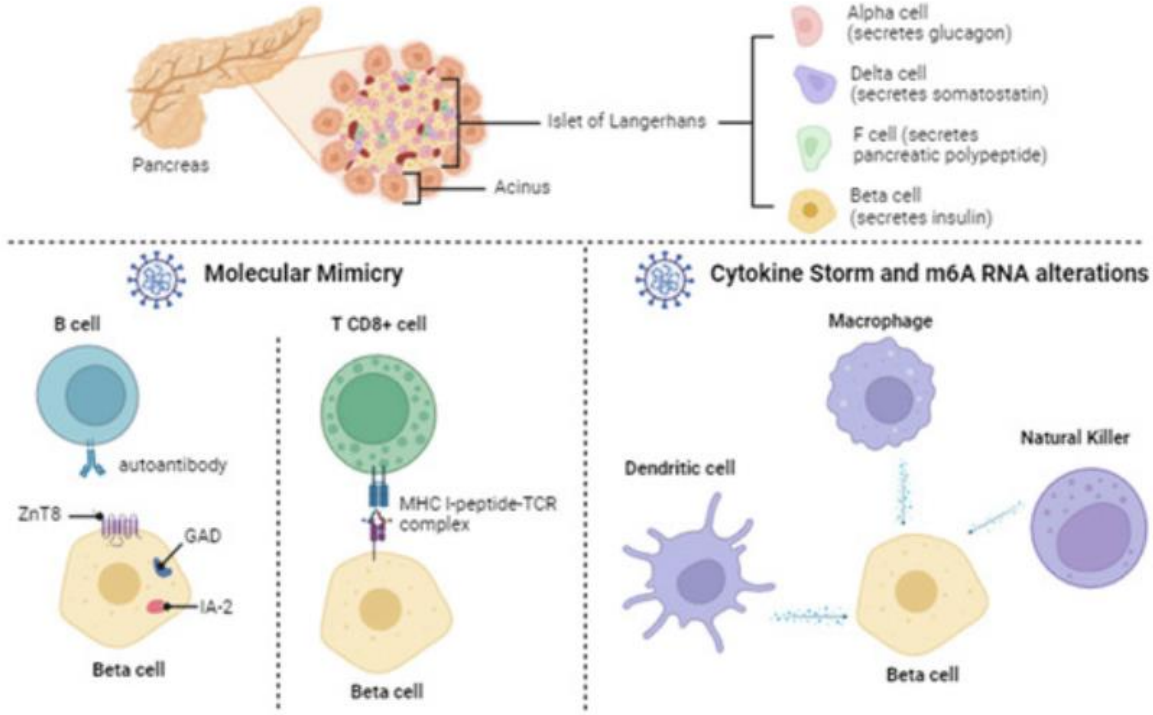


Рисунок 1. Потенциальные иммунные механизмы повреждения β-клеток поджелудочной железы после инфекции SARS-CoV-2.

Примечание: β-клетки могут повреждаться аутоагрессивными Т- и В-лимфоцитами вследствие молекулярной мимикрии. Перекрёстная иммунная реактивность между белками SARS-CoV-2 и одним или несколькими белками человека возникает, когда иммунные клетки распознают как вирусный антиген, так и аутоантиген вследствие сходства их аминокислотной последовательности. Антитела против SARS-CoV-2 могут обладать перекрёстной реактивностью с транспортером цинка 8 (ZnT8), глутаматдекарбоксилазой (GAD), антигеном инсулиномы-2 (IA-2) или другими высоко экспрессируемыми белками поджелудочной железы. Т-лимфоциты (CD8+) распознают, посредством Т-клеточного рецептора (TCR), пептиды, производные белков SARS-CoV-2, которые представлены на поверхности инфицированных β-клеток молекулами главного комплекса гистосовместимости I класса (MHC-I). β-клетки также могут разрушаться клетками врождённого иммунитета, такими как дендритные клетки, макрофаги и натуральные киллеры, через различные механизмы, включающие провоспалительные цитокины. Воспроизведено из [35] (CC BY 4.0).

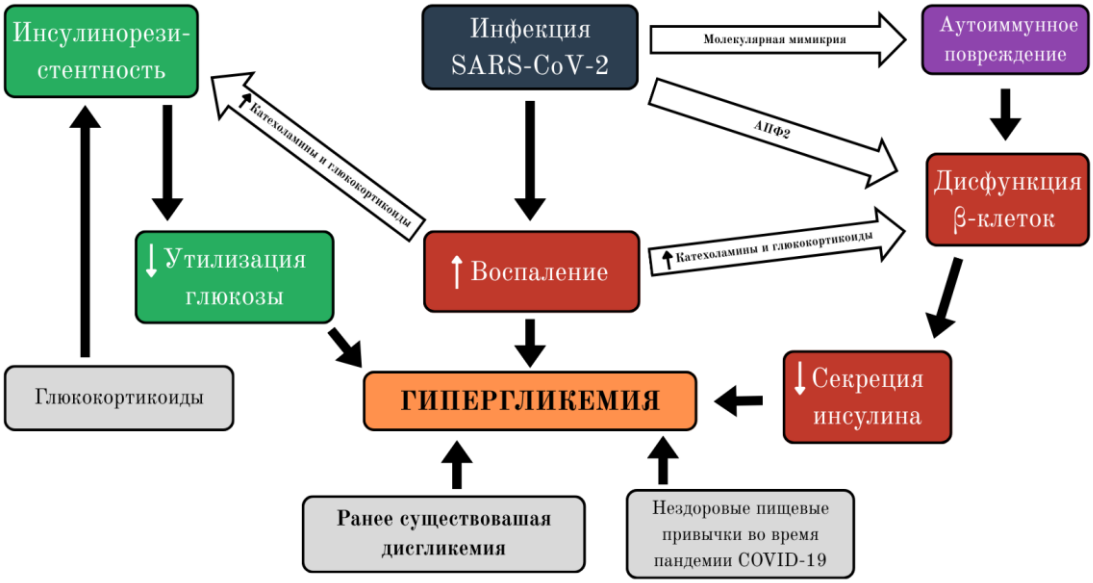


Рисунок 2. Предполагаемые механизмы развития гипергликемии при инфекции SARS-CoV-2.

Примечание: АПФ2, ангиотензинпревращающий фермент 2. Адаптировано из [12] (CC BY 4.0).

UDC 612.338

Dana Bekaryssova

Department for Coordination and Development of Scientific Journals, South Kazakhstan Medical Academy, Shymkent, Kazakhstan.

Corresponding author:

Dana Bekaryssova, MD, PhD

Department for Coordination and Development of Scientific Journals, South Kazakhstan Medical Academy, Shymkent, Kazakhstan.

Email: bekaryssova.da@gmail.com

ORCID IDs:

Dana Bekaryssova[1] (https://orcid.org/0000-0002-9651-7295)

THE MICROBIOTA–GUT–BRAIN AXIS: AN UP-TO-DATE REVIEW OF MECHANISTIC PATHWAYS AND CLINICAL SIGNIFICANCE

Abstract

The microbiota–gut–brain axis (MGBA) is a complex, bidirectional communication network connecting the intestinal microbiota with the central nervous system and playing an essential role in maintaining physiological homeostasis and coordinating key functions of the human body. This review summarizes current knowledge on the main mechanisms involved in MGBA signaling and highlights its growing clinical relevance.

The gut microbiota is composed of trillions of microorganisms that together form a highly dynamic ecosystem. It is actively involved in regulating immune responses, metabolic processes, and neurophysiological functions. Microbiota development begins early in life and is shaped by multiple factors, including the environment, diet, and mode of birth. In adulthood, it becomes a relatively stable yet highly active system with significant metabolic and genetic capabilities that influence host physiology on many levels.

Communication between the gut and the brain occurs through several interconnected pathways. These include neural routes, primarily the enteric nervous system and the vagus nerve, immune signaling mediated by cytokines and immune cells, endocrine pathways involving the hypothalamic–pituitary–adrenal axis and gut hormones, as well as metabolic communication through microbial metabolites such as short-chain fatty acids and other neuroactive compounds. Together, these systems enable continuous two-way signaling that affects mood, cognition, stress regulation, and energy balance.

Disruption of this system, known as dysbiosis, has been associated with increased intestinal and blood–brain barrier permeability, chronic low-grade inflammation, and alterations in neurotransmitter systems. These changes are increasingly linked to a range of conditions, including depression, anxiety disorders, neurodevelopmental abnormalities, and neurodegenerative diseases.

Although research in this field has advanced significantly in recent years, many questions remain, particularly regarding causal relationships and inter-individual variability. The MGBA is now widely considered a promising target for therapeutic intervention, and microbiota-based strategies such as dietary modulation, probiotics, and related approaches are gaining attention. Future studies integrating multi-omics technologies and systems biology will be essential for translating these findings into personalized clinical applications.

Keywords: *gut-brain axis, gut, microbiota, brain, dysbiosis*

Бекарысова Дана
Отдел координации и развития научных журналов, Южно-Казахстанская Медицинская Академия, Шымкент, Казахстан

ОСЬ «МИКРОБИОТА–КИШЕЧНИК–МОЗГ»: СОВРЕМЕННЫЕ ПРЕДСТАВЛЕНИЯ О МЕХАНИЗМАХ ВЗАИМОДЕЙСТВИЯ И КЛИНИЧЕСКОЙ ЗНАЧИМОСТИ

Аннотация

Ось «микробиота–кишечник–мозг» (MGBA) представляет собой сложную двунаправленную коммуникационную сеть, соединяющую кишечную микробиоту с центральной нервной системой и играющую ключевую роль в поддержании физиологического гомеостаза и координации основных функций организма. В данном обзоре обобщены современные данные о ключевых механизмах передачи сигналов в рамках MGBA, а также подчеркнута её возрастающая клиническая значимость.

Кишечная микробиота состоит из триллионов микроорганизмов, формирующих высокодинамичную экосистему. Она активно участвует в регуляции иммунных реакций, метаболических процессов и нейрофизиологических функций. Формирование микробиоты начинается на ранних этапах жизни и определяется множеством факторов, включая окружающую среду, питание и способ родоразрешения. Во взрослом возрасте она становится относительно стабильной, но при этом остаётся высокоактивной системой с выраженными метаболическими и генетическими возможностями, влияющими на физиологию организма на различных уровнях.

Коммуникация между кишечником и головным мозгом осуществляется через несколько взаимосвязанных путей. К ним относятся нейрональные механизмы, в первую очередь энтеральная нервная система и блуждающий нерв, иммунная сигнализация, опосредованная цитокинами и иммунными клетками, эндокринные пути, включающие гипоталамо-гипофизарно-надпочечниковую ось и кишечные гормоны, а также метаболическая коммуникация через микробные метаболиты, такие как короткоцепочечные жирные кислоты и другие нейроактивные соединения. В совокупности эти системы обеспечивают непрерывную двустороннюю передачу сигналов, влияющую на настроение, когнитивные функции, регуляцию стресса и энергетический баланс.

Нарушение функционирования данной системы, известное как дисбиоз, ассоциировано с повышенной проницаемостью кишечного и гематоэнцефалического барьеров, хроническим

низкоинтенсивным воспалением и изменениями в нейромедиаторных системах. Эти изменения всё чаще связывают с развитием различных состояний, включая депрессию, тревожные расстройства, нарушения нейроразвития и нейродегенеративные заболевания.

Несмотря на значительный прогресс в данной области в последние годы, остаётся множество нерешённых вопросов, особенно в отношении причинно-следственных связей и межиндивидуальной вариабельности. В настоящее время MGBA рассматривается как перспективная мишень для терапевтических вмешательств, а стратегии, направленные на модификацию микробиоты, включая диетические подходы, пробиотики и смежные методы, привлекают всё большее внимание. Будущие исследования с использованием мультиомных технологий и системной биологии будут иметь ключевое значение для трансляции этих данных в персонализированные клинические подходы.

Ключевые слова: *ось «кишечник–мозг», кишечник, микробиота, мозг, дисбиоз*

Бекарысова Дана

Ғылыми журналдарды үйлестіру және дамыту бөлімі, Оңтүстік Қазақстан Медицина Академиясы, Шымкент, Қазақстан

«МИКРОБИОТА–ІШЕК–МИ» ОСІ: ӨЗАРА ӘРЕКЕТТЕСУ МЕХАНИЗМДЕРІ МЕН КЛИНИКАЛЫҚ МАҢЫЗДЫЛЫҒЫ ТУРАЛЫ ЗАМАНАУИ ТҮСІНІКТЕР

Аңдатпа

«Микробиота–ішек–ми» осі (MGBA) – ішек микробиотасын орталық жүйке жүйесімен байланыстыратын және физиологиялық гомеостазды сақтауда, сондай-ақ ағзаның негізгі функцияларын үйлестіруде маңызды рөл атқаратын күрделі екіжақты коммуникациялық жүйе болып табылады. Осы шолуда MGBA аясындағы сигнал беру механизмдерінің негізгі бағыттары бойынша заманауи деректер жүйеленіп, оның клиникалық маңыздылығының артып келе жатқаны көрсетілген.

Ішек микробиотасы триллиондаған микроорганизмдерден тұрады және жоғары динамикалы экожүйе қалыптастырады. Ол иммундық жауаптарды, метаболикалық процестерді және нейрофизиологиялық функцияларды реттеуге белсенді қатысады. Микробиотаның қалыптасуы өмірдің ерте кезеңдерінде басталып, қоршаған орта, тамақтану және туу тәсілі сияқты көптеген факторлардың әсерімен айқындалады. Ересек жаста микробиота салыстырмалы түрде тұрақты болғанымен, жоғары белсенді жүйе

ретінде сақталып, айқын метаболикалық және генетикалық мүмкіндіктері арқылы ағзаның физиологиясына әртүрлі деңгейде ықпал етеді.

Ішек пен ми арасындағы байланыс бірнеше өзара байланысты жолдар арқылы жүзеге асады. Оларға нейрондық механизмдер, ең алдымен энтерикалық жүйке жүйесі мен кезбе жүйке, цитокиндер мен иммундық жасушалар арқылы жүзеге асатын иммундық сигнализация, гипоталамус–гипофиз–бүйрекүсті безі осін және ішек гормондарын қамтитын эндокриндік жолдар, сондай-ақ қысқа тізбекті май қышқылдары мен басқа да нейроактивті қосылыстар сияқты микробтық метаболиттер арқылы жүзеге асатын метаболикалық байланыс жатады. Бұл жүйелер жиынтығында көңіл күйге, когнитивтік функцияларға, стресс реттелуіне және энергетикалық теңгерімге әсер ететін үздіксіз екіжақты сигнал алмасуды қамтамасыз етеді.

Бұл жүйенің бұзылуы, дисбиоз деп аталатын жағдай, ішек және гематоэнцефалдық тосқауылдардың өткізгіштігінің артуымен, созылмалы төмен деңгейлі қабынумен және нейромедиаторлық жүйелердегі өзгерістермен байланысты. Аталған өзгерістер депрессия, үрейлік бұзылыстар, нейродаму бұзылыстары және нейродегенеративті аурулар сияқты түрлі патологиялық жағдайлардың дамуымен жиі байланыстырылуда.

Соңғы жылдары бұл салада айтарлықтай жетістіктерге қол жеткізілгеніне қарамастан, әсіресе себеп-салдарлық байланыстар мен жеке айырмашылықтарға қатысты көптеген сұрақтар әлі де ашық күйінде қалып отыр. Қазіргі таңда MGBA терапиялық әсер ету үшін перспективалы нысана ретінде қарастырылуда, ал микробиотаны модификациялауға бағытталған стратегиялар, соның ішінде диеталық тәсілдер, пробиотиктер және соған ұқсас әдістер, үлкен қызығушылық тудыруда. Болашақта мультиомдық технологиялар мен жүйелік биологияны қолданатын зерттеулер алынған нәтижелерді дербестендірілген клиникалық тәжірибеге енгізуде шешуші рөл атқарады.

Түйін сөздер: *«ішек–ми» осі, ішек, микробиота, ми, дисбиоз*

Introduction

The human gastrointestinal tract is home to trillions of microorganisms, including bacteria, viruses, and fungi, which together form the gut microbiota and exist in a symbiotic relationship with the host organism. The stability of this delicate balance is maintained, in part, by a tolerant intestinal immune system enriched with regulatory cells [1]. The gut is not only a central organ for digestion and immune regulation but also a highly complex and dynamic microbial ecosystem. The

gut microbiota closely interacts with the host and influences the development and function of the immune, metabolic, and nervous systems [2]. In a broader sense, it represents the community of microorganisms inhabiting the gastrointestinal tract and plays a fundamental role in supporting the physiological functions of multiple body systems [3, 4].

In recent years, increasing attention has been given to the microbiota–gut–brain axis, a bidirectional communication network between intestinal microorganisms and the central nervous system [5, 6]. This axis is actively studied both under physiological conditions and in various disease states, where the gut microbiota acts as a key mediator of signaling between distant organs and systems [7, 8]. Functionally, gut–brain communication involves both peripheral and central regulatory mechanisms. Signals generated in the gut in response to food intake are transmitted to the central nervous system and contribute to the regulation of energy balance, food intake, and glucose homeostasis, with the hypothalamus playing a central integrative role [9].

Alterations in the composition and metabolic activity of the gut microbiota (dysbiosis) disrupt regulatory mechanisms and increase the permeability of both the intestinal and blood–brain barriers, thereby contributing to the development of neurological as well as gastrointestinal disorders. Importantly, this regulation is bidirectional: the central nervous system, through the autonomic nervous system and the hypothalamic–pituitary–adrenal (HPA) axis, influences gut function, including motility, secretion, permeability, and microbial composition [10]. In turn, the gut microbiota affects the central nervous system via microbial metabolites, neuroactive compounds, and gut-derived hormones, which can reach the brain through the vagus nerve, systemic circulation, the enteric nervous system, and immune pathways [11]. Moreover, stress-related signals originating from the brain, including activation of the HPA axis and the release of norepinephrine, can alter the composition of the microbiota and promote the growth of pathogenic microorganisms.

In recent years, interest in the gut microbiota and the microbiota–gut–brain axis has grown substantially, as reflected in the increasing number of studies in this field [12]. Despite significant progress, further large-scale research is still needed to deepen our understanding of the bidirectional gut–brain interaction. Such efforts may not only expand current knowledge of the microbiota–gut–brain axis but also help identify novel therapeutic targets for neurological and psychiatric disorders [13]. The aim of this review is to systematize current data on the mechanisms underlying the microbiota–gut–brain axis and to analyze its role in physiological processes as well as in the development of neurological and gastrointestinal diseases.

Search strategy

A comprehensive and structured literature search was conducted to identify relevant studies on the microbiota–gut–brain axis. The search was performed across major biomedical databases, including PubMed/MEDLINE, Scopus, and Web of Science, to ensure broad coverage of both experimental and clinical research. The search strategy combined Medical Subject Headings (MeSH) terms and free-text keywords, including "gut microbiota," "microbiota–gut–brain axis," "gut-brain communication," "neuroinflammation," "intestinal permeability," "vagus nerve," "enteric nervous system," and "microbial metabolites." Boolean operators (AND, OR) were applied to optimize and refine the search process.

Inclusion criteria comprised peer-reviewed articles published in English between 2014 and 2025, including original research articles, systematic reviews, meta-analyses, and high-quality narrative reviews. Both human and animal studies were included to ensure a comprehensive understanding of mechanistic and translational aspects of the field.

Exclusion criteria included studies with insufficient methodological detail, non-peer-reviewed publications, conference abstracts without full-text availability, and articles not directly addressing microbiota–gut–brain axis mechanisms. Studies focusing exclusively on unrelated gastrointestinal or neurological conditions without MGBA relevance were also excluded. The selected literature was systematically analyzed and synthesized to summarize current knowledge on gut microbiota composition, communication pathways within the microbiota–gut–brain axis, and its role in both physiological processes and disease development.

Historical Development and Current Understanding of the Microbiota–Gut–Brain Axis

The concept of a bidirectional interaction between the gastrointestinal tract and the brain, now known as the gut–brain axis, began to take shape as early as the 19th century. One of the first researchers to highlight this connection was Beaumont, who in the 1840s demonstrated that emotional states could directly influence digestive processes [14]. These early observations laid the foundation for the idea that a functional link exists between the central nervous system and the gastrointestinal tract.

In the following decades, scientific interest in this relationship gradually increased. However, it was not until the 1980s that the gut–brain axis gained more solid experimental support. In particular, studies showed that hormonal signals produced by the intestinal endocrine system could influence neuronal structures in the brain, thereby confirming the existence of complex neuroendocrine regulation [15]. At this stage, however, the role of the microbiota had not yet been considered, despite its later recognition as a key component of this system.

A more complete understanding of the gut–brain axis as a multi-layered integrative system emerged only by the late 20th and early 21st centuries [16]. During this period, it became clear that communication between the gut and the central nervous system is mediated by a complex network of neural, immune, and endocrine pathways. Moreover, accumulating evidence led to a shift in how the gut was viewed—not merely as a digestive organ, but also as an important center of neuroimmune regulation.

Modern research has significantly expanded this concept by incorporating the gut microbiota as an active participant in inter-system communication. Today, the microbiota is regarded as a dynamic and responsive system capable of modulating central nervous system functions under both physiological and pathological conditions [17]. Thus, the evolution of scientific understanding has led to the development of the microbiota–gut–brain axis concept, which reflects a highly integrated regulatory network essential for maintaining overall physiological homeostasis.

Composition, Development, and Functional Characteristics of the Gut Microbiota

The human gut represents a unique and highly organized ecosystem inhabited by trillions of microorganisms, with bacteria being the dominant group, forming a complex and dynamic community [18]. These microorganisms exist in a close symbiotic relationship with the host, performing a wide range of essential functions, including participation in metabolism, immune regulation, and the maintenance of intestinal barrier integrity.

The development of the gut microbiota begins even before birth, as suggested by the detection of microorganisms in placental tissues. In early postnatal life, its composition is shaped by multiple factors, such as the mode of delivery, feeding practices, and environmental exposures [19]. As an individual matures, the microbiota undergoes continuous and substantial changes, gradually stabilizing into a more resilient and relatively stable adult-like configuration.

In adults, more than 90% of gut microorganisms reside in the large intestine, where they function almost as a “metabolic organ” in their own right. They actively contribute to metabolic regulation, vitamin synthesis, and modulation of immune responses [20]. The total microbial mass can reach up to 1 kg, while its composition varies considerably depending on age, lifestyle, geographic location, and environmental conditions [21]. The gut microbiome comprises approximately 2,000 microbial species, and its collective genetic potential far exceeds that of the human genome, highlighting its profound functional importance [22].

From a taxonomic perspective, the dominant phyla are Bacteroidetes and Firmicutes, which together account for approximately 75–80% of the gut microbiota [23]. At the same time, less abundant groups such as Proteobacteria, Actinobacteria, Verrucomicrobia, and Cyanobacteria,

although present in smaller proportions, play a crucial role in maintaining microbial balance and ecosystem stability [24]. Interactions between these microbial communities and the host are governed by processes of mutual selection, ensuring both stability and adaptability of the microbiota.

Diet represents one of the most influential factors shaping the composition of the gut microbiota. Dietary habits not only alter the structure of microbial communities but also modulate the functional activity of the microbiota–gut–brain axis [25]. For instance, a high-calorie diet may impair intestinal barrier integrity, increase gut permeability, and activate pro-inflammatory signaling pathways, leading to elevated levels of cytokines such as TNF-α, IL-1β, and IL-6 [26]. In contrast, moderate shifts in microbiota composition are increasingly viewed as a physiological adaptive response, reflecting the organism's ability to maintain homeostasis under changing internal and external conditions [27].

Mechanisms of Interaction within the Microbiota–Gut–Brain Axis

Communication between the gut and the central nervous system occurs through a complex and highly interconnected network of mechanisms, including neural, immune, and endocrine components. These systems function in close coordination, enabling the integration of signals at multiple levels and ensuring efficient bidirectional communication across the body [28]. Rather than operating independently, these pathways complement one another and together form a unified regulatory network that allows the organism to adapt to both internal and external changes.

The gut microbiota plays a central role in regulating neurodevelopment and central nervous system function through three main pathways: immune, neural, and endocrine signaling [29]. Each of these routes contributes in a distinct yet interconnected way to gut–brain communication, influencing both physiological processes and systemic homeostasis.

To provide a structured overview of these mechanisms and the key mediators involved in bidirectional gut–brain communication, Table 1 summarizes the main signaling pathways within the microbiota–gut–brain axis. It includes neural, immune, and endocrine components, as well as their associated functional effects.

Table 1. Key components, mechanisms, and clinical implications of the microbiota–gut–brain axis

Category	Key Components / Factors	Mechanisms of Action	Clinical Implications
Neural pathways	Enteric nervous system (ENS), vagus nerve	Transmission of afferent and efferent signals; modulation of	Regulation of mood, cognition, stress response; involvement

		neurotransmission	in depression and anxiety
Immune system	Cytokines (IL-6, TNF-α), immune cells	Immune activation, neuroinflammation, systemic inflammation	Contribution to neurodegenerative diseases, psychiatric disorders
Endocrine pathways	HPA axis, cortisol, gut hormones (ghrelin, leptin)	Stress response, hormonal signaling, metabolic regulation	Impact on stress-related disorders, obesity, metabolic syndrome
Microbial metabolites	SCFAs (butyrate, acetate), neurotransmitters (GABA, serotonin)	Modulation of brain function, inflammation, blood–brain barrier integrity	Role in neuroprotection, epilepsy, depression
Intestinal barrier	Tight junction proteins, mucosal layer	Regulation of permeability (“leaky gut”)	Increased inflammation, risk of CNS disorders
Blood–brain barrier	BBB integrity, endothelial function	Control of molecule transport to CNS	Neuroinflammation, neurodegeneration
Neurological disorders	Alzheimer’s disease, Parkinson’s disease, epilepsy	Dysbiosis, neuroinflammation, neurotransmitter imbalance	Cognitive decline, motor dysfunction, seizures
Psychiatric disorders	Depression, anxiety, autism spectrum disorders	Altered microbiota, immune activation, neurotransmitter dysregulation	Behavioral and emotional disturbances
Metabolic diseases	Obesity, type 2 diabetes	Altered energy metabolism, inflammation	Insulin resistance, metabolic dysregulation
Therapeutic strategies	Probiotics, prebiotics, synbiotics, diet	Restoration of microbiota balance, modulation of MGBA	Potential treatment for GI, metabolic, and mental disorders

Key Mechanisms of the Microbiota–Gut–Brain Axis

One of the central components of this system is the enteric nervous system (ENS), an autonomous neural network composed of hundreds of millions of neurons that is capable of functioning independently of the central nervous system [30]. Due to its anatomical location within the gut wall, it is among the first to detect signals originating from the gut microbiota, including microbial metabolites [31].

The microbiota can modulate the expression of various receptors within the ENS, including serotonergic receptors, thereby contributing to the activation of the vagus nerve—one of the principal communication pathways between the gut and the brain [32]. In turn, the vagus nerve is involved in regulating a wide range of physiological processes, including feeding behavior, energy metabolism, and emotional responses [33]. Signal transmission occurs both through direct neural pathways and via circulating blood-borne molecules, enabling multi-channel communication between the gut and distant organs [34].

A particularly important role in this system is played by gut microbial metabolites, including short-chain fatty acids, neurotransmitters, and hormone-like compounds. These molecules can influence the central nervous system either directly, by crossing the blood–brain barrier, or indirectly, by modulating immune and endocrine signaling pathways [35–37]. Cholinergic signaling mechanisms further coordinate interactions between the enteric and central nervous systems, enhancing the integration and fine-tuning of gut–brain communication [38].

Overall, the microbiota–gut–brain axis represents a multi-level and highly dynamic system in which diverse mechanisms continuously interact to maintain physiological balance and support the organism’s adaptation to changing internal and external environments.

Role of Dysbiosis and the Clinical Significance of the Gut–Brain Axis

Disruption of the composition and functional activity of the gut microbiota, known as dysbiosis, is increasingly recognized as an important risk factor for a wide range of diseases. These include not only gastrointestinal disorders but also systemic conditions such as cardiovascular, metabolic, and oncological diseases, as well as neurological and psychiatric disorders. This broad spectrum of associations highlights the systemic influence of the gut microbiota on human health. Several key factors contribute to the development of dysbiosis, including excessive use of antibiotics, chronic stress, and exposure to various environmental and medical influences, such as chemotherapy [39]. These factors can reduce microbial diversity, impair functional stability of the microbiota, and increase host susceptibility to disease [40]. Moreover, stress-related conditions may promote the overgrowth of pathogenic microorganisms, further intensifying inflammatory processes.

Both clinical and experimental evidence suggests a close relationship between dysbiosis and the development of psychiatric disorders, including depression, anxiety disorders, and autism spectrum disorders [41, 42]. In individuals with autism, characteristic alterations in gut microbiota composition have been observed, indicating a potential role of microbial factors in shaping behavioral and cognitive outcomes [43]. Microbial metabolites, particularly short-chain fatty acids,

play a key role in regulating neuroimmune processes by influencing microglial activity, inflammatory responses, and neurotransmitter balance [44]. Disruptions in their production have been associated with depression and other psychiatric conditions [45]. In addition, alterations in the gut microbiota may contribute to the development of neurodegenerative diseases, including Alzheimer's disease and Parkinson's disease [46].

The immune component is of particular importance, as a large proportion of immune cells is located within gut-associated lymphoid tissue. This makes the gut microbiota a major regulator of immune responses and inflammatory activity [47]. Through T-cell activation and cytokine production, the microbiota indirectly influences the central nervous system, contributing to complex neuroimmune interactions [48].

Furthermore, imbalances in key neurotransmitters, including GABA, glutamate, dopamine, and serotonin, have been linked to dysbiotic changes and may play a role in conditions such as schizophrenia and epilepsy [49, 50]. Collectively, these findings indicate that the microbiota–gut–brain axis represents a central pathway in the pathogenesis of a wide range of diseases, and its further investigation offers promising opportunities for developing novel therapeutic strategies aimed at modulating the gut microbiota and restoring physiological homeostasis.

Limitations and Future Directions

Despite substantial progress in elucidating the microbiota–gut–brain axis (MGBA), several important limitations continue to constrain both mechanistic interpretation and clinical translation of current findings. A significant proportion of evidence is still derived from animal models, particularly rodent studies, which, although highly informative for mechanistic exploration, do not fully capture the complexity of human microbiome architecture, interindividual variability, environmental exposures, and lifestyle-related determinants. Consequently, direct extrapolation of these findings to human physiology remains limited.

In addition, there is marked heterogeneity across studies in experimental design, cohort characteristics, and analytical methodologies. Factors such as age, diet, geographic location, medication use, and comorbid conditions exert profound effects on gut microbial composition and function, thereby introducing substantial variability and limiting reproducibility across studies. Methodological differences in microbiome profiling approaches, including 16S rRNA gene sequencing, shotgun metagenomics, and metabolomic platforms, further contribute to inconsistencies in data interpretation. A persistent lack of standardized protocols for sample collection, processing, and bioinformatic analysis remains a major barrier to cross-study comparability.

Importantly, current evidence is often pathway-specific rather than integrative. Although the MGBA is recognized as a multidimensional system involving neural, immune, endocrine, metabolic, and barrier-related mechanisms (as summarized in Table 1), most studies investigate these components in isolation. This fragmented approach limits the development of a unified systems-level model capable of fully capturing the dynamic interactions between the gut microbiota, intestinal barrier, immune signaling, hypothalamic–pituitary–adrenal (HPA) axis, and central nervous system. In particular, the coordinated role of intestinal permeability and blood–brain barrier integrity within this integrated network remains incompletely understood.

Another critical limitation lies in the difficulty of establishing causality. While numerous associations between dysbiosis and neurological, psychiatric, and metabolic disorders have been reported, it remains unclear whether microbial alterations are a cause, consequence, or epiphenomenon of disease states. Longitudinal cohort studies and well-controlled interventional trials are required to delineate temporal and causal relationships within the MGBA.

Furthermore, microbiome-targeted interventions, including probiotics, prebiotics, synbiotics, and dietary modulation, demonstrate highly variable and often strain-specific effects. Clinical outcomes are frequently inconsistent across studies, reflecting differences in microbial strains, dosing regimens, host background, and disease context. This variability highlights the need for precision-based microbiome therapies rather than generalized approaches.

Finally, while multi-omics technologies have advanced understanding of microbial composition and function, the integration of metagenomic, transcriptomic, proteomic, and metabolomic data into coherent functional frameworks remains incomplete. Future research should therefore prioritize systems biology approaches, large-scale multicenter studies, and standardized analytical pipelines to improve reproducibility and clinical translatability.

Conclusion

The microbiota–gut–brain axis represents a complex, dynamic, and bidirectionally regulated system that integrates neural, immune, endocrine, and metabolic signaling pathways to maintain physiological homeostasis. Within this framework, the gut microbiota actively participates in host communication through multiple interconnected routes, including the enteric nervous system, the vagus nerve, circulating microbial metabolites, immune mediators, and neuroendocrine signaling pathways such as the hypothalamic–pituitary–adrenal axis.

Accumulating evidence demonstrates that perturbations in gut microbial composition and function can significantly influence central nervous system processes, contributing to alterations in neurodevelopment, cognition, emotional regulation, and behavior. Dysbiosis, increased intestinal

permeability, systemic immune activation, and disruption of blood–brain barrier integrity emerge as key convergent mechanisms linking the gut environment to neurological and psychiatric dysfunction. Conversely, central nervous system activity, particularly stress-related signaling via the HPA axis and autonomic nervous system, exerts reciprocal effects on gut physiology and microbial ecology, reinforcing the bidirectional nature of this axis.

Importantly, the MGBA provides a promising conceptual framework for the development of novel diagnostic and therapeutic strategies. Microbiota-targeted interventions—including probiotics, prebiotics, synbiotics, dietary modulation, and emerging microbiome-based therapies—hold significant potential for modulating disease trajectories across gastrointestinal, metabolic, and neuropsychiatric disorders. However, clinical translation remains limited by heterogeneity in study design, incomplete mechanistic understanding, and variability in therapeutic responsiveness.

Future advances in the field will depend on the identification of robust microbial and metabolic signatures associated with specific disease phenotypes, as well as the integration of multi-omics technologies within systems-level analytical frameworks. In addition, the development of personalized microbiome-based interventions will require rigorous validation in large-scale, well-controlled clinical trials.

In summary, a deeper mechanistic understanding of the microbiota–gut–brain axis will not only refine current models of gut–brain communication but also pave the way toward precision medicine approaches targeting host–microbiome interactions in health and disease.

Conflicts of Interest

None declared.

Funding

None.

Author contributions

Conceptualization: DB. Study design: DB. Data acquisition and review of the literature: DB. Data analysis: DB. Making interpretations: DB. Drafting the manuscript: DB. Critically reviewing and editing the manuscript: DB. Final approval: DB. All co-authors take full responsibility for the integrity and accuracy of all aspects of the work.

Data availability

The data that support the finding of this study are available on a reasonable request from the corresponding author.

References

1. Zhuang, M., Zhang, X., & Cai, J. (2024). Microbiota-gut-brain axis: interplay between microbiota, barrier function and lymphatic system. Gut microbes, 16(1), 2387800. https://doi.org/10.1080/19490976.2024.2387800

2. Gwak, M. G., & Chang, S. Y. (2021). Gut-Brain Connection: Microbiome, Gut Barrier, and Environmental Sensors. Immune network, 21(3), e20. https://doi.org/10.4110/in.2021.21.e20

3. Barrio, C., Arias-Sánchez, S., & Martín-Monzón, I. (2022). The gut microbiota-brain axis, psychobiotics and its influence on brain and behaviour: A systematic review. Psychoneuroendocrinology, 137, 105640. https://doi.org/10.1016/j.psyneuen.2021.105640

4. Lu, H., Zhang, H., Wu, Z., & Li, L. (2024). Microbiota-gut-liver-brain axis and hepatic encephalopathy. Microbiome research reports, 3(2), 17. https://doi.org/10.20517/mrr.2023.44

5. Wen, C., Wei, S., Zong, X., Wang, Y., & Jin, M. (2021). Microbiota-gut-brain axis and nutritional strategy under heat stress. Animal nutrition (Zhongguo xu mu shou yi xue hui), 7(4), 1329–1336. https://doi.org/10.1016/j.aninu.2021.09.008

6. Ohara, T. E., & Hsiao, E. Y. (2025). Microbiota-neuroepithelial signalling across the gut-brain axis. Nature reviews. Microbiology, 23(6), 371–384. https://doi.org/10.1038/s41579-024-01136-9

7. Bertollo, A. G., Santos, C. F., Bagatini, M. D., & Ignácio, Z. M. (2025). Hypothalamus-pituitary-adrenal and gut-brain axes in biological interaction pathway of the depression. Frontiers in neuroscience, 19, 1541075. https://doi.org/10.3389/fnins.2025.1541075

8. Aburto, M. R., & Cryan, J. F. (2024). Gastrointestinal and brain barriers: unlocking gates of communication across the microbiota-gut-brain axis. Nature reviews. Gastroenterology & hepatology, 21(4), 222–247. https://doi.org/10.1038/s41575-023-00890-0

9. Wachsmuth, H. R., Weninger, S. N., & Duca, F. A. (2022). Role of the gut-brain axis in energy and glucose metabolism. Experimental & molecular medicine, 54(4), 377–392. https://doi.org/10.1038/s12276-021-00677-w

10. Sasso, J. M., Ammar, R. M., Tenchov, R., Lemmel, S., Kelber, O., Grieswelle, M., & Zhou, Q. A. (2023). Gut Microbiome-Brain Alliance: A Landscape View into Mental and Gastrointestinal Health and Disorders. ACS chemical neuroscience, 14(10), 1717–1763. https://doi.org/10.1021/acschemneuro.3c00127

11. Liu, L., Huh, J. R., & Shah, K. (2022). Microbiota and the gut-brain-axis: Implications for new therapeutic design in the CNS. EBioMedicine, 77, 103908. https://doi.org/10.1016/j.ebiom.2022.103908

12. Song, Z., Song, R., Liu, Y., Wu, Z., & Zhang, X. (2023). Effects of ultra-processed foods on the microbiota-gut-brain axis: The bread-and-butter issue. Food research international (Ottawa, Ont.), 167, 112730. https://doi.org/10.1016/j.foodres.2023.112730

13. Bhatia, N. Y., Jalgaonkar, M. P., Hargude, A. B., Sherje, A. P., Oza, M. J., & Doshi, G. M. (2023). Gut-Brain Axis and Neurological Disorders-How Microbiomes Affect our Mental Health. CNS & neurological disorders drug targets, 22(7), 1008–1030. https://doi.org/10.2174/1871527321666220822172039

14. Doenyas, C., Clarke, G., & Cserjési, R. (2025). Gut-brain axis and neuropsychiatric health: recent advances. Scientific reports, 15(1), 3415. https://doi.org/10.1038/s41598-025-86858-3

15. Chang, L., Wei, Y., & Hashimoto, K. (2022). Brain-gut-microbiota axis in depression: A historical overview and future directions. Brain research bulletin, 182, 44–56. https://doi.org/10.1016/j.brainresbull.2022.02.004

16. He, Y., Wang, K., Su, N., Yuan, C., Zhang, N., Hu, X., Fu, Y., & Zhao, F. (2024). Microbiota-gut-brain axis in health and neurological disease: Interactions between gut microbiota and the nervous system. Journal of cellular and molecular medicine, 28(18), e70099. https://doi.org/10.1111/jcmm.70099

17. Kuijer, E. J., & Steenbergen, L. (2023). The microbiota-gut-brain axis in hippocampus-dependent learning and memory: current state and future challenges. Neuroscience and biobehavioral reviews, 152, 105296. https://doi.org/10.1016/j.neubiorev.2023.105296

18. Filho, A. M. C., Gomes, N. S., Lós, D. B., Leite, I. B., Tremblay, M. È., & Macêdo, D. S. (2024). Microglia and Microbiome-Gut-Brain Axis. Advances in neurobiology, 37, 303–331. https://doi.org/10.1007/978-3-031-55529-9_17

19. Aagaard, K., Ma, J., Antony, K. M., Ganu, R., Petrosino, J., & Versalovic, J. (2014). The placenta harbors a unique microbiome. Science translational medicine, 6(237), 237ra65. https://doi.org/10.1126/scitranslmed.3008599

20. Tan H. E. (2023). The microbiota-gut-brain axis in stress and depression. Frontiers in neuroscience, 17, 1151478. https://doi.org/10.3389/fnins.2023.1151478

21. Micic, D., Polovina, S., Micic, D., & Macut, D. (2023). OBESITY AND GUT-BRAIN AXIS. Acta endocrinologica (Bucharest, Romania : 2005), 19(2), 234–240. https://doi.org/10.4183/aeb.2023.234

22. Loh, J. S., Mak, W. Q., Tan, L. K. S., Ng, C. X., Chan, H. H., Yeow, S. H., Foo, J. B., Ong, Y. S., How, C. W., & Khaw, K. Y. (2024). Microbiota-gut-brain axis and its therapeutic applications in neurodegenerative diseases. Signal transduction and targeted therapy, 9(1), 37. https://doi.org/10.1038/s41392-024-01743-1

23. Toader, C., Dobrin, N., Costea, D., Glavan, L. A., Covache-Busuioc, R. A., Dumitrascu, D. I., Bratu, B. G., Costin, H. P., & Ciurea, A. V. (2024). Mind, Mood and Microbiota-Gut-Brain Axis in Psychiatric Disorders. International journal of molecular sciences, 25(6), 3340. https://doi.org/10.3390/ijms25063340

24. Sommer, F., & Bäckhed, F. (2013). The gut microbiota--masters of host development and physiology. Nature reviews. Microbiology, 11(4), 227–238. https://doi.org/10.1038/nrmicro2974

25. Schneider, E., O'Riordan, K. J., Clarke, G., & Cryan, J. F. (2024). Feeding gut microbes to nourish the brain: unravelling the diet-microbiota-gut-brain axis. Nature metabolism, 6(8), 1454–1478. https://doi.org/10.1038/s42255-024-01108-6

26. Chae, Y. R., Lee, Y. R., Kim, Y. S., & Park, H. Y. (2024). Diet-Induced Gut Dysbiosis and Leaky Gut Syndrome. Journal of microbiology and biotechnology, 34(4), 747–756. https://doi.org/10.4014/jmb.2312.12031

27. Zhu, F., Tu, H., & Chen, T. (2022). The Microbiota-Gut-Brain Axis in Depression: The Potential Pathophysiological Mechanisms and Microbiota Combined Antidepression Effect. Nutrients, 14(10), 2081. https://doi.org/10.3390/nu14102081

28. Asadi, A., Shadab Mehr, N., Mohamadi, M. H., Shokri, F., Heidary, M., Sadeghifard, N., & Khoshnood, S. (2022). Obesity and gut-microbiota-brain axis: A narrative review. Journal of clinical laboratory analysis, 36(5), e24420. https://doi.org/10.1002/jcla.24420

29. Wang, Q., Yang, Q., & Liu, X. (2023). The microbiota-gut-brain axis and neurodevelopmental disorders. Protein & cell, 14(10), 762–775. https://doi.org/10.1093/procel/pwad026

30. Fleming, M. A., 2nd, Ehsan, L., Moore, S. R., & Levin, D. E. (2020). The Enteric Nervous System and Its Emerging Role as a Therapeutic Target. Gastroenterology research and practice, 2020, 8024171. https://doi.org/10.1155/2020/8024171

31. Ahmed, H., Leyrolle, Q., Koistinen, V., Kärkkäinen, O., Layé, S., Delzenne, N., & Hanhineva, K. (2022). Microbiota-derived metabolites as drivers of gut-brain communication. Gut microbes, 14(1), 2102878. https://doi.org/10.1080/19490976.2022.2102878

32. Qu, S., Yu, Z., Zhou, Y., Wang, S., Jia, M., Chen, T., & Zhang, X. (2024). Gut microbiota modulates neurotransmitter and gut-brain signaling. Microbiological research, 287, 127858. https://doi.org/10.1016/j.micres.2024.127858

33. Wang, Y., Duan, C., Du, X., Zhu, Y., Wang, L., Hu, J., & Sun, Y. (2025). Vagus Nerve and Gut-Brain Communication. The Neuroscientist : a review journal bringing neurobiology, neurology and psychiatry, 31(3), 262–278. https://doi.org/10.1177/10738584241259702

34. Mayer, E. A., Nance, K., & Chen, S. (2022). The Gut-Brain Axis. Annual review of medicine, 73, 439–453. https://doi.org/10.1146/annurev-med-042320-014032

35. Yan, M., Man, S., Sun, B., Ma, L., Guo, L., Huang, L., & Gao, W. (2023). Gut liver brain axis in diseases: the implications for therapeutic interventions. Signal transduction and targeted therapy, 8(1), 443. https://doi.org/10.1038/s41392-023-01673-4

36. Tao, R., Liu, S., Crawford, J., & Tao, F. (2023). Gut-Brain Crosstalk and the Central Mechanisms of Orofacial Pain. Brain sciences, 13(10), 1456. https://doi.org/10.3390/brainsci13101456

37. Agirman, G., Yu, K. B., & Hsiao, E. Y. (2021). Signaling inflammation across the gut-brain axis. Science (New York, N.Y.), 374(6571), 1087–1092. https://doi.org/10.1126/science.abi6087

38. Momen, Y. S., Mishra, J., & Kumar, N. (2024). Brain-Gut and Microbiota-Gut-Brain Communication in Type-2 Diabetes Linked Alzheimer's Disease. Nutrients, 16(15), 2558. https://doi.org/10.3390/nu16152558

39. Rykalo, N., Riehl, L., & Kress, M. (2024). The gut microbiome and the brain. Current opinion in supportive and palliative care, 18(4), 282–291. https://doi.org/10.1097/SPC.0000000000000717

40. Doroszkiewicz, J., Groblewska, M., & Mroczko, B. (2021). The Role of Gut Microbiota and Gut-Brain Interplay in Selected Diseases of the Central Nervous System. International journal of molecular sciences, 22(18), 10028. https://doi.org/10.3390/ijms221810028

41. Park, J. C., Chang, L., Kwon, H. K., & Im, S. H. (2025). Beyond the gut: decoding the gut-immune-brain axis in health and disease. Cellular & molecular immunology, 22(11), 1287–1312. https://doi.org/10.1038/s41423-025-01333-3

42. Suda, K., & Matsuda, K. (2022). How Microbes Affect Depression: Underlying Mechanisms via the Gut-Brain Axis and the Modulating Role of Probiotics. International journal of molecular sciences, 23(3), 1172. https://doi.org/10.3390/ijms23031172

43. Park, J. C., & Im, S. H. (2022). The gut-immune-brain axis in neurodevelopment and neurological disorders. Microbiome research reports, 1(4), 23. https://doi.org/10.20517/mrr.2022.11

44. Xie, X., Wang, L., Dong, S., Ge, S., & Zhu, T. (2024). Immune regulation of the gut-brain axis and lung-brain axis involved in ischemic stroke. Neural regeneration research, 19(3), 519–528. https://doi.org/10.4103/1673-5374.380869

45. Patel, R. A., Panche, A. N., & Harke, S. N. (2025). Gut microbiome-gut brain axis-depression: interconnection. The world journal of biological psychiatry : the official journal of the World Federation of Societies of Biological Psychiatry, 26(1), 1–36. https://doi.org/10.1080/15622975.2024.2436854

46. Szandruk-Bender, M., Wiatrak, B., & Szeląg, A. (2022). The Risk of Developing Alzheimer's Disease and Parkinson's Disease in Patients with Inflammatory Bowel Disease: A Meta-Analysis. Journal of clinical medicine, 11(13), 3704. https://doi.org/10.3390/jcm11133704

47. Al Bander, Z., Nitert, M. D., Mousa, A., & Naderpoor, N. (2020). The Gut Microbiota and Inflammation: An Overview. International journal of environmental research and public health, 17(20), 7618. https://doi.org/10.3390/ijerph17207618

48. Zhang, R., Ding, N., Feng, X., & Liao, W. (2025). The gut microbiome, immune modulation, and cognitive decline: insights on the gut-brain axis. Frontiers in immunology, 16, 1529958. https://doi.org/10.3389/fimmu.2025.1529958

49. Ju, S., Shin, Y., Han, S., Kwon, J., Choi, T. G., Kang, I., & Kim, S. S. (2023). The Gut-Brain Axis in Schizophrenia: The Implications of the Gut Microbiome and SCFA Production. Nutrients, 15(20), 4391. https://doi.org/10.3390/nu15204391

50. Ding, M., Lang, Y., Shu, H., Shao, J., & Cui, L. (2021). Microbiota-Gut-Brain Axis and Epilepsy: A Review on Mechanisms and Potential Therapeutics. Frontiers in immunology, 12, 742449. https://doi.org/10.3389/fimmu.2021.742449

UDC 616.12-008

Dana Bekaryssova[1], Yekaterina Gavrikova[2], Gulmira Mutalipova[3]

[1] Department for Coordination and Development of Scientific Journals, South Kazakhstan Medical Academy, Shymkent, Kazakhstan.

[2] Department of Consultation and Diagnostics, Shymkent Heart Center, Shymkent, Kazakhstan.

[3] Department of Biology and Biochemistry, South Kazakhstan Medical Academy, Shymkent, Kazakhstan.

Corresponding author:

Dana Bekaryssova, MD, PhD

Department for Coordination and Development of Scientific Journals, South Kazakhstan Medical Academy, Shymkent, Kazakhstan.

Email: bekaryssova.da@gmail.com

ORCID IDs:

Dana Bekaryssova[1] (https://orcid.org/0000-0002-9651-7295)

Yekaterina Gavrikova[2] (https://orcid.org/0009-0004-0266-0923)

Gulmira Mutalipova[3] (https://orcid.org/0000-0001-8336-0711)

ISCHAEMIC HEART DISEASE IN AN ELDERLY PATIENT WITH ARTERIAL HYPERTENSION AND METABOLIC DISORDERS: A CASE REPORT

Abstract

Introduction. *Combined cardiovascular pathology, including ischaemic heart disease (IHD), arterial hypertension (AH), and metabolic disorders, represents a significant clinical challenge, particularly in elderly patients.*

Case report. *We describe the case of an 88-year-old man with a long-standing history of grade III AH, coronary heart disease (CHD), and hyperuricaemia. The patient had previously experienced a myocardial infarction and subsequently underwent coronary artery stenting. Electrocardiographic evaluation revealed first-degree atrioventricular (AV) block and left ventricular hypertrophy. To contextualize this case within the existing evidence, a systematic literature search was conducted in Medline, Scopus, and Web of Science using keywords and MeSH terms related to ischaemic heart disease, arterial hypertension, older age, and metabolic disorders.*

Conclusion. *This case highlights the importance of a personalised and comprehensive management approach in elderly patients with combined cardiovascular pathology. Such an approach should include effective blood pressure and lipid profile control, optimisation of heart rate, correction of metabolic abnormalities, and regular dynamic monitoring to reduce the risk of complications and maintain functional status.*

Keywords: *Ischaemic heart disease, arterial hypertension, hyperuricaemia, elderly patient, heart failure*

Бекарысова Дана[1], Гаврикова Екатерина[2], Муталипова Гульмира[3]

[1] Отдел координации и развития научных журналов, Южно-Казахстанская Медицинская Академия, Шымкент, Казахстан

[2] Консультативно-диагностическое отделение, Центр Сердца Шымкент, Шымкент, Казахстан

[3] Кафедра биологии и биохимии, Южно-Казахстанская Медицинская Академия, Шымкент, Казахстан

ИШЕМИЧЕСКАЯ БОЛЕЗНЬ СЕРДЦА У ПОЖИЛОГО ПАЦИЕНТА С АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ И МЕТАБОЛИЧЕСКИМИ НАРУШЕНИЯМИ: КЛИНИЧЕСКИЙ СЛУЧАЙ

Аннотация

Введение. *Сочетанная сердечно-сосудистая патология, включающая ишемическую болезнь сердца (ИБС), артериальную гипертензию (АГ) и метаболические нарушения, представляет собой значимую клиническую проблему, особенно у пациентов пожилого возраста.*

Описание клинического случая. *Представлен случай 88-летнего мужчины с длительным анамнезом артериальной гипертензии III степени, ишемической болезни сердца и гиперурикемии. В анамнезе у пациента имелся перенесённый инфаркт миокарда, после чего было выполнено стентирование коронарных артерий. При электрокардиографическом исследовании выявлены атриовентрикулярная (AV) блокада I степени и гипертрофия левого желудочка. Для сопоставления данного случая с имеющимися научными данными был проведён систематический поиск литературы в базах Medline, Scopus и Web of Science с использованием ключевых слов и MeSH-терминов, связанных с ишемической болезнью сердца, артериальной гипертензией, пожилым возрастом и метаболическими нарушениями.*

Заключение. *Данный клинический случай подчёркивает важность персонализированного и комплексного подхода к ведению пожилых пациентов с сочетанной сердечно-сосудистой патологией. Такой подход должен включать эффективный контроль артериального давления и липидного профиля, оптимизацию частоты сердечных сокращений, коррекцию метаболических нарушений и регулярное динамическое наблюдение с целью снижения риска осложнений и сохранения функционального статуса.*

Ключевые слова: *ишемическая болезнь сердца, артериальная гипертензия, гиперурикемия, пожилой пациент, сердечная недостаточность*

Бекарысова Дана[1], Гаврикова Екатерина[2], Муталипова Гүлмира[3]

[1] Ғылыми журналдарды үйлестіру және дамыту бөлімі, Оңтүстік Қазақстан Медицина Академиясы, Шымкент, Қазақстан

[2] Консультациялық-диагностикалық бөлім, Шымкент Жүрек Орталығы, Шымкент, Қазақстан

[3] Биология және биохимия кафедрасы, Оңтүстік Қазақстан Медицина Академиясы, Шымкент, Қазақстан

АРТЕРИЯЛЫҚ ГИПЕРТЕНЗИЯСЫ ЖӘНЕ МЕТАБОЛИКАЛЫҚ БҰЗЫЛЫСТАРЫ БАР ЕГДЕ ЖАСТАҒЫ НАУҚАСТАҒЫ ИШЕМИЯЛЫҚ ЖҮРЕК АУРУЫ: КЛИНИКАЛЫҚ ЖАҒДАЙ

Аңдатпа

Кіріспе. *Ишемиялық жүрек ауруын (ИЖА), артериялық гипертензияны (АГ) және метаболикалық бұзылыстарды қамтитын біріктірілген жүрек-қантамыр патологиясы, әсіресе егде жастағы науқастар арасында, маңызды клиникалық мәселе болып табылады.*

Клиникалық жағдай сипаттамасы. *88 жастағы ер адамда артериялық гипертензияның III дәрежесі, ишемиялық жүрек ауруы және гиперурикемия ұзақ уақыт бойы байқалған. Анамнезінде миокард инфаркті болған, кейін коронарлық артерияларға стенттеу жүргізілген. Электрокардиографиялық зерттеу нәтижесінде I дәрежелі атриовентрикулярлық (AV) блокада және сол жақ қарыншаның гипертрофиясы анықталды. Бұл клиникалық жағдайды қолда бар ғылыми деректермен салыстыру мақсатында Medline, Scopus және Web of Science дерекқорларында ишемиялық жүрек ауруы, артериялық гипертензия, егде жас және метаболикалық бұзылыстарға қатысты кілт сөздер мен MeSH терминдерін пайдалана отырып, жүйелі әдебиет іздеуі жүргізілді.*

Қорытынды. *Бұл клиникалық жағдай егде жастағы науқастардағы біріктірілген жүрек-қантамыр патологиясын басқаруда жекелендірілген және кешенді тәсілдің маңыздылығын көрсетеді. Мұндай тәсіл артериялық қысымды және липидтік профильді тиімді бақылауды, жүрек соғу жиілігін оңтайландыруды, метаболикалық бұзылыстарды түзетуді және асқынулар қаупін төмендету мен функционалдық жағдайды сақтау мақсатында тұрақты динамикалық бақылауды қамтуы тиіс.*

Түйін сөздер: *ишемиялық жүрек ауруы, артериялық гипертензия, гиперурикемия, егде жастағы науқас, жүрек жеткіліксіздігі*

Introduction

Cardiovascular diseases (CVD) remain the leading cause of mortality worldwide and represent one of the most significant challenges in modern medicine [1]. According to the World Health Organization, CVD account for approximately 17.9 million deaths annually, representing nearly 32% of all deaths globally, with ischaemic heart disease (IHD) and stroke responsible for the majority of these cases [2].

The development of cardiovascular disease is associated with a complex interaction of multiple risk factors, which are generally classified as non-modifiable and modifiable. Non-modifiable factors include genetic predisposition, age, sex, and race, whereas modifiable factors include smoking, unhealthy dietary habits, physical inactivity, and chronic stress [3]. Among the modifiable risk factors, arterial hypertension (AH) plays a particularly important role, as it is considered one of the key predictors of IHD and other cardiovascular complications. According to epidemiological data, the prevalence of AH among the adult population exceeds 1.28 billion people worldwide; however, only about 46% of patients achieve adequate blood pressure control.

The management of elderly and very elderly patients represents a particular clinical challenge, as advanced age itself is an independent risk factor for cardiovascular disease [4]. Patients in this age group frequently present with significant comorbidities, including a combination of cardiovascular and metabolic disorders. In addition, inflammatory mechanisms, including the activity of various interleukins identified in certain rheumatic diseases, may further contribute to increased cardiovascular risk [5].

Against the background of age-related physiological changes, the coexistence of arterial hypertension, ischaemic heart disease, cardiac conduction abnormalities, and metabolic disturbances such as hyperuricaemia can significantly complicate the clinical course and worsen the prognosis. In such cases, a comprehensive and multidisciplinary approach to patient diagnosis and management becomes particularly important [6].

The analysis and description of complex clinical cases contribute to a better understanding of disease pathogenesis and allow for the evaluation of diagnostic and therapeutic strategies in patients with multiple comorbidities.

The aim of this study was to describe a clinical case of ischaemic heart disease combined with grade III arterial hypertension and hyperuricaemia in an elderly patient, with an analysis of the

diagnostic features, treatment approach, and clinical course of the disease in the context of current international recommendations.

Search strategy

A targeted and systematic literature search was conducted to identify previously published clinical case reports and case series describing ischaemic heart disease in elderly patients with cardiovascular and metabolic comorbidities. The search was performed in the Medline/PubMed, Scopus, and Web of Science databases in accordance with established recommendations for comprehensive and reproducible literature searches. The search strategy combined Medical Subject Headings (MeSH) and free-text keywords using Boolean operators. The main search terms included “Ischaemic Heart Disease” OR “Coronary Artery Disease” OR “Myocardial Infarction” in combination with “Arterial Hypertension” OR “Hypertension,” “Elderly” OR “Older Adults” OR “Advanced Age,” “Hyperuricaemia” OR “Metabolic Comorbidity,” and “Case Report” OR “Case Series.”

Eligible publications included peer-reviewed case reports and small case series describing adult and elderly patients (aged 65 years and older) with ischaemic heart disease accompanied by arterial hypertension and/or metabolic risk factors, with particular attention to conduction abnormalities and structural cardiac changes. Only articles published in English were considered.

Studies involving pediatric populations, animal models, narrative reviews without original clinical data, and reports focusing exclusively on isolated coronary artery disease without relevant cardiovascular or metabolic comorbidities were excluded. Articles lacking sufficient clinical, diagnostic, or therapeutic detail were also excluded. The identified publications were reviewed and analyzed to contextualize the clinical presentation, diagnostic approach, management strategies, and outcomes of the present case within the existing body of evidence.

Case report

An 88-year-old male patient was examined by a cardiologist at a specialized cardiology center due to periodic episodes of dizziness. At the time of admission, the patient did not report chest pain, shortness of breath at rest or during routine physical activity, palpitations, or an irregular heartbeat. Physical exertion was not associated with angina pectoris, suggesting relative clinical stability.

According to the medical history, the patient had suffered from arterial hypertension for many years, with maximum recorded blood pressure values reaching 170/90 mm Hg. In 2018, he experienced an acute myocardial infarction, after which percutaneous coronary intervention with stenting of the right coronary artery was performed. Following this acute coronary event, the patient has been under regular outpatient cardiology follow-up and has received comprehensive

pharmacological therapy, including β-blockers, antiplatelet agents, lipid-lowering drugs, and antihypertensive medications. Despite ongoing treatment, episodes of suboptimal blood pressure control were periodically observed.

The patient's medical history was negative for tuberculosis, viral hepatitis, and chronic infectious diseases. No history of drug or food allergies was reported. During the two weeks preceding the examination, the patient did not report fever and had no known contact with individuals with acute respiratory infections or COVID-19. Social status: retired. During physical examination, the patient's general condition was assessed as relatively satisfactory. He was conscious and oriented to time and place. The skin had normal coloration without signs of peripheral cyanosis. Multiple subcutaneous nodular formations consistent with gouty tophi were observed on the patient's upper and lower extremities, particularly in the area of the fingers and around the joints. These nodules were firm, painless on palpation, and characteristic of chronic tophaceous gout (Figure 1).

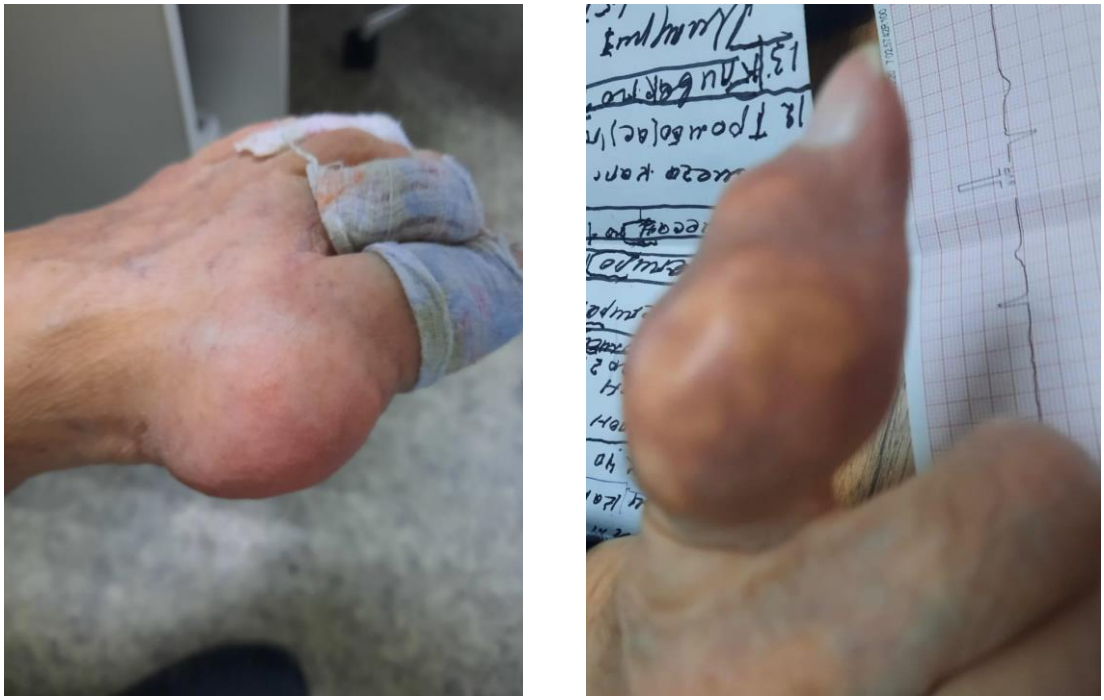


Figure 1. Clinical images of the patient's limbs illustrating the presence of gouty tophi

The patient had a normosthenic body habitus. His height was 160 cm and body weight was 63 kg, with a body mass index (BMI) of 24.6 kg/m², which falls within the normal range. Vesicular breathing was auscultated in the lungs, with no pathological rales detected. Heart sounds were somewhat muffled but rhythmic. The heart rate was 60 beats per minute. Blood pressure measured on both arms was symmetrical and recorded at 120/65 mm Hg. The abdomen was soft and non-

tender on palpation, and there were no signs of systemic venous congestion or peripheral edema. Electrocardiography demonstrated sinus rhythm with a heart rate of 58–60 beats per minute. Prolongation of the PR interval to 0.26 seconds was observed, corresponding to first-degree atrioventricular (AV) block. Signs of left ventricular hypertrophy and left atrial enlargement were also detected.

Echocardiography revealed preserved left ventricular systolic function with an ejection fraction of 54%, concentric hypertrophy of the left ventricular myocardium, and dilatation of both atria. Atherosclerotic changes were noted in the walls of the aortic root and ascending aorta. Moderate valvular regurgitation was also identified, including grade I aortic and mitral regurgitation and grade I–II tricuspid regurgitation. Left ventricular diastolic function was preserved, and no pericardial effusion was detected.

Laboratory testing revealed marked hyperuricaemia, with a serum uric acid level of 590 μmol/L, exceeding the recommended target range and representing an additional adverse metabolic risk factor for cardiovascular complications.

Based on the combination of clinical, instrumental, and laboratory findings, the patient was diagnosed with ischaemic heart disease with a history of myocardial infarction and coronary artery stenting, grade III arterial hypertension with very high cardiovascular risk, chronic heart failure with New York Heart Association (NYHA) functional class II, first-degree AV block, left ventricular hypertrophy, and hyperuricaemia. The patient was advised to optimize pharmacological therapy aimed at strict control of blood pressure, heart rate, lipid profile, and uric acid levels. In addition, 24-hour Holter ECG monitoring was recommended to further assess cardiac rhythm and conduction abnormalities.

Discussion

The presented clinical case illustrates a typical yet clinically complex presentation of ischaemic heart disease in an elderly patient with multiple comorbidities. The combination of long-standing arterial hypertension, a history of myocardial infarction, conduction disturbances, and metabolic disorders reflects the cumulative cardiovascular risk characteristic of the elderly population.

According to international studies, the prevalence of ischaemic heart disease increases significantly with age and reaches its highest levels among individuals over 80 years of age. A similar trend is observed for arterial hypertension, which affects more than 70% of elderly individuals and represents one of the leading factors contributing to myocardial remodeling. Prolonged pressure overload promotes the development of left ventricular hypertrophy, diastolic

dysfunction, and heart failure with preserved ejection fraction. In the present clinical case, the detected left ventricular hypertrophy and atrial dilatation are likely the result of chronic pressure overload associated with previously insufficient control of arterial hypertension.

The presence of first-degree atrioventricular (AV) block is also of particular clinical interest. Although this conduction abnormality is often considered relatively benign, in elderly patients with ischaemic heart disease receiving β-blocker therapy it may contribute to symptoms of hypoperfusion. In the present case, the patient experienced episodes of dizziness, which may be associated with the characteristics of atrioventricular conduction. Similar clinical observations have been described in the literature, emphasizing the importance of an individualized assessment of the clinical significance of conduction disturbances in older patients.

It should also be noted that cardiovascular diseases may develop both independently and in association with other comorbid conditions. In recent years, increasing attention has been paid to the relationship between cardiovascular diseases and autoimmune as well as metabolic disorders [7]. One such condition is gout, a systemic disease characterized by the deposition of monosodium urate crystals in the joints and surrounding tissues, leading to the development of inflammatory arthropathy [8]. Currently, hyperuricaemia, which often accompanies gout and was detected in the present patient, is considered an independent risk factor for cardiovascular disease. Several cohort studies have demonstrated an association between elevated uric acid levels and the progression of arterial hypertension, atherosclerosis, and chronic heart failure [9]. In this case, the presence of hyperuricaemia may have further contributed to vascular dysfunction and the progression of atherosclerotic changes.

Comparison of the present case with previously published clinical series and registry data highlights the importance of a comprehensive and personalized approach to the management of elderly patients with ischaemic heart disease. In this context, in addition to pharmacological therapy, non-pharmacological interventions—including regular physical activity and a balanced diet—play a significant role and are associated with a reduction in the incidence of cardiovascular events [10]. Furthermore, current clinical guidelines emphasize the importance of achieving optimal blood pressure and lipid targets even in older patients, provided that treatment is well tolerated. These principles were applied in the management of the present case.

The strengths of this clinical observation include the detailed description of the clinical course in an elderly patient, the comprehensive assessment of structural and functional cardiac changes, and the emphasis on the role of metabolic risk factors in the progression of cardiovascular disease.

Moreover, this case reflects real-world clinical practice in the management of complex patients, who are often underrepresented in randomized clinical trials.

However, this observation has several limitations. First, it is based on the description of a single clinical case, which limits the generalizability of the findings to a broader patient population. In addition, advanced myocardial imaging techniques and long-term dynamic follow-up were not available.

Conclusion

This clinical case demonstrates the complexity of managing an elderly patient with multimorbid cardiovascular pathology, including ischaemic heart disease, grade III arterial hypertension, conduction disorders, and hyperuricaemia. The accumulation of cardiovascular risk factors—such as a history of myocardial infarction, left ventricular hypertrophy, and metabolic disturbances—highlights the importance of a comprehensive assessment of the patient's condition, taking into account age-related structural and functional cardiac changes.

This observation confirms the value of a personalized management approach that includes careful monitoring of blood pressure, lipid profile, heart rate, and metabolic parameters, as well as regular dynamic follow-up. Such an approach may help reduce the risk of cardiovascular complications and maintain satisfactory functional status in elderly patients. Overall, this case underscores the need for further research aimed at optimizing management strategies for multimorbid patients in the context of an aging population.

Informed consent

Written informed consent was obtained from the patient for publication of this report.

Conflicts of Interest

None declared.

Funding

None.

Author contributions

Conceptualization: DB, YG, GM. Study design: DB. Data acquisition and review of the literature: DB. Data analysis: DB, YG, GM. Making interpretations: DB, YG, GM. Drafting the manuscript: DB, GM. Critically reviewing and editing the manuscript: DB. Final approval: DB, YG, GM. All co-authors take full responsibility for the integrity and accuracy of all aspects of the work.

Data availability

The data that support the finding of this study are available on a reasonable request from the corresponding author.

References

1. Chen, X., Xu, L., & Li, Z. (2022). Autonomic Neural Circuit and Intervention for Comorbidity Anxiety and Cardiovascular Disease. Frontiers in physiology, 13, 852891. https://doi.org/10.3389/fphys.2022.852891

2. Ahmad F. (2023). Dietary patterns and the risk of cardiovascular diseases. Nutrition and health, 29(4), 609–610. https://doi.org/10.1177/02601060231216523

3. Bernatova, I., Liskova, S., & Bartekova, M. (2022). Hypertension and Cardiovascular Diseases: From Etiopathogenesis to Potential Therapeutic Targets. International journal of molecular sciences, 23(14), 7742. https://doi.org/10.3390/ijms23147742

4. Cruz-Ávila, H. A., Ramírez-Alatriste, F., Martínez-García, M., & Hernández-Lemus, E. (2024). Comorbidity patterns in cardiovascular diseases: the role of life-stage and socioeconomic status. Frontiers in cardiovascular medicine, 11, 1215458. https://doi.org/10.3389/fcvm.2024.1215458

5. Madenidou, A. V., Mavrogeni, S., & Nikiphorou, E. (2023). Cardiovascular Disease and Cardiac Imaging in Inflammatory Arthritis. Life (Basel, Switzerland), 13(4), 909. https://doi.org/10.3390/life13040909

6. Vinjerui, K. H., Boeckxstaens, P., Douglas, K. A., & Sund, E. R. (2020). Prevalence of multimorbidity with frailty and associations with socioeconomic position in an adult population: findings from the cross-sectional HUNT Study in Norway. BMJ open, 10(6), e035070. https://doi.org/10.1136/bmjopen-2019-035070

7. Sagtaganov, Z., Yessirkepov, M., Bekaryssova, D., & Suigenbayev, D. (2024). Managing rheumatoid arthritis and cardiovascular disease: the role of physical medicine and rehabilitation. Rheumatology international, 44(9), 1749–1756. https://doi.org/10.1007/s00296-024-05651-z

8. Bekaryssova, D., Yessirkepov, M., & Mahmudov, K. (2023). Structure, demography, and medico-social characteristics of articular syndrome in rheumatic diseases: a retrospective monocentric analysis of 2019-2021 data. Rheumatology international, 43(11), 2057–2064. https://doi.org/10.1007/s00296-023-05435-x

9. Pei, H., He, L., Wang, S., Mo, C., Wang, J., Cui, X., Li, X., Zheng, J., & Liang, F. (2026). Association between gout and cardiovascular disease: A register-based cohort study.

Progress in cardiovascular diseases, S0033-0620(26)00008-3. Advance online publication. https://doi.org/10.1016/j.pcad.2026.02.003

10. Khalil A. (2024). Nutrition, Lipoproteins and Cardiovascular Diseases. Nutrients, 16(15), 2530. https://doi.org/10.3390/nu16152530

Содержание