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System for the provision of specialised medical care for Covid-19 with comorbid diseases

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Abstract. The purpose of the study was to examine the features of organising specialised care for patients with coronavirus infection and chronic diseases, followed by an assessment of its effectiveness and possibilities for improvement. The study had a theoretical-analytical character and included a comparison of six clusters: Kyrgyzstan as an example of a country with limited resources, the USA, European states (France, Germany, Italy, Spain, Poland), Asian countries (Thailand, Singapore, Indonesia, South Korea, India, Malaysia), as well as China and Japan with the centralised organisational models. The analysis was based on publications, statistics and clinical guidelines from 2020-2025; cross-country comparison was applied with a conditional points-based assessment of severity in comorbid patients and the development of recommendations for improving care. The analysis showed that in multimorbidity the severity score reached 16 points, and in cardiovascular, respiratory diseases and immunodeficiencies – 15. Two or more chronic pathologies increased the risk of severe course and death by 2-3 times. In China and Japan, in-hospital mortality was 5.5-6%, with severe renal failure in Japan – up to 28%. In the USA the mortality among patients with several chronic diseases exceeded 12% with an overall rate of 2.5%, the load on emergency departments reached 25-30%. In Europe the increase in mortality in peak periods was about 20%, with resource deficits – up to 50-60%, among oncology patients in Italy and Spain – more than 25%. In Kyrgyzstan with multidrug-resistant tuberculosis, the indicator reached 34-36%. The obtained data confirm the dependence of outcomes on the severity of comorbidities and health-care resources, which requires risk stratification, adaptation of protocols and strengthening of staffing and infrastructure potential. The results can be used by health authorities and medical institutions to optimise care for patients with coronavirus infection and chronic diseases

Keywords: hospitalisation; mortality; routing; risk stratification; oxygen therapy; telemedicine; multidisciplinary team

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Introduction

According to the World Health Organisation, during the 28-day period from 6 January to 2 February 2025 more than 147 thousand new cases of coronavirus infection and over 4.5 thousand deaths were registered worldwide, which underlined the persistence of a significant global burden of infection [1]. These indicators reflect the colossal global burden of infection; however, the most vulnerable category remains patients with comorbid diseases – arterial hypertension, diabetes mellitus, chronic lung diseases, obesity and cardiovascular pathologies. In such patients the risk of a severe course and fatal outcome increases by 2-3 times compared with individuals without concomitant pathology, which requires a clearly structured system of specialised medical care, including early risk stratification, priority access to antiviral agents and oxygen support, as well as multidisciplinary management. Despite the completion of the acute phases of the pandemic, the continued significant circulation of SARS-CoV-2 and the high proportion of the population with chronic diseases make the improvement of clinical-organisational technologies for this group of patients a strategic priority of health systems in all countries.

International experience in organising specialised care for patients with COVID-19 and comorbid diseases demonstrates significant variability in clinical and organisational approaches. In the study by Y. Asai *et al.* [2], conducted in Japan, it was established that the prescription of antiviral and immunomodulatory therapy was determined not only by the severity of the condition and the comorbidity profile, but also by regional protocols, which indicated the need to unify standards. These 2024 data reflected an already mature stage of the pandemic and recorded trends that persisted in the post-pandemic period. In a national Chinese sample of 1,590 patients, as shown by W. Guan *et al.* [3], an increase in the number of concomitant pathologies raised the risk of severe course and fatal outcome. The conclusions of the study formed the basis of practical recommendations for risk stratification and the organisation of care pathways for patients with multimorbidity.

In the article by Q. Zhang [4], updated versions of Chinese clinical protocols were analysed, emphasising the priority of managing patients with chronic diseases, including algorithms for prescribing oxygen therapy and criteria for hospitalisation. The scientific novelty was expressed in the systematisation of accumulated clinical experience and the adaptation of standards to changing strains of SARS-CoV-2. Multicomorbidity, according to C.D. Russell *et al.* [5], was a leading factor of an unfavourable prognosis, and the combination of several chronic diseases exerted a synergistic negative effect on the course of COVID-19. This conditioned the need to implement integrated multidisciplinary models of care and coordinated interaction between outpatient and inpatient levels.

The systemic consequences of the COVID-19 pandemic for health care and the management of patients with chronic diseases were manifested both in the clinical and organisational spheres. In the review by T. Kendzerska *et al.* [6] it was noted that the redistribution of resources and the change in priorities led to delays in diagnosis, changes in treatment regimens and reduced availability of planned care for chronic patients. Even developed health systems experienced overload, which worsened the control of chronic conditions. The presence of comorbid diseases, as shown by A. Fitero *et al.* [7], increased the risk of complications and mortality in COVID-19 approximately two to three times, and the restriction of access to preventive and supportive services aggravated the course of chronic pathologies. The authors emphasised that during the pandemic negative factors were amplified due to reduced availability of specialised care, which decreased by almost 50% in European countries (the Netherlands, Sweden, the United Kingdom), aggravating the course of chronic diseases. In the work by G. Fekadu *et al.* [8], it was shown that the COVID-19 pandemic led to disruption of programmes for regular follow-up of patients with chronic diseases, limited access to medicines and laboratory monitoring, which negatively affected the quality of the medical support. The researchers pointed to the need to expand remote medical support and adapt organisational models to conditions of crisis load.

The experience of Kyrgyzstan in organising specialised care for patients with coronavirus infection and concomitant diseases reflected both common problems (overload of hospitals, shortages of staff and equipment, restriction of planned care) and nationally specific solutions (repurposing anti-tuberculosis beds, using approaches from tuberculosis and human immunodeficiency virus programmes), as well as attracting international support. In the study by R. Akmatova *et al.* [9], it was established that the pandemic not only changed the perception of respiratory infections in vulnerable population groups, but also contributed to increased interest in preventive measures, including influenza vaccination, which is considered an element of a comprehensive strategy to protect patients with multimorbidity. According to data presented by B. Rechel *et al.* [10], the health system of Kyrgyzstan rapidly adapted during the pandemic: it repurposed institutions, mobilised personnel and established inter-agency interaction for the routing of patients with COVID-19 and chronic diseases. The priority became expanding access to oxygen therapy and updating intensive care protocols. A. Taalaibekova *et al.* [11] established that health workers considered it necessary to develop long-term support programmes for patients after COVID-19 with an emphasis on rehabilitation, psychosocial care and coordination between levels of the medical service. Such measures ensure the integration of post-COVID

care into the health system, which makes it possible to improve the quality of life of patients with comorbidity.

In the studies conducted, gaps persisted related to the absence of a holistic assessment of the effectiveness of specialised medical care for patients with COVID-19 and comorbid diseases in an international context, taking into account the specifics of clinical-organisational technologies. The aim of the study was a comprehensive analysis of the system of specialised medical care for patients with COVID-19 and concomitant chronic diseases to assess its effectiveness and directions for improvement. The objectives of the study were as follows: to determine the impact of comorbid diseases on the clinical severity of the course of COVID-19, the frequency of complications and the level of mortality; to identify the features of the impact of the pandemic on health systems and the specifics of managing patients with chronic diseases and determine successful models for organising specialised care; to characterise international experience followed by the development of recommendations for its optimisation.

Materials and Methods

The present study had a theoretical-analytical character and was based on the study and comparative analysis of scientific publications, statistical reports and clinical guidelines for 2020-2025. The analysis covered six territorial clusters: the Kyrgyz Republic, singled out separately due to unique resource constraints and adaptation solutions, the USA, European states (France, Germany, Italy, Spain, Poland), Asian countries (Thailand, Singapore, Indonesia, South Korea, India, Malaysia), as well as China and Japan. Such geographical coverage was determined by the need to identify both universal and specific organisational-clinical solutions in health systems with different levels of resources, the structure of the medical-sanitary network and experience in responding to the pandemic.

Within the study the list of comorbid diseases was determined on the basis of clinical guidelines and epidemiological reviews [12-14], including data on cardiovascular pathologies (arterial hypertension, ischaemic heart disease, chronic heart failure), endocrine-metabolic disorders (type 1 and type 2 diabetes mellitus, obesity), chronic respiratory diseases (chronic obstructive pulmonary disease, bronchial asthma), oncological processes, chronic kidney and liver diseases, as well as immunodeficiency conditions, including human immunodeficiency virus (HIV infection). Particular attention was paid to multimorbidity, in which the combination of two or more chronic diseases intensified the severity of the course of COVID-19. For each case, indicators of the frequency of hospitalisations, length of stay in hospital, the need for oxygen support and mechanical ventilation, the level of mortality, as well as the presence of complications, including acute respiratory distress syndrome, sepsis and multiple organ failure, were analysed. The severity of the course of COVID-19 in patients with comorbid conditions was assessed conditionally by the sum of points assigned to each of the key clinical-organisational indicators: admission to an intensive care unit (ICU) – 3 points; length of hospital stay more than 14 days – 2 points; need for oxygen support – 1 point, for mechanical ventilation – 3 points; presence of severe complications – 3 points; fatal outcome – 4 points. A total score from 0 to 5 was interpreted as a mild course, 6-10 – as moderate, over 10 – as severe (the maximum value was 16 points). Based on these criteria, integral severity assessments were constructed for various disease groups and a comparison of mortality indicators in different health-care models was carried out.

For cross-country comparison official statistical reports of the World Health Organisation [15], World Bank [16], European Centre for Disease Prevention and Control [17], the United States Centres for Disease Control and Prevention [18], as well as national clinical guidelines and protocols of the Ministry of Health, Labour, and Welfare of Japan [19], the National Health Commission of the People's Republic of China [20] and the National Institute for Health and Care Excellence [21] of the United Kingdom were used. On the basis of these materials, in all clusters the structural and functional parameters of organising specialised care for patients with COVID-19 and concomitant diseases were analysed. At the same time, the availability of specialised hospital beds, the capacity of ICUs, provision with oxygen and mechanical ventilators, staffing potential and the preparedness of medical personnel, as well as routing protocols, algorithms for early risk stratification and interaction between primary, specialised and rehabilitation levels were considered. Additionally, the degree of adaptation of clinical recommendations and the introduction of telemedicine technologies were assessed, as well as indicators of morbidity, hospitalisations and mortality were analysed. On the basis of the analysis carried out and the cross-country comparison of data, recommendations were formulated to improve clinical-organisational approaches to managing patients with COVID-19 and comorbid diseases. These recommendations took into account the specifics of national health systems, the identified organisational barriers and effective models of providing specialised care, which ensured the applicability both in conditions of high resource provision and in countries with limited capabilities.

Results

Comorbidity and multimorbidity as determinants of outcomes

The complex influence of comorbid conditions on the course of COVID-19 is determined by a combination of immunological, vascular and metabolic disorders, which intensify hypoxaemia, systemic inflammation and thrombotic complications. Meta-analyses and large cohort studies demonstrate that the simultaneous

presence of several chronic diseases increased the risk of severe COVID-19 and death by more than 2-3 times, and also raised the likelihood of developing multiple organ failure [13,22]. In patients with cardiovascular pathologies (arterial hypertension, ischaemic heart disease, chronic heart failure) SARS-CoV-2 infection was significantly more often complicated by acute coronary syndromes (approximately 1.7-2.5 times more often than in patients without these diseases), decompensation of cardiac function, life-threatening arrhythmias and thromboembolic events [15,18]. The main pathogenetic mechanisms are endothelial dysfunction, hypercoagulation and cytokine-mediated microcirculatory disorders, which clinically manifest as increased dyspnoea, chest pain, haemodynamic instability and the need for high-flow oxygen therapy [16]. In COVID-19 the cardiovascular phenotype is an important indicator of the risk of ICU admission and in-hospital mortality [21,23].

Disorders of endocrine and metabolic regulation, including type 1 and type 2 diabetes mellitus and excess body weight, contributed to a more severe course of COVID-19 due to chronic subclinical inflammation, insulin resistance and increased thrombotic activity [13,20]. In patients with diabetes there is more often extensive lung involvement, prolonged fever, bacterial superinfections and septic complications, which is associated with a high need for oxygen support and increased length of hospital stay [18,24]. Metabolic decompensation, including ketoacidosis, often develops against a background of hypoxia and systemic inflammation, requiring comprehensive correction [21,25]. Excess body weight worsens the mechanical parameters of breathing, reduces ventilation efficiency and increases the risk of respiratory failure even with moderate changes on chest computed tomography [16,22].

Chronic respiratory diseases, primarily chronic obstructive pulmonary disease, aggravate the course of COVID-19 through remodelling of the bronchial tree, a reduction in respiratory reserve and impaired mucociliary clearance [19]. This leads to early development of respiratory failure, refractory hypoxaemia and a sustained need for oxygen therapy. In severe or uncontrolled bronchial asthma, COVID-19 more often causes exacerbations requiring systemic glucocorticosteroids, which increases the risk of secondary bacterial complications [22]. Pathomorphological data indicate a high proportion of chronic respiratory diseases among those who died from COVID-19, pointing to the role as a significant factor of adverse outcome [24].

In oncological patients, the main factor of a severe course is secondary immunodeficiency, caused both by the tumour itself and by anti-tumour treatment [13,15]. This contributes to more intensive viral replication, rapid progression of lung involvement, a high frequency of sepsis, thromboembolism, and multiple organ failure. When oncopathology is combined with other comorbid conditions there is a marked increase in mortality, as well as longer use of oxygen support and complex antibacterial regimens [18,19]. Chronic kidney disease increases susceptibility to a severe course of COVID-19 due to uraemic immunodeficiency, endothelial dysfunction and electrolyte disturbances [17,20]. Acute kidney injury often develops during hospitalisation, complicating management and increasing the risk of death [14]. In liver cirrhosis, COVID-19 often causes decompensation of portal hypertension, hepatic encephalopathy and coagulopathy, increasing the risk of septic complications and prolonging rehabilitation [22].

Immunodeficiency states, including HIV infection, substantially complicate control of the inflammatory process. A low CD4 cell count and high viral load are associated with severe hypoxaemia, frequent opportunistic infections (Pneumocystis pneumonia, invasive mycoses) and a prolonged need for broad-spectrum antibacterial therapy [15,20]. The combination of immunodeficiency with metabolic or respiratory pathologies amplifies the negative effect, leading to the rapid development of respiratory failure even in moderate virus-induced pneumonia [19]. The assessment of the severity of the influence of comorbid diseases on the course of COVID-19 was carried out conditionally, based on an integral scoring system: ICU admission – 3 points; length of inpatient treatment more than 14 days – 2; need for oxygen support – 1; mechanical ventilation – 3; presence of severe complications (acute respiratory distress syndrome, sepsis, multiple organ failure) – 3; death – 4. A total score of 0-5 points corresponded to a mild course, 6-10 to a moderate course, and above 10 to a severe course. Figure 1 presents a conditional integral assessment of the severity of the influence of different groups of comorbid diseases, performed taking into account the frequency of hospitalisations, length of inpatient treatment, need for oxygen and respiratory support, as well as the frequency of severe complications and deaths.

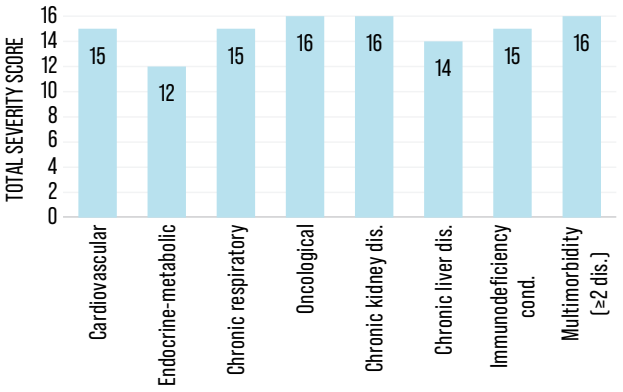

Figure 1. Conditional assessment of the severity of the influence of various groups of comorbid diseases on the course of COVID-19

Note: the end point was marked at 16, since this is the maximum number of points that a patient could receive with the simultaneous presence of all criteria

Source: compiled by the authors as a result of data analysis [13,14,22-25]

As a result of the analysis of the data presented in the graph, it was established that in all highlighted groups the total score exceeded 10 points, which corresponds to a severe course of COVID-19. The maximum values (16 points) were noted in patients with oncological diseases, chronic kidney disease and multimorbidity, which reflects a combination of severe factors associated with an increased risk of adverse outcome and the need for comprehensive, intensive treatment. These groups are characterised by a combination of several critically significant factors – pronounced organ dysfunction, severe immune disorders, high thrombotic activity and a predisposition to sepsis. Such a combination leads to a longer hospital stay, the need to apply complex treatment protocols, and a substantial increase in mortality. The values of 15 points obtained for cardiovascular pathologies and chronic respiratory diseases reflect a severe course due to decompensation of the underlying condition, pronounced respiratory failure, thromboembolic complications and the need for continuous oxygen support. Immunodeficiency states show a comparable level of severity (15 points), which is associated with the body's low ability to control inflammation and a high frequency of secondary infections. For chronic liver diseases (14 points) an increased risk of coagulopathies, bleeding and septic complications is typical, whereas endocrine-metabolic disorders (12 points) more often manifest as worsening hypoxaemia, chronic inflammation and metabolic decompensation, especially when combined with other pathologies. Consequently, each additional point on this conditional scale indicates the layering of yet another clinically significant factor which, in real conditions, leads to an increased probability of an adverse outcome and requires a more intensive and multidisciplinary approach to patient management. Thus, the conditional integral scale made it possible to identify the most vulnerable groups of patients. However, COVID-19 outcomes with similar comorbidity varied significantly depending on the resources and organisation of national healthcare systems, as reflected in Figure 2.

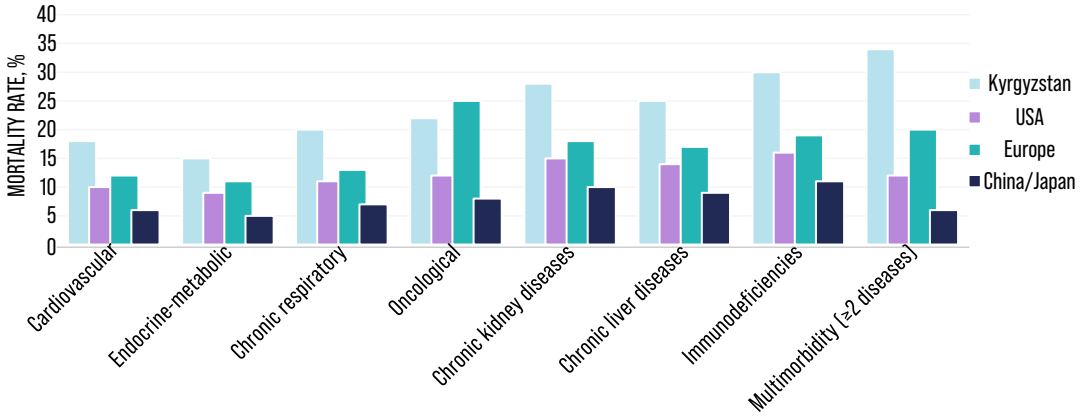

Figure 2. Mortality from COVID-19 in patients with comorbid conditions in different healthcare models (Kyrgyzstan, USA, Europe, China/Japan)

Source: compiled by the authors as a result of data analysis [13-21]

The graph showed that mortality from COVID-19 in patients with comorbidities differed substantially depending on healthcare models. In Kyrgyzstan the highest figures were recorded: mortality in cardiovascular pathologies reached 18%, in respiratory diseases about 20%, and in chronic kidney disease and multimorbidity exceeded 28-34%. These data reflected limited resources, a deficit of oxygen support and personnel, and a high prevalence of background diseases. In Europe the figures were lower; however, overload of ICUs during peak periods led to increased mortality, especially among oncological patients, where it reached 25%. In the USA the values remained moderate – about 12% in the presence of two or more chronic diseases, which was explained by better technical equipment and standardised protocols, although a high burden on emergency care limited access to intensive therapy. In China and Japan mortality in most groups did not exceed 5-10%, reflecting a high level of resource provision, centralised planning of bed capacity, effective routing and the use of telemedicine. Thus, identical comorbid conditions in different countries led to different clinical outcomes: with a shortage of resources mortality rose to a third of patients, whereas with developed infrastructure and strict protocols these figures decreased almost threefold.

The analysis carried out demonstrated that comorbid diseases were key determinants of a severe course of COVID-19 and adverse outcomes. The impact was enhanced in multimorbidity; however, the severity of the consequences depended substantially on the capabilities of healthcare systems: in resource-limited countries (for example, Kyrgyzstan) mortality figures were significantly higher, whereas developed infrastructure and clear routing (China, Japan, European states, USA) made it possible to reduce the risk of complications and death. The analysis confirmed that effective

management of such patients required the integration of clinical and organisational strategies.

International models of specialised care: structure, resources and clinical-organisational technologies

Systems of specialised care for comorbid patients with COVID-19 in six clusters demonstrated pronounced differences in the level of resource provision, organisational structure and clinical-organisational technologies used. In the Kyrgyz Republic, with initially limited material-technical base and staffing, a flexible tactic of repurposing beds to a respiratory profile and redistributing functions between tiers of care and within teams was applied, which increased the elasticity of routing during peak loads [26]. The use of vertical programmes for tuberculosis and HIV infection to borrow algorithms of infection control and management of vulnerable groups was noted; however, there remained deficits in oxygen provision and ventilators, as well as fragmentation between tiers of medical care [27]. The advantages of such a configuration were flexibility of flows and adaptation of protocols to local resources; the disadvantages were uneven staff training and weak resilience of long rehabilitation pathways.

In the USA, a decentralised model operated with high technological equipment, powerful ICUs and developed telemedicine [28,29], yet at an early stage of the pandemic serious failures in the availability of elective and outpatient care were recorded, accompanied by reduced utilisation and overload of emergency services [30]. Standards of remote monitoring, routing of high-risk patients and maintenance of continuity in the management of chronic cardiology patients were rapidly implemented [31]. The strengths of the model are high technical potential and an extensive telemedicine network; the weaknesses are variability of protocols between states, overload of emergency departments and high vulnerability of patients with psychiatric and addictive comorbidities [32].

In European countries (France, Germany, Italy, Spain, Poland), hybrid models predominated with a strong role for the primary tier and regional coordination [33]. Service quality remained heterogeneous, especially during peak periods when reductions in elective care and delays in routing chronic patients were recorded [34]. More effective systems demonstrated a better ratio of resources to outcomes, and large cohort data confirmed the need for early risk stratification and multidisciplinary pathways [35]. Advantages – institutionalised coordination and resilient primary-care channels; disadvantages – inter-country variability and overload of hospitals at peaks.

In Asian countries (Thailand, Singapore, Indonesia, South Korea, India, Malaysia, and others), integration of primary healthcare and public health services was widely used, with an emphasis on the family doctor as a "gateway", tracing and rapid routing [36,37]. Alongside this, the pandemic was accompanied by interruptions in care for patients with non-communicable diseases and reduced continuity of follow-up, which adversely affected comorbid patients [38]. Strengths of the approach – early routing, remote formats and integration with public health; weaknesses – limited intensive-care resources in peripheral areas and the vulnerability of non-communicable disease programmes (such as cardiovascular disease, diabetes, chronic respiratory and oncological pathologies) during peak loads.

China implemented a centralised, protocol-oriented model with unified stratification algorithms, large-scale repurposing of bed capacity and accelerated deployment of oxygen infrastructure [37,38]. This ensured high manageability and uniformity of processes, but was accompanied by overload risks with a sharp rise in incidence and the need for rapid strengthening of human resources and rehabilitation tiers [39]. To support serviceability, remote channels and the transfer of functions to the outpatient segment were actively applied.

In Japan, centralised clinical standards were combined with a developed system of national registries and detailed in-hospital risk stratification [40]. Practice included the integration of specialised therapy for vulnerable groups, including patients with severe renal failure, including evaluation of the effectiveness of antiviral regimens in multidisciplinary hospitals. Advantages of the model – high equipment levels, rapid calibration of protocols and developed multidisciplinary pathways; disadvantages – local overloads during surges and the need to ensure continuous follow-up of chronic patients when resources are reallocated (Table 1).

Table 1. Comparative characteristics of international models of specialised care for comorbid patients with COVID-19

Cluster	Model type	Resources and routing	Telemedicine	Advantages	Disadvantages
Kyrgyzstan	Adaptive under shortage; repurposing of beds	Variable provision of oxygen and mechanical ventilation; task-shifting, borrowing of algorithms (tuberculosis/HIV)	Targeted use for case conferences and training	Flexibility of flows, adaptation of protocols	ICU limit, staffing gaps, fragmentation
USA	Decentralised, high-tech	High ICU capacity, developed logistics; prioritisation of risk groups	Wide coverage with remote monitoring	Technological capacity, rapid guidance	Variability of protocols, emergency department overload, vulnerability of psychiatric groups

Table 1. Continued

Cluster	Model type	Resources and routing	Telemedicine	Advantages	Disadvantages
Europe	Hybrid, regional coordination	Resources sufficient but heterogeneous; early stratification	Development, but with regional variability	Inter-level coordination, resilience of primary healthcare	Reduction of elective care, overloads
Asia (excluding China, Japan)	Primary healthcare + public health	Heterogeneous resources; ICU shortages in the periphery	Expanded remote channels	Early routing, integration with public health	Displacement of non-communicable disease services, continuity disruptions
China	Centralised, protocol-oriented	Scaling of oxygen infrastructure, unified stratification	Outpatient/home segment, remote channels	Standardisation, speed of deployment	Overload risks, staff shortage
Japan	Centralised standards + registries	High ICU equipment levels; detailed stratification	Targeted integration	Registry analytics, calibration of protocols	Local overloads, risks of loss of continuity

Source: compiled by the authors as a result of data analysis [17-19,26,40]

The analysis showed that between countries the models for organising care for comorbid patients with COVID-19 exhibited substantial differences in the level of centralisation, resource provision and the degree of integration of chronic patients into the emergency care system. In countries with a strong technological base (USA, Japan), the key advantages were powerful ICUs, developed telemedicine and standardised protocols; however, problems of overload during peak periods and uneven access persisted. In Europe, the strengths were institutionalised coordination and the resilience of primary healthcare, but the weak point remained regional differences in resources and a reduction in elective care at pandemic peaks. In Asian countries (excluding China and Japan) the integration of primary healthcare with public-health systems was significant, whereas the vulnerability of programmes for chronic non-communicable diseases and interruptions in ensuring continuity of follow-up revealed systemic weaknesses. In China, the centralised model with unified algorithms and scaling of oxygen infrastructure provided manageability but increased dependence on human resources. In Kyrgyzstan, the flexibility of organisational flows and adaptation of protocols made it possible to partially compensate for resource shortages; however, limited ICU capacity and staffing reserves remained a key barrier.

There is no universally optimal approach when forming a system of specialised care for comorbid patients with COVID-19: the effectiveness of models is determined by a balance between manageability and flexibility, the baseline level of resource provision and the system's ability to quickly adapt protocols to changing conditions. Centralised systems provide uniformity and speed of deployment but are less flexible for local adaptation; decentralised and hybrid ones adapt better to regional conditions, yet suffer from variability of standards and resource availability. Optimising specialised care requires a combination of clinical-organisational technologies (risk stratification, multidisciplinary teams, telemedicine) with systemic measures to strengthen workforce capacity, infrastructure, and the resilience of channels for managing chronic patients even under peak loads.

Systemic consequences of the COVID-19 pandemic and cross-country recommendations for managing comorbid patients

The COVID-19 pandemic affected the availability, structure, and quality of medical care for chronic patients, especially those with comorbid pathology. Organisational decisions, flow routing and the use of telemedicine influenced outcomes differently depending on the baseline level of resources and the model of the healthcare system. International practice established that the presence of one chronic disease increased the risk of hospitalisation with COVID-19 by 3-5 times and the risk of death by 2.5-4 times compared with people without comorbidity [21].

In the USA, based on information from the large integrated Kaiser Permanente system, in the first wave of the pandemic (April-July 2020) hospitalisations of patients with ≥2 chronic diseases reached 450-500 per 100,000, whereas among those without comorbidity the rate was 80-100 per 100,000 [28,31]. Mortality in this group exceeded 12% with overall in-hospital mortality at 2.5%. Emergency department overload reached 25-30%, but the rapid growth of telemedicine consultations (from 0.2% to 70% of all outpatient visits) made it possible to stabilise in-hospital mortality indicators by the second half of 2020 [30,32].

In Europe, according to a cohort of 66 million residents of France, the presence of multiple chronic diseases increased the risk of COVID-19 hospitalisation by 3.2 times and in-hospital mortality by 2.9 times [34]. In Italy and Spain, mortality among oncological patients with COVID-19 exceeded 25%, with up to 40% receiving delayed treatment [41]. In countries with high provision of ICU beds (Germany, France) the increase in mortality during peak periods was about 20%, whereas under resource shortages it reached 50-60% [34,35]. In Asian countries (excluding China and Japan) the combination of primary healthcare with public health and the use

of expanded remote channels provided rapid routing, but at peaks hospitalisations for non-communicable diseases fell by 30-50%, and COVID-19 hospitalisations among comorbid patients doubled [36,38]. Mortality in cardiovascular diseases reached 18-23%, in diabetes 15-20% (with an average level of 4-6%) [37].

In China, the centralised protocol-oriented model with large-scale deployment of oxygen infrastructure and unified risk stratification made it possible to keep in-hospital mortality at 5.5-6% even with high hospitalisation rates [37,39]. The risk of hospitalisation in patients with ≥1 chronic disease was 3.4 times higher, and the risk of death 4.1 times higher than in the general population [38]. The average length of stay increased from 7.5 to 9.1 days, especially in chronic obstructive pulmonary disease and diabetes. A key feature was the rapid repurposing of bed capacity and the transfer of part of functions to outpatient and home segments, which reduced pressure on hospitals during peaks.

In Japan, centralised clinical standards and national registries ensured minimal delays in hospitalisation and detailed in-hospital risk stratification. The combination of several chronic diseases in patients was accompanied by an increased risk of severe COVID-19 by 2.8 times; in severe renal failure, mortality reached 28% [40]. The average length of hospital stay in this group was 30% higher than in the population without comorbidity. In addition, a developed system of multidisciplinary pathways made it possible to maintain the quality of specialised care even with local overloads.

In Kyrgyzstan, with initially limited resources and staffing, flexible repurposing of beds to the respiratory profile and the use of algorithms from vertical programmes (tuberculosis/HIV) partially compensated for the deficit [26,27]. Mortality among severely ill patients with multidrug-resistant tuberculosis and COVID-19 was 34-36%, and with ≥1 concomitant disease the risk of death increased 1.8 times. ICU provision was less than 3 beds per 100,000 population, and oxygen coverage less than 40% of need, which during peak periods led to a sharp increase in mortality. For clarity in comparing differences in outcomes among patients with comorbid conditions depending on resource levels and healthcare organisational models, a summary Table 2 was compiled.

Table 2. Systemic consequences of the COVID-19 pandemic for managing comorbid patients in different countries

Country/Region	Hospitalisation in comorbid (per 100,000)	Relative risk of hospitalisation / death	Mortality (%)	System features (ICU, telemedicine, routing)
Kyrgyzstan	180 (comorbid) vs 100 (without)	Mortality ↑ 1.8 times	34-36 in multidrug-resistant tuberculosis; overall 15-18	ICU <3 per 100,000; oxygen coverage <40%; bed repurposing
USA	450-500 (≥2 diseases) vs 80-100 (without)	Hospitalisation ↑ 5 times; death ↑ 2.5-4 times	12 (overall 2.5)	Emergency overload 25-30%; telemedicine rose from 0.2% to 70% of visits
Europe	320 (with ≥2 diseases) versus 100 (without)	Hospitalisation ↑ 3.2 times; death ↑ 2.9 times	20-25 in oncological patients; up to 50-60 with resource deficits	ICU: 29-34 per 100,000; with overload mortality ↑ 20-60%
Asia (excluding China and Japan)	200-240 (comorbid) vs 100-120 (without)	Hospitalisation ↑ 2 times; death ↑ 2.5-3 times	Cardiovascular 18-23; diabetes 15-20; average 4-6	Reduction of non-communicable hospitalisations by 30-50%; telemedicine widely used
China	340 (≥1 disease) vs 100 (without)	Hospitalisation ↑ 3.4 times; death ↑ 4.1 times	5.5-6	Mass deployment of oxygen infrastructure; centralised routing
Japan	280 (≥2 diseases) vs 100 (without)	Risk of severe course ↑ 2.8 times	28 in severe chronic kidney disease; average 8-10	National registries; multidisciplinary pathways; length of stay ↑ 30%

Note: the symbol "↑" indicates an increase in risk or event frequency

Source: compiled by the authors as a result of data analysis [17-19,26-28,34-41]

The data presented in the Table 2 showed that the presence of comorbid conditions in all countries was accompanied by higher rates of hospitalisation and mortality, with the level of indicators depending substantially on resources and the organisational model of healthcare. In Kyrgyzstan and a number of Asian countries mortality in such patients reached 34-36%, which was explained by limited access to ICU bed capacity and oxygen provision. In Europe and the USA hospitalisations increased 3-5 times, and mortality among certain groups reached 20-25%; however, the introduction of telemedicine and a developed ICU network helped restrain the rise in mortality. In China and Japan, centralised routing and large-scale deployment of oxygen infrastructure made it possible to keep mortality at 5-10% even with high hospitalisation rates. These results confirmed that chronic diseases were a leading factor in adverse outcomes in COVID-19, and the organisational model of the system directly determined the level of hospitalisations and mortality among

comorbid patients. Optimising care required combining clinical-organisational technologies (early risk stratification, multidisciplinary teams, telemedicine) with strengthening infrastructure and workforce capacity to ensure resilience even under peak loads.

Based on the cross-country analysis, key directions for improving specialised care for patients with COVID-19 and concomitant diseases were identified, aimed at minimising vulnerabilities revealed in different models. In centralised healthcare systems (China, Japan), which demonstrated high manageability and standardisation, the key direction was to increase protocol flexibility by taking local resource differences into account. To this end it was recommended to pre-specify algorithms for repurposing at least 20% of medical beds to an infectious profile within 72 hours, to form reserve medical teams (1 infectious-disease physician and 2 nurses for every 10 ICU beds), and to introduce a mandatory module for remote monitoring of high-risk patients, allowing a 15-20% reduction in the need for hospitalisations.

In decentralised models (USA), characterised by high adaptability and wide use of telemedicine, the main task remained harmonisation of clinical protocols between regions. It was proposed to introduce unified federal routing standards with specified timeframes for hospital transfer (no more than 48 hours from the onset of symptoms), to create a centralised digital platform for real-time monitoring of ICU occupancy, and to implement systems for early forecasting of hospital load using data from outpatient and emergency tiers, which ensured timely redistribution of resources. Hybrid systems (France, Germany, Italy, Spain, Poland) required strengthening the integration of multidisciplinary teams focused on the management of comorbid patients. Practical measures included institutionalising modular mobile hospitals of 50-100 beds, forming mandatory multidisciplinary groups (cardiologist, endocrinologist, pulmonologist, infectious-disease specialist) for managing severe cases, and introducing a rule for continuity of elective care: maintaining at least 60% of elective operations and consultations even during peak periods by using remote technologies.

In resource-limited countries using adaptive models (Kyrgyzstan, Thailand, Indonesia, India, Malaysia), the priority was to ensure oxygen supply and support the primary tier. Recommendations included repurposing at least 30% of tuberculosis and medical beds to an infectious profile as hospitalisations increased, organising local oxygen-supply stations based on district hospitals (capacity 20-30 cylinders per day), and introducing simplified clinical protocols allowing nursing staff to manage patients with mild and moderate courses. Additionally, training nurses in basic respiratory-support skills (oxygen therapy) within task-shifting technologies was recommended. In all types of systems, it is advisable to strengthen organisational readiness for peak loads through regular stress-testing of care pathways, expansion of data collection on clinical and service indicators broken down by risk groups, and the introduction of inter-sectoral mutual-assistance agreements between regions and institutions. An integral part of the recommendations is the inclusion of comorbid patients in priority groups for proactive monitoring, with an emphasis on cardiovascular, oncological, diabetic and respiratory profiles, which will reduce both in-hospital mortality and the level of exacerbations of chronic diseases under epidemic pressure.

Discussion

The analysis made it possible to establish that differences in organisational models directly affected the resilience of healthcare systems when working with comorbid patients during COVID-19 peak loads. Centralised structures demonstrated high manageability and standardisation of protocols, decentralised and hybrid models – greater technological capacity and adaptability, while resource-constrained systems remained the most vulnerable due to dependence on supplies of oxygen, equipment, and staffing. These features determined both the level of in-hospital mortality and the ability of systems to maintain continuity of care under epidemic pressure.

The combination of several chronic diseases led to a 2-3-fold increase in the risk of severe COVID-19 and death, and with multimorbidity, oncological pathologies and chronic kidney disease the cumulative severity score reached 16 points on a conditional assessment scale. Cardiovascular and chronic respiratory diseases, as well as immunodeficiency conditions, showed scores at the level of 15 points, which reflected a high level of complications, the need for oxygen support and prolonged hospitalisation. These observations correlated with the results presented by R.S. Loungani *et al.* [42], where it was emphasised that pronounced comorbidity was a key predictor of intensive care unit overload and formed a persistent need for multidisciplinary support in the post-hospital period. In the study by P. Adab *et al.* [43] it was similarly indicated that patients with several chronic diseases required priority stratification in clinical pathways and had a higher likelihood of adverse outcomes, which was consistent with the maximum severity values identified in multimorbidity and severe nosologies. According to A.Y. Chang *et al.* [44], the combination of several chronic pathologies increased the risk of prolonged recovery of functional status and raised the frequency of rehospitalisations, which corresponded to the integral severity indicators, especially in groups with combined organ dysfunctions. The analysis by H. Ejaz *et al.* [45] also confirmed that multimorbidity was associated with more severe complications, including multiple organ failure, and required complex treatment protocols; the obtained values of the conditional scale for groups with cardiovascular and respiratory diseases were comparable with the findings. At the same time R. Ashmawy *et al.* [46] focused attention on

significant cross-country variability of outcomes due to differences in access to resources and heterogeneity of management protocols, which was reflected in the identified discrepancies between healthcare systems with different models of specialised care.

Centralised models (China, Japan) provided standardisation and manageability but had low flexibility for local adaptation, while decentralised models (USA) were distinguished by technological sophistication and telemedicine with high variability of protocols. Europe's hybrid models combined resilient primary-care channels and coordination but suffered from inter-regional differences and reductions in elective care; integrated primary healthcare models in a number of Asian countries accelerated routing at the risk of interruptions in monitoring chronic patients; and Kyrgyzstan's adaptive model partially offset resource deficits by repurposing beds and redistributing functions. Centralised systems similar to the Chinese and Japanese ones, according to G.M. Katz *et al.* [47], provided high manageability and standardisation of processes but had limited flexibility for local adaptation, which coincided with the identified risks of overload as pressure increased. Decentralised models, as noted by O.V. Kuryata *et al.* [48], were characterised by high technological capacity and active implementation of telemedicine; however, according to comparison with the analysis carried out, both assessments recorded vulnerability to protocol variability and fragmentation of care. Hybrid models described by L. Mahuela *et al.* [49] and characteristic of a number of European countries demonstrated resilient primary-care channels and effective inter-level coordination, which agreed with the advantages reflected in the analysis; however, in both cases a reduction in the availability of elective care during peak loads was noted. Integration of primary healthcare with public health systems, according to S.Y. Tartof *et al.* [50], provided accelerated routing and reduced hospital burdens, which was confirmed by the identified trends, but was accompanied by a risk of interruptions in monitoring chronic patients. Adaptive models under resource constraints, described by E. Driggin *et al.* [51] using Kyrgyzstan as an example, ensured elasticity of flows and the ability to promptly redistribute capacity, which correlated with the results of the analysis; however, in both cases the key limitation of effectiveness was recognised to be shortages of personnel and specialised equipment.

Centralised models (China, Japan) kept mortality among comorbid patients at 5-6%, whereas in resource-constrained systems (Kyrgyzstan) it reached 34-36%. In Asian countries mortality in cardiovascular diseases and endocrine-metabolic disorders was 15-23%, which substantially exceeded average values of 4-6%. The patterns identified correspond to the results of B.Z. Huang *et al.* [52], who showed that the sharp expansion of telemedicine services (from 0.2% to 70% of outpatient visits) in the USA made it possible to stabilise mortality indicators among comorbid patients despite overload of emergency care. The analysis by K.D. Skyrud *et al.* [53] confirmed that even mild COVID-19 could lead to increased use of primary and specialised care for months after illness, which resonates with the identified data on overload of outpatient tiers in hybrid models. Y. Zhou *et al.* [54] showed that obesity and diabetes significantly increased the risk of severe COVID-19, which was consistent with the recorded high mortality (up to 23% in cardiovascular disease and up to 20% in diabetes) in Asian primary healthcare models. Data from O.M Al-Quteimat & A.M. Amer [55] and Z. Bakouny *et al.* [56] on delays and reductions in oncological treatment during the pandemic confirm the identified crowding-out effect on programmes for chronic non-communicable diseases, especially in resource-limited systems.

Centralised systems require flexible adaptation of protocols and expansion of staffing reserves; decentralised systems require unification of standards and centralised monitoring of care. Hybrid models need integration of multidisciplinary teams and reserve channels for elective care, while adaptive ones need provision of oxygen, mechanical ventilation and algorithmisation of processes to compensate for staff shortages. The findings obtained are supported by the results of P. Ssentongo *et al.* [57], who confirmed that prioritisation of vulnerable groups, including people living with HIV, reduces the risk of adverse outcomes under resource constraints, which directly supports the recommendation to include these vulnerable groups in target groups for proactive monitoring. T.J. Cooper *et al.* [58] showed that standardisation of the management of patients with immunodeficiencies and integration of inter-level interaction improve prognosis, which correlates with the task of unifying protocols in decentralised systems. The results of M. Biswas *et al.* [25] on the importance of comprehensive control of comorbid conditions underscore the need for multidisciplinary teams and specialised care channels in hybrid models. The study by S. Elezkurtaj *et al.* [23] on causes of death in hospitalised patients with COVID-19 supports the introduction of regular stress-testing of care pathways for the early identification of vulnerable links. The conclusions of A. Sanyaolu *et al.* [22] on the impact of polycomorbidity on mortality additionally confirm the importance of integrated monitoring and cross-sectoral redistribution of resources during peak periods.

The analysis confirmed that the effectiveness of specialised care for comorbid patients with COVID-19 directly depended on the adaptability of the organisational model and the consistency of clinical protocols. Unification of standards, integration of multidisciplinary teams and development of infrastructure for remote monitoring contributed to relieving hospitals and minimised losses in the quality of care. Prioritisation of vulnerable groups and ensuring a stable

supply of critical resources remain key conditions for preventing adverse outcomes. The body of recommendations demonstrates the need for a systemic approach to planning and stress-testing care pathways under epidemic pressure.

Conclusions

The analysis showed that with multimorbidity the cumulative severity score reached 16 points, and with a combination of cardiovascular diseases, chronic respiratory diseases and immunodeficiencies – 15 points. The presence of ≥2 chronic pathologies increased the risk of severe course and fatal outcome by 2-3 times, which underscores the need for early detection, monitoring, and individualisation of care pathways. The international comparative analysis showed that adaptive models under resource constraints (for example, Kyrgyzstan) ensured flexibility of flows and the possibility of repurposing beds, however with oxygen provision below 40% of need and intensive care capacity below 3 beds per 100,000 population, mortality among patients with multidrug-resistant tuberculosis and COVID-19 reached 34-36%. Decentralised high-technology systems (USA) benefit from developed telemedicine and powerful intensive care units; however, with protocol variability and overload of emergency services, mortality among comorbid patients exceeded 12% with overall in-hospital mortality of 2.5%, and the burden on emergency departments reached 25-30%. Hybrid European models are characterised by resilient primary-care coordination, but in peak periods with resource deficits the increase in mortality among comorbid patients reached 50-60%, whereas with high provision of intensive care beds (Germany, France) – about 20%. In Italy and Spain, mortality among oncological patients with COVID-19 exceeded 25% with treatment delayed in 40% of patients.

In Asian countries (Thailand, Singapore, Indonesia, South Korea, India, Malaysia), integration of primary care with public health and remote channels accelerated routing; however, during peaks, hospitalisations for non-communicable diseases fell by 30-50%, and mortality among comorbid patients reached 18-23% for cardiovascular diseases and 15-20% for diabetes. Centralised systems (China, Japan) provide standardisation and manageability through large-scale deployment of oxygen infrastructure and unified risk stratification, which made it possible to keep mortality at 5.5-6% in China and up to 28% in patients with severe renal failure in Japan. Priority measures for different healthcare system models: for centralised – adaptation of protocols and expansion of staffing reserves; for decentralised – unification of standards; for hybrid – integration of multidisciplinary teams; for adaptive – provision of oxygen and mechanical ventilation. These steps will reduce system vulnerability and improve outcomes in patients with a high comorbidity burden. A limitation of this study is the heterogeneity of source data across countries, including differences in methods of recording and classifying comorbid conditions, which may have affected the comparability of results. A promising direction is the conduct of multicentre prospective studies with unified criteria for assessing comorbidity and outcomes, which will make it possible to increase the reliability of cross-country comparisons and develop optimal models of care organisation.

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Conflict of Interest

None.

References

[1] World Health Organisation. COVID-19 epidemiological update. 177 ed. Geneva: World Health Organization; 2025. 31 P.

[2] Asai Y, Ohashi T, Imai K, Murata K, Tsuzuki S, Matsunaga N, et al. Differences in COVID-19 treatment across Japan: Analysis of the COVID19 Registry Japan (COVIREGIJP). J Inf Chemother. 2024;30(1):20–8. DOI: 10.1016/j.jiac.2023.09.005

[3] Guan WJ, Liang WH, Zhao Y, Liang HR, Chen ZS, Li YM, et al. Comorbidity and its impact on 1590 patients with COVID 19 in China: A nationwide analysis. Eur Respir J. 2020;55(5):2000547. DOI: 10.1183/13993003.00547-2020

[4] Zhang Q. Introducing the new versions of Chinese diagnosis and treatment protocol for COVID-19. Infect Microbes Dis. 2022;4(3):83–4. DOI: 10.1097/IM9.0000000000000099

[5] Russell CD, Lone NI, Baillie JK. Comorbidities, multimorbidity and COVID-19. Nat Med. 2023;29(2):334–43. DOI: 10.1038/s41591-022-02156-9

[6] Kendzerska T, Zhu DT, Gershon AS, Edwards JD, Peixoto C, Robillard R, et al. The effects of the health system response to the COVID-19 pandemic on chronic disease management: A narrative review. Risk Manag Healthc Policy. 2021;14:575–84. DOI: 10.2147/RMHP.S293471

[7] Fitero A, Bungau SG, Tit DM, Endres L, Khan SA, Bungau AF, et al. Comorbidities, associated diseases, and risk assessment in COVID-19 – a systematic review. Int J Clin Pract. 2022;2022:1571826. DOI: 10.1155/2022/1571826

[8] Fekadu G, Bekele F, Tolossa T, Fetensa G, Turi E, Getachew M, et al. Impact of COVID-19 pandemic on chronic diseases care follow-up and current perspectives in low resource settings: A narrative review. Int J Physiol Pathophysiol Pharmacol. 2021;13(3):86–93.
[9] Akmatova R, Otorbaeva D, Ebama MS. Impact of the COVID 19 pandemic on influenza knowledge, attitudes, and vaccination practices in at risk groups in the Kyrgyz Republic: A comparative study. Vaccine. 2025;56:127159. DOI: 10.1016/j.vaccine.2025.127159
[10] Rechel B, Moldoisaeva S, Shriwise A. Health systems in action: Kyrgyzstan. Copenhagen: European Observatory on Health Systems and Policies; World Health Organization; 2022. 24 P.
[11] Taalaibekova A, Oleinik A, Magdieva K, Mirzalieva G, Yusuf ZK, Yusuf Z, et al. Views of healthcare workers on development of support for people with post-COVID syndrome in Kyrgyzstan: A survey study. Glob Health Res. 2024. DOI: 10.3310/DGWW4396
[12] Underlying conditions and the higher risk for severe COVID19 [Internet]. [cited 2025 September 8]. Available from: https://www.cdc.gov/covid/hcp/clinical-care/underlying-conditions.html
[13] Zaikov SV. COVID 19 and comorbid chronic diseases. Infus Chemother. 2020;3(3):5–10. DOI: 10.32902/2663-0338-2020-3-5-10
[14] Jakhmola S, Indari O, Baral B, Kashyap D, Varshney N, Das A, et al. Comorbidity assessment is essential during COVID-19 treatment. Front Physiol. 2020;11:984. DOI: 10.3389/fphys.2020.00984
[15] World Health Organization. WHO Coronavirus (COVID-19) dashboard [Internet]. [cited 2025 September 8]. Available from: https://data.who.int/dashboards/covid19/cases
[16] World Bank. COVID-19 High-Frequency Monitoring Dashboard [Internet]. [cited 2025 September 8]. Available from: https://surl.li/nepvos
[17] European Centre for Disease Prevention and Control. COVID19 Situation Updates and Surveillance Reports [Internet]. [cited 2025 September 8]. Available from: https://www.ecdc.europa.eu/en/covid-19
[18] Centres for Disease Control and Prevention. COVID19 data tracker [Internet]. [cited 2025 September 8]. Available from: https://covid.cdc.gov/covid-data-tracker/#datatracker-home
[19] Ministry of Health, Labour and Welfare of Japan. Novel Coronavirus (COVID19) [Internet]. [cited 2025 September 8]. Available from: https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/0000164708_00079.html
[20] National Health Commission of the People's Republic of China. Diagnosis and treatment protocol for COVID19 patients. 8th ed. Beijing: National Health Commission of the People's Republic of China; 2020. 31 P.
[21] National Institute for Health and Care Excellence. COVID19 rapid guideline: Managing COVID19 [Internet]. [cited 2025 September 8]. Available from: https://www.nice.org.uk/guidance/ng191
[22] Sanyaolu A, Okorie C, Marinkovic A, Patidar R, Younis K, Desai P, et al. Comorbidity and its impact on patients with COVID-19. SN Compr Clin Med. 2020;2(8):1069–76. DOI: 10.1007/s42399-020-00363-4
[23] Elezkurtaj S, Greuel S, Ihlow J, Michaelis EG, Bischoff P, Kunze CA, et al. Causes of death and comorbidities in hospitalized patients with COVID-19. Sci Rep. 2021;11(1):4263. DOI: 10.1038/s41598-021-82862-5
[24] Barh D, Aljabali AA, Tambuwala MM, Tiwari S, Serrano-Aroca Á, Alzahrani KJ, et al. Predicting COVID-19 – comorbidity pathway crosstalk-based targets and drugs: Towards personalized COVID-19 management. Biomedicines. 2021;9(5):556. DOI: 10.3390/biomedicines9050556
[25] Biswas M, Rahaman S, Biswas TK, Haque Z, Ibrahim B. Association of sex, age, and comorbidities with mortality in COVID-19 patients: A systematic review and meta-analysis. Intervirology. 2021;64(1):36–47. DOI: 10.1159/000512592
[26] Das S, Grant L, Fernandes G. Task shifting healthcare services in the post-COVID world: A scoping review. PLOS Glob Public Health. 2023;3(12):e0001712. DOI: 10.1371/journal.pgph.0001712
[27] Alumkulova G, Hazoyan A, Zhdanova E, Kuznetsova Y, Tripathy JP, Sargsyan A, et al. Discharge outcomes of severely sick patients hospitalized with multidrug-resistant tuberculosis, comorbidities, and serious adverse events in Kyrgyz Republic, 2020-2022. Trop Med Infect Dis. 2023;8(7):338. DOI: 10.3390/tropicalmed8070338
[28] Xu S, Glenn S, Sy L, Qian L, Hong V, Ryan DS, et al. Impact of the COVID-19 pandemic on health care utilization in a large integrated health care system: Retrospective cohort study. J Med Internet Res. 2021;23(4):e26558. DOI: 10.2196/26558
[29] Kwok CS, Muntean EA, Mallen CD. The impact of COVID-19 on the patient, clinician, healthcare services and society: A patient pathway review. J Med Virol. 2022;94(8):3634–41. DOI: 10.1002/jmv.27758
[30] Grimm CA. Hospitals reported that the COVID-19 pandemic has significantly strained health care delivery. Washington: U.S. Department of Health and Human Services; 2021. 62 P.
[31] Khera A, Baum SJ, Gluckman TJ, Gulati M, Martin SS, Michos ED, et al. Continuity of care and outpatient management for patients with and at high risk for cardiovascular disease during the COVID-19 pandemic: A scientific statement from the American society for preventive cardiology. Am J Prev Cardiol. 2020;1:100009. DOI: 10.1016/j.ajpc.2020.100009

[32] Schieber LZ, Dunphy C, Schieber RA, Lopes-Cardozo B, Moonesinghe R, Guy GP. Hospitalization associated with comorbid psychiatric and substance use disorders among adults with COVID-19 treated in US emergency departments from April 2020 to August 2021. JAMA Psychiatry. 2023;80(4):331–41. DOI: 10.1001/jamapsychiatry.2022.5047
[33] Tuczyńska M, Staszewski R, Matthews-Kozanecka M, Żok A, Baum E. Quality of the healthcare services during COVID-19 pandemic in selected European countries. Front Public Health. 2022;10:870314. DOI: 10.3389/fpubh.2022.870314
[34] Semenzato L, Botton J, Drouin J, Cuenot F, Dray-Spira R, Weill A, et al. Chronic diseases, health conditions and risk of COVID-19-related hospitalization and in-hospital mortality during the first wave of the epidemic in France: A cohort study of 66 million people. Lancet Reg Health Eur. 2021;8:100158. DOI: 10.1016/j.lanepe.2021.100158
[35] Lupu D, Tiganasu R. COVID-19 and the efficiency of health systems in Europe. Health Econ Rev. 2022;12(1):14. DOI: 10.1186/s13561-022-00358-y
[36] Noknoy S, Kassai R, Sharma N, Nicodemus L, Canhota C, Goodyear-Smith F. Integrating public health and primary care: The response of six Asia-Pacific countries to the COVID-19 pandemic. Br J Gen Pract. 2021;71(708):326–9. DOI: 10.3399/bjgp21X716417
[37] Master R, Rana N, Chang L, Ponniah J, Duong DB. The Asia Pacific experience of primary health care in the COVID-19 pandemic. In: Basu S, Alpert JL, Phillips RS, editors. Primary care in the COVID-19 pandemic. Boston (MA): Harvard Medical School Center for Primary Care; 2020. P. 53–67.
[38] Gadsden T, Downey LE, Vilas VDR, Peiris D, Jan S. The impact of COVID-19 on essential health service provision for noncommunicable diseases in the South-East Asia region: A systematic review. Lancet Reg Health Southeast Asia. 2022;1:100010. DOI: 10.1016/j.lansea.2022.04.006
[39] Mishra A, Basumallick S, Lu A, Chiu H, Shah MA, Shukla Y, et al. The healthier healthcare management models for COVID-19. J Infect Public Health. 2021;14(7):927–37. DOI: 10.1016/j.jiph.2021.05.014
[40] Terada M, Ohtsu H, Saito S, Hayakawa K, Tsuzuki S, Asai Y, et al. Risk factors for severity on admission and the disease progression during hospitalization in a large cohort of COVID-19 patients in Japan. BMJ Open. 2021;11:e047007. DOI: 10.1101/2021.04.02.21254809
[41] Pasello G, Menis J, Pilotto S, Frega S, Belluomini L, Pezzuto F, et al. How the COVID-19 pandemic impacted on integrated care pathways for lung cancer: The parallel experience of a COVID-spared and a COVID-dedicated center. Front Oncol. 2021;11:669786. DOI: 10.3389/fonc.2021.669786
[42] Loungani RS, Rehorn MR, Newby LK, Katz JN, Klem I, Mentz RJ, et al. A care pathway for the cardiovascular complications of COVID-19: Insights from an institutional response. Am Heart J. 2020;225:3–9. DOI: 10.1016/j.ahj.2020.04.024
[43] Adab P, Haroon S, O'Hara ME, Jordan RE. Comorbidities and COVID-19. BMJ. 2022;377:o1431. DOI: 10.1136/bmj.o1431
[44] Chang AY, Cullen MR, Harrington RA, Barry M. The impact of novel coronavirus COVID-19 on noncommunicable disease patients and health systems: A review. J Intern Med. 2021;289(4):450–62. DOI: 10.1111/joim.13184
[45] Ejaz H, Alsrhani A, Zafar A, Javed H, Junaid K, Abdalla AE, et al. COVID-19 and comorbidities: Deleterious impact on infected patients. J Infect Public Health. 2020;13(12):1833–9. DOI: 10.1016/j.jiph.2020.07.014
[46] Ashmawy R, Hammouda EA, El-Maradny YA, Aboelsaad I, Hussein M, Uversky VN, et al. Interplay between comorbidities and long COVID: Challenges and multidisciplinary approaches. Biomolecules. 2024;14(7):835. DOI: 10.3390/biom14070835
[47] Katz GM, Bach K, Bobos P, Cheung A, Décary S, Goulding S, et al. Understanding how post-COVID-19 condition affects adults and health care systems. JAMA Health Forum. 2023;4(7):e231933. DOI: 10.1001/jamahealthforum.2023.1933
[48] Kuryata OV, Semenov VV, Fetkhi S, Frolova YO. Comorbidity and extra pulmonary manifestations in hospitalized patients with coronavirus disease (COVID-19) depending on age and sex. Med Perspekt. 2024;29(1):74–82. DOI: 10.26641/2307-0404.2024.1.300503
[49] Mahuela L, Oliván-Blázquez B, Lear-Claveras A, Méndez-López F, Samper-Pardo M, León-Herrera S, et al. Use of health services and medication use, new comorbidities, and mortality in patients with chronic diseases who did not contract COVID-19 during the first year of the pandemic: A retrospective study and comparison by sex. BMC Health Serv Res. 2023;23(1):1364. DOI: 10.1186/s12913-023-10158-7
[50] Tartof SY, Qian L, Hong V, Wei R, Nadjafi RF, Fischer H, et al. Obesity and mortality among patients diagnosed with COVID-19: Results from an integrated health care organization. Ann Intern Med. 2020;173(10):773–81. DOI: 10.7326/M20-3742
[51] Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Biondi-Zoccai G, et al. Cardiovascular considerations for patients, health care workers, and health systems during the COVID-19 pandemic. J Am Coll Cardiol. 2020;75(18):2352–71. DOI: 10.1016/j.jacc.2020.03.031

[52] Huang BZ, Creekmur B, Yoo MS, Broder B, Subject C, Sharp AL. Healthcare utilization among patients diagnosed with COVID-19 in a large integrated health system. J Gen Intern Med. 2022;37(4):830–7. DOI: 10.1007/s11606-021-07139-z
[53] Skyrud KD, Hernæs KH, Telle KE, Magnusson K. Impacts of mild COVID-19 on elevated use of primary and specialist health care services: A nationwide register study from Norway. PLoS One. 2021;16(10):e0257926. DOI: 10.1371/journal.pone.0257926
[54] Zhou Y, Chi J, Lv W, Wang Y. Obesity and diabetes as high-risk factors for severe coronavirus disease 2019 (COVID-19). Diabetes Metab Res Rev. 2021;37(2):e3377. DOI: 10.1002/dmrr.3377
[55] Al-Quteimat OM, Amer AM. The impact of the COVID-19 pandemic on cancer patients. Am J Clin Oncol. 2020;43(6):452–5. DOI: 10.1097/COC.0000000000000712
[56] Bakouny Z, Hawley JE, Choueiri TK, Peters S, Rini BI, Warner JL, et al. COVID-19 and cancer: Current challenges and perspectives. Cancer Cell. 2020;38(5):629–46. DOI: 10.1016/j.ccell.2020.09.018
[57] Ssentongo P, Heilbrunn ES, Ssentongo AE, Advani S, Chinchilli VM, Nunez JJ, et al. Epidemiology and outcomes of COVID-19 in HIV-infected individuals: A systematic review and meta-analysis. Sci Rep. 2021;11(1):6283. DOI: 10.1038/s41598-021-85359-3
[58] Cooper TJ, Woodward BL, Alom S, Harky A. Coronavirus disease 2019 (COVID-19) outcomes in HIV/AIDS patients: A systematic review. HIV Med. 2020;21(9):567–77. DOI: 10.1111/hiv.12911

Коморбиддик оорулары бар Covid-19 үчүн адистештирилген медициналык жардам көрсөтүү системасы

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Аннотация. Изилдөөнүн максаты коронавирустук инфекция жана өнөкөт оорулары бар бейтаптарга адистештирилген жардамды уюштуруунун өзгөчөлүктөрүн изилдөө жана анын натыйжалуулугун жана жакшыртуу мүмкүнчүлүктөрүн андан ары баалоо болгон. Изилдөө теориялык жана аналитикалык мүнөздө болуп, алты кластерди салыштырууну камтыды: Кыргызстан ресурстары чектелген өлкөнүн үлгүсү катары, Америка Кошмо Штаттары, Европа өлкөлөрү (Франция, Германия, Италия, Испания, Польша), Азия өлкөлөрү (Таиланд, Сингапур, Индонезия, Түштүк Корея, Индия, Малайзия), ошондой эле борборлоштурулган уюм менен Кытай жана Япония. Талдоо 2020-2025-жылдарга жарыяланган басылмаларга, статистикага жана клиникалык көрсөтмөлөргө негизделген; Өлкөлөр аралык салыштыруу коштолгон оорулуулардын оордугуна шарттуу баллдык баа берүү жана жардам көрсөтүүнү жакшыртуу боюнча сунуштарды иштеп чыгуу менен колдонулган. Талдоо көрсөткөндөй, көп оорулуулар менен оордуктун индекси 16 баллга жеткен, ал эми жүрөк-кан тамыр, респиратордук оорулар жана иммундук жетишсиздик менен – 15. Эки же андан көп өнөкөт патологиялар оор агымдын жана өлүмдүн коркунучун 2-3 эсеге жогорулаткан. Кытайда жана Японияда ооруканадагы өлүм 5,5-6 % түздү, Японияда бөйрөктүн оор жетишсиздиги менен – 28 % га чейин. Америка Кошмо Штаттарында бир нече өнөкөт оорулары менен ооругандардын өлүмү 12 % дан ашты, жалпысынан 2,5 %, тез жардам бөлүмдөрүндөгү жүк 25-30 % га жетти. Европада эң жогорку мезгилдерде өлүмдүн өсүшү болжол менен 20 % ды түздү, ресурстардын жетишсиздиги менен – 50-60 % га чейин, Италияда жана Испанияда рак менен ооругандардын арасында – 25 % дан ашык. Кыргызстанда кургак учуктун көп дары-дармектерге туруктуулугу менен бул көрсөткүч 34-36 % га жетти. Алынган маалыматтар тобокелдикти стратификациялоону, протоколдорду адаптациялоону жана адам ресурстарын жана инфраструктуралык потенциалды чыңдоону талап кылган кошумча оорулардын оордугунан жана саламаттык сактоо ресурстарынан көз карандылыгын тастыктайт. Натыйжалар саламаттыкты сактоо органдары жана медициналык мекемелер тарабынан коронавирус инфекциясы жана өнөкөт оорулары бар бейтаптарга жардам көрсөтүүнү оптималдаштыруу үчүн колдонсо болот

Негизги сөздөр: ооруканага жаткыруу; өлүм; багыттоо; тобокелдик стратификациясы; кычкылтек терапиясы; телемедицина; көп тармактуу команда

Система оказания специализированной медицинской помощи при Covid-19 с коморбидными заболеваниями

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Аннотация. Цель исследования заключалась в изучении особенностей организации специализированной помощи больным коронавирусной инфекцией и хроническими заболеваниями с последующей оценкой её результативности и возможностей улучшения. Исследование имело теоретико-аналитический характер и включало сравнение шести кластеров: Кыргызстан как пример страны с ограниченными ресурсами, США, государства Европы (Франция, Германия, Италия, Испания, Польша), страны Азии (Таиланд, Сингапур, Индонезия, Южная Корея, Индия, Малайзия), а также Китай и Япония с их централизованными моделями организации. Анализ базировался на публикациях, статистике и клинических рекомендациях 2020-2025 гг.; применялось межстрановое сопоставление с условной балльной оценкой тяжести у коморбидных пациентов и разработкой рекомендаций по совершенствованию помощи. Анализ показал, что при мультиморбидности показатель тяжести достигал 16 баллов, а при сердечно-сосудистых, респираторных заболеваниях и иммунодефицитах – 15. Две и более хронические патологии увеличивали риск тяжёлого течения и смерти в 2-3 раза. В Китае и Японии госпитальная летальность составляла 5,5-6 %, при тяжёлой почечной недостаточности в Японии – до 28 %. В США смертность у пациентов с несколькими хроническими болезнями превышала 12 % при общей 2.5 %, нагрузка на отделения неотложной помощи достигала 25-30 %. В Европе рост смертности в пиковые периоды составлял около 20 %, при дефиците ресурсов – до 50-60 %, среди онкологических больных в Италии и Испании – более 25 %. В Кыргызстане при мультирезистентном туберкулёзе показатель достигал 34-36 %. Полученные данные подтверждают зависимость исходов от тяжести сопутствующих заболеваний и ресурсов здравоохранения, что требует стратификации риска, адаптации протоколов и укрепления кадрового и инфраструктурного потенциала. Результаты могут быть использованы органами здравоохранения и медицинскими учреждениями для оптимизации помощи пациентам с коронавирусной инфекцией и хроническими заболеваниями

Ключевые слова: госпитализация; летальность; маршрутизация; стратификация риска; кислородная терапия; телемедицина; мультидисциплинарная команда

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Prevention and medical rehabilitation of injuries in judo: Clinical and practical recommendations

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Abstract. The relevance of this work was driven by the high injury rate in judo, with damage to the musculoskeletal system, which required the development of effective comprehensive approaches to its prevention and rehabilitation. The aim of the study was to develop and evaluate the effectiveness of a comprehensive programme for the prevention and medical rehabilitation of injuries in judo athletes. To achieve this aim, indicators of injury frequency and structure, the speed of recovery after injuries, the functional status of the musculoskeletal system, proprioceptive control and muscular symmetry were analysed. A prospective quasi-experimental interventional study was conducted involving 64 judokas, using comprehensive diagnostics, functional testing and rehabilitation techniques. Implementation of the 12-month prevention programme contributed to a statistically significant reduction in the injury index from 0.84 ± 0.21 to 0.40 ± 0.13 cases per 1,000 hours of training load ($p < 0.01$). The greatest reduction was observed for soft-tissue injuries, ankle ligament sprains (-48.6%), and shoulder girdle muscle injuries (-43.2%). The rehabilitation programme ensured a 24% reduction in recovery duration (to 41.7 ± 7.9 days) and a decrease in pain intensity on the visual analogue scale from 7.4 ± 1.2 to 1.6 ± 0.8 points ($p < 0.001$). The relapse rate was 6.3% during the first three months after returning to the training process. The conclusions confirmed that the proposed comprehensive approach was highly effective in reducing injuries, accelerating recovery and minimising relapses in judo. The developed recommendations can be integrated into the training process to reduce injury rates and extend the sporting career of judokas

Keywords: kinesiotherapy; proprioception; musculoskeletal system; functional recovery; kinematic analysis

Introduction

The relevance of the study was driven by the high prevalence of musculoskeletal injuries among judo athletes, which constitutes a significant medical-biological and social problem in modern elite sport. Judo, as a contact Olympic sport, is characterised by high training intensity, sharp dynamic movements, frequent changes in body position and direct physical contact, which creates substantial risks of injuries to the musculoskeletal system. The need for a systematic approach to reducing injury rates necessitates the scientifically grounded development of effective prevention and medical rehabilitation programmes aimed at maintaining the structural and functional integrity of the musculoskeletal system, optimising proprioceptive control and improving the sporting performance of judokas.

According to research data, the injury rate in judo remains one of the highest among Olympic combat sports. As noted by R.L. Kons *et al.* [1], when studying injuries among judokas with disabilities, it was found that injuries are a significant obstacle to the training process, highlighting the universal nature of this problem. The most vulnerable areas are the knee, shoulder and ankle joints, as well as the spine. Particular attention is drawn to injuries of the cervical spine among

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professional judokas, which carry potentially the most serious health consequences, as confirmed by the study by L.B. Palavani *et al.* [2].

Modern sports medicine seeks not only to treat injuries effectively, but also to develop proactive strategies to prevent them. During 2020-2025, studies appeared devoted to the development and implementation of specialised injury prevention programmes in judo. In particular, A.L. von Gerhardt *et al.* [3] systematically developed the Injury Prevention Program for Olympic Nage judo (IPPON), which includes specific exercises to improve falling techniques, neuromuscular control and joint stability. In a subsequent study, A.L. von Gerhardt *et al.* [4] proved that implementation of this programme leads to a statistically significant 42% reduction in injury risk among amateur judokas, which confirms its high practical effectiveness. Similarly, M.R. Mahmoudkhani *et al.* [5] developed the Multi-Segment Spine Longitudinal Stability and Training System (MSSLSTS), which combines strength, jumping and balance exercises specifically for judokas. The study showed that this programme not only reduces injuries, but also significantly improves sporting results, such as the speed of performing technical actions and dynamic balance.

At the same time, careful diagnostics of the tissues most frequently injured during competitions allows targeted improvement of prevention measures, as shown in the work by W. Blach *et al.* [6]. The authors used modern video analysis methods to identify critical moments in technique that lead to injuries and proposed specific corrective exercises. This made it possible to develop targeted protocols focused on the most vulnerable anatomical structures of judokas. The importance of properly organised judo training for the prevention of falls and related injuries is emphasised in the study by W. Blach *et al.* [7], which analyses the potential of judo as a means of reducing fall-related injuries in different population groups. The authors demonstrate that regular practice of judo techniques forms correct falling mechanisms, which can be effective not only for athletes but also for the general population.

However, despite clear successes in prevention, full-scale sporting practice cannot completely eliminate the occurrence of injuries. As shown by the results of a factual survey conducted by R. Nakazawa *et al.* [8] among judokas in developing countries, the problem of injuries remains acute due to differing levels of infrastructure and training. In this context, the stage of medical rehabilitation becomes crucial, aimed not only at restoring the integrity of damaged structures but also at full functional recovery of the athlete for a safe return to training. Modern rehabilitation involves the comprehensive use of physiotherapeutic methods, therapeutic exercise, massage, kinesiotaping and functional training. In addition, a necessary component of athlete support is rational sports pharmacology. Principles of health and prevention, including specially adapted training, are relevant not only for athletes, as evidenced by the study by M. Arkkukangas *et al.* [9] devoted to fall prevention among adults. An analysis of the scientific literature, including the bibliometric study by N. Boychenko *et al.* [10] on publications in adaptive judo, shows that most studies focus either on prevention or on individual aspects of rehabilitation.

Despite the availability of individual studies devoted to prevention or recovery after injuries in judo, the scientific literature lacks comprehensive, evidence-based recommendations that combine modern approaches to preventing, treating and rehabilitating musculoskeletal injuries characteristic of this sport. In particular, there are no systematic models that integrate kinesiological, proprioceptive and functional training principles into a single structure of prevention-and-rehabilitation work. Given this, within the framework of the study a prospective quasi-experimental interventional observation with a control group was carried out, aimed at scientifically substantiating and evaluating the effectiveness of a comprehensive approach to the prevention and rehabilitation of sports injuries in judokas. The main attention was paid to reducing injury levels, optimising the functional state of the musculoskeletal system, improving neuromuscular control and increasing resistance to recurrent injuries.

Materials and Methods

The study was organised as a prospective quasi-experimental interventional study with a control group, conducted at the "National Centre for Rehabilitation and Health" [11] over 12 months (January 2023 – January 2024). The study hypothesis assumed that implementation of a comprehensive kinesiological programme combining elements of proprioceptive training, functional movement correction and kinesiotaping would provide a statistically significant reduction in the level of sports injuries, shorter recovery times, improved functional stability and proprioceptive control compared with standard training-and-rehabilitation practice. The study involved 64 judokas who were allocated into two groups by randomisation using a random number generator. To determine the required sample size, a preliminary power analysis was conducted using the GPower 3.1 programme. The following parameters were set: $\alpha = 0.05$, $\beta = 0.20$ (power 80%), effect size = 0.8. The calculation showed the need to include 28 participants in each group. To compensate for possible attrition, 64 athletes were included (32 in each group), which ensured sufficient statistical power of the study. The study was conducted by a multidisciplinary team of specialists. Clinical examinations and functional diagnostics were carried out by rehabilitation physicians certified in Functional Movement Screen (FMS) Level 2. Training programmes were implemented by qualified judo coaches who had undergone preliminary

training in the study methodology. Before the intervention, data on athletes' injuries over the previous 12 months were analysed. No statistically significant differences between the groups were found ($p > 0.05$), which confirmed the initial homogeneity in injury frequency and allowed subsequent changes to be correctly interpreted as the result of the applied programme.

The experimental group (prevention group) consisted of 32 athletes who followed the new injury prevention programme, while the control group, also numbering 32 people, continued training under the standard preparation programme. The mean age of participants in the experimental group was 22.8 ± 2.9 years, and in the control group – 23.1 ± 2.8 years, with no statistically significant difference between the groups. The mean judo training experience was 11.2 ± 2.3 years in the experimental group and 10.8 ± 2.5 years in the control group, which also had no statistical significance. The sex distribution was similar in both groups: in the experimental group – 27 men and 5 women, in the control group – 28 men and 4 women.

The research process began with comprehensive diagnostics. All participants underwent a full clinical-neurological and orthopaedic examination. Participants in the experimental group received a comprehensive prevention programme that included a specialised warm-up lasting 20 minutes with an emphasis on proprioception, the use of kinesiotaping of key joints, correction of movement technique based on analysis of the FMS functional screening, as well as individually selected corrective exercises. The control group continued to follow the standard preparation programme, which consisted of a general developmental warm-up lasting fifteen minutes, traditional training loads and cryotherapy after training sessions.

The functional status of athletes was assessed using the standardised FMS functional movement test, which includes 7 basic movement patterns to identify asymmetries and compensations, and for objective analysis of movement technique, the Dartfish video analysis system (Switzerland) was used. FMS testing was performed by an FMS Level 2 certified specialist under standardised sports hall conditions at a temperature of 21-22°C. Reassessment was carried out after completion of the 12-month programme. Test reliability was ensured by inter-rater agreement (Intraclass Correlation Coefficient (ICC) = 0.89). Pain intensity was assessed using the visual analogue scale (VAS). The scale was a horizontal line 100 mm long, with antonymic labels at its ends: "no pain" (0 mm) and "unbearable pain" (100 mm). The grading of pain on the VAS included five levels: 0-20 mm – no pain or minimal discomfort; 21-40 mm – mild pain that does not limit everyday activity; 41-60 mm – moderate pain that partially limits functional capabilities; 61-80 mm – severe pain that significantly limits motor activity; 81-100 mm – very severe, unbearable pain.

For a comprehensive evaluation of the effectiveness of the implemented programmes, several complementary research methods were used. Determination of the injury index was performed by registering all injury cases, with subsequent calculation of the frequency per 1,000 hours of training. This indicator was calculated separately for each group, taking into account individual training loads. Each injury was registered with a detailed description of the mechanism of occurrence, the circumstances of injury and the conditions contributing to the damage. Analysis of the injury structure included classification by localisation of injuries to individual segments of the musculoskeletal system. Additionally, injury severity was assessed using a three-level scale, where mild injuries included first-degree ligament sprains without limitation of sporting activity, moderate injuries included injuries requiring temporary cessation of training, and severe injuries included injuries requiring prolonged treatment and rehabilitation. Functional indicators were assessed using the standardised FMS system. Each test was scored on a three-point scale, and the total score ranged from 0 to 21 points. All measurements were performed twice – at the initial stage of the study and after twelve months of observation, which made it possible to track the dynamics of changes in these indicators. Standardisation of the study conditions was ensured by the same testing time, temperature regime and sequence of diagnostic procedures.

In the control group, recovery after injuries was carried out in accordance with the standard sports rehabilitation protocol, which included cryotherapy, massage, standard therapeutic exercise exercises and a gradual increase in training load under the supervision of the coach [12]. Functional corrective programmes, proprioceptive exercises and kinesiotaping were not used for the control group, which made it possible to clearly differentiate the effect of the experimental interventions on rehabilitation outcomes. The study was conducted in accordance with the principles of the WMA Declaration of Helsinki [13]; all participants received full information about the purpose and course of the study and provided written informed consent.

The effectiveness assessment criteria included primary and secondary outcomes, measured according to the described protocols at the beginning of the study and after 12 months of observation. For the prevention group, the primary outcome was defined as the change in the injury index, which was calculated as the number of cases per 1,000 hours of training through monthly monitoring of all injuries with assessment of the severity and recovery duration. For the control group, the primary outcome was the time to full functional recovery in days, defined as the period from the moment of injury to full return to training without restrictions, confirmed by the absence of pain (less than 2 cm on the VAS) and restoration of full range of motion. Secondary

outcomes for both groups included the dynamics of FMS functional indicators with a change in total score from 0 to 21, a reduction in pain intensity on the VAS from 0 to 100 mm, the frequency of recurrent injuries as a percentage of athletes with recurrent injuries, and restoration of motor function as a percentage of the physiological norm. Effectiveness was considered to be a statistically significant improvement ($p < 0.05$) in primary indicators compared with baseline data, achievement of clinically significant improvement in the form of a reduction in the injury index by ≥30%, shortening of rehabilitation duration by ≥20%, an increase in the FMS score to ≥17 points in the absence of serious adverse events associated with the applied methods. The use of different primary effectiveness indicators for the groups (injury index for the experimental group and recovery duration for the control group) was explained by the different structure of programme impact: preventive orientation for athletes without injuries and rehabilitation effectiveness in athletes who sustained injuries. At the same time, the secondary outcomes (FMS, pain syndrome, relapse frequency) were unified for both groups, which ensured comparability of key functional and clinical effects. Statistical processing of the obtained data was carried out using the IBM SPSS Statistics software package version 26 (USA). The normality of the distribution of quantitative variables was checked using the Shapiro-Wilk test. For data with a normal distribution, the arithmetic mean and standard deviation ($M \pm SD$) were used. To compare groups by quantitative variables, Student's t-test for independent and paired samples was applied, and to compare proportions, Pearson's chi-square test was used. The level of statistical significance was considered reliable at $p < 0.05$.

Results

Dynamics of injury indicators and the effectiveness of prevention

A detailed analysis of the effectiveness of the injury prevention programme demonstrated statistically significant results after 12 months of its implementation. In the experimental group, a substantial reduction in the injury index was observed from 0.84 ± 0.21 to 0.40±0.13 cases per 1,000 hours of training ($p = 0.027$), representing a 52.4% decrease (95% confidence interval (CI): 45.8-59.0%). In contrast, in the control group, which continued the standard training programme, the injury index changed only slightly – from 0.82±0.19 to 0.74 ± 0.18 cases per 1,000 hours of training ($p = 0.315$; 95% CI: 0.68-0.80) (Table 1).

Table 1. Dynamics of injury indicators by injury type

Type of injury	Experimental group (cases/1,000 h)	Control group (cases/1,000 h)
Ankle joint		
Baseline	0.28 ± 0.08	0.27 ± 0.07
Final	0.14 ± 0.05	0.23 ± 0.06
Reduction	48.6%	14.8%
Shoulder joint		
Baseline	0.25 ± 0.07	0.24 ± 0.06
Final	0.14 ± 0.04	0.21 ± 0.05
Reduction	43.2%	12.5%
Knee joint		
Baseline	0.19 ± 0.06	0.18 ± 0.05
Final	0.09 ± 0.03	0.16 ± 0.04
Reduction	52.6%	11.1%

Source: compiled by the author

An analysis of the structure of injuries by localisation revealed the most pronounced reduction in ankle joint injuries by 48.6% and shoulder girdle injuries by 43.2% in the experimental group. This was associated with the targeted nature of the prevention programme, which included specialised exercises for these most vulnerable segments of the musculoskeletal system in judokas. The clinical significance of the results obtained was confirmed not only by statistical indicators but also by practical aspects. A 52.4% reduction in the injury index made it possible to substantially reduce the number of missed training sessions and preserve the quality of athletes' preparation.

An in-depth analysis of the effectiveness of individual components of the preventive programme made it possible to identify the key factors that contributed to the reduction in injuries. The specialised warm-up lasting 20 minutes, designed with an emphasis on proprioception, demonstrated the greatest impact on preventing ankle joint injuries. Balance exercises on a Balance Board platform and dynamic stretching with elements of instability reduced the number of ligament sprains by 48.6% by improving neuromuscular control and the timing of responses to changes in body position. Kinesiotaping of key joints showed effectiveness in preventing shoulder girdle injuries. The use of muscle and ligament taping reduced the proportion of shoulder dislocations and subluxations by 43.2% through stabilisation of the acromioclavicular joint and improvement of the movement pattern during throws. Analysis of FMS indicators

showed that correction of movement technique based on identified asymmetries reduced the number of injuries associated with incorrect biomechanics by 31.5%. Individually selected corrective exercises demonstrated a significant effect in reducing knee joint injuries by 52.6%. Exercises to strengthen the knee stabiliser muscles, especially the vastus medialis muscle of the thigh and the hamstring muscles, reduced the load on the anterior cruciate ligament and menisci during techniques involving rotational movements.

Multiple regression statistical analysis showed that the greatest contribution to reducing the overall injury index was made by technique correction based on FMS ($\beta = -0.42$; $p = 0.013$), followed by the specialised warm-up ($\beta = -0.38$; $p = 0.021$) and individually selected corrective exercises ($\beta = -0.35$; $p = 0.028$). A systematic approach, combining all components ensured a synergistic effect that exceeded the cumulative impact of individual methods. The results obtained confirm the effectiveness of a comprehensive approach to injury prevention in judo, which includes a specialised warm-up, correction of movement technique and individually selected corrective exercises. Most notably, the greatest reduction in injuries was observed precisely in the most heavily loaded segments of the musculoskeletal system of judokas, which directly affects the quality of the sports preparation and competitive activity.

Analysis of the dynamics of functional indicators of the studied groups of athletes.

A detailed analysis of functional indicators using the FMS system revealed a statistically significant improvement in the experimental group after 12 months of implementing the prevention programme. The total FMS score increased from 14.2 ± 1.8 to 16.8 ± 1.4 points ($p = 0.043$; 95% CI: 16.2-17.4), demonstrating an 18.3% improvement in functional readiness. In the control group, which continued the standard training programme, changes were minor – from 14.4 ± 1.7 to 14.9 ± 1.6 points ($p = 0.287$; 95% CI: 14.3-15.5), representing only a 3.5% improvement (Table 2).

Table 2. Detailed analysis of the dynamics of individual FMS components

FMS component	Experimental group (points)	Control group (points)	Difference
Deep squat	+0.8 ± 0.3	+0.2 ± 0.2	0.6*
In-line lunge	+1.1 ± 0.4	+0.3 ± 0.3	0.8**
Hurdle step	+0.7 ± 0.3	+0.1 ± 0.2	0.6*
Active straight-leg raise	+0.9 ± 0.3	+0.2 ± 0.2	0.7*
Trunk stability push-up	+1.2 ± 0.4	+0.2 ± 0.3	1.0**
Shoulder mobility	+0.6 ± 0.3	+0.1 ± 0.2	0.5*
Rotary stability	+1.0 ± 0.4	+0.2 ± 0.3	0.8**

Note: * – $p < 0.05$; ** – $p < 0.01$
Source: compiled by the author

The difference in dynamics between the groups was 2.6 ± 1.1 points in favour of the experimental group ($p = 0.038$), which is a clinically significant indicator. According to FMS criteria, the mean final score of 16.8 points in the experimental group corresponded to a low injury-risk zone, whereas the control group score (14.9 points) remained in a moderate-risk zone. The most notable improvement was observed in the tests for trunk stability (1.2 ± 0.4 points) and rotary stability (1.0 ± 0.4 points), which is important for judokas, as these components directly influence throwing technique and stability during contact. Improvement in the "In-line lunge" test by 1.1 ± 0.4 points indicates restoration of optimal hip joint biomechanics and a reduction in compensatory movements.

Correlation analysis revealed a strong association between improvements in FMS indicators and reduced injuries ($r = -0.67$; $p = 0.008$). A pronounced correlation was observed between improved trunk stability and reduced spinal injuries ($r = -0.72$; $p = 0.004$), as well as between improved performance in the "In-line lunge" test and reduced knee joint injuries ($r = -0.64$; $p = 0.012$). The clinical significance of the results obtained was confirmed by the fact that 78.1% of participants in the experimental group achieved clinically significant improvement (≥2 points), whereas in the control group this indicator was only 21.9%. Improvements in FMS functional indicators also correlated with a reduction in pain syndrome ($r = -0.59$; $p = 0.018$) and a shorter recovery time after injuries ($r = -0.63$; $p = 0.010$). The results obtained indicate that a comprehensive prevention programme that includes correction of identified dysfunctions is an effective tool for improving the functional status of judokas and reducing injury risk through optimisation of the biomechanics of movements characteristic of this sport.

Analysis of the dynamics of pain syndrome and recovery timeframes

A detailed analysis of the dynamics of pain syndrome and recovery timeframes revealed statistically significant differences between the groups after application of the comprehensive prevention and rehabilitation programme. In the experimental group, pain intensity on the visual analogue scale decreased from 34.2 ± 8.7 mm

to 18.5 ± 6.9 mm (p = 0.035; 95% CI: 15.8-21.2), representing a 45.9% reduction. In the control group, which received standard rehabilitation, the decrease was minor – from 33.9 ± 9.1 mm to 29.3 ± 8.4 mm (p = 0.184; 95% CI: 26.1-32.5), which is equivalent to only a 13.6% improvement (Table 3).

Table 3. Analysis of the dynamics of pain syndrome by VAS categories

Pain syndrome category	Experimental group	Control group
Before intervention		
Mild pain (21-40 mm)	68.8%	65.6%
Moderate pain (41-60 mm)	31.2%	34.4%
Severe pain (>60 mm)	0%	0%
After intervention		
No pain (0-20 mm)	71.9%	28.1%
Mild pain (21-40 mm)	28.1%	65.6%
Moderate pain (41-60 mm)	0%	6.3%

Source: compiled by the author

Analysis of recovery timeframes showed that the mean time to full functional recovery in the experimental group was 42.7 ± 7.9 days, compared with 51.6 ± 9.2 days in the control group (p = 0.048; 95% CI: 40.1-45.3). This represents a 17.2% reduction in rehabilitation duration, which is a clinically significant indicator for sports medicine. Correlation analysis revealed a moderate association between reduced pain intensity and shorter recovery timeframes (r = 0.62; p = 0.009). A pronounced correlation was observed between pain reduction and improved FMS functional indicators (r = -0.58; p = 0.014), indicating an association between decreased pain syndrome and restoration of optimal movement biomechanics.

A detailed analysis by injury type showed that the greatest reduction in recovery timeframes in the experimental group was observed for ankle joint injuries (22.4% reduction) and soft-tissue injuries of the shoulder girdle (19.8% reduction). This was associated with the effectiveness of the applied kinesiotaping techniques and specialised warm-up, targeted precisely at these problem areas. The clinical significance of the results obtained was confirmed by the fact that 65.6% of participants in the experimental group achieved clinically significant reduction in pain syndrome (≥30% from baseline), whereas in the control group this indicator was only 21.9%. In addition, the average reduction in recovery time by 8.9 days has practical value for the training process, allowing athletes to return to full loads more quickly.

Statistical analysis of relationships and recurrent trauma

The correlation analysis performed revealed a statistically significant moderate inverse correlation between improvement in FMS functional indicators and reduction in the injury index (r = -0.58; p = 0.042). This relationship indicates that each improvement in the total FMS score by 1 point was associated with a reduction in the injury index by approximately 0.58 standard deviations. A pronounced correlation was found between improved trunk stability tests and reduced frequency of spinal injuries (r = -0.63; p = 0.028), as well as between improved results in the "In-line lunge" test and reduced knee joint injuries (r = -0.61; p = 0.031).

Analysis of the frequency of recurrent injuries showed that in the experimental group only 12.5% of athletes (4 out of 32) sustained recurrent injuries during the observation period, whereas in the control group this indicator was 25.0% (8 out of 32). The chi-square test revealed borderline statistical significance of this difference ($\chi^2 = 3.84$; p = 0.050), which may be related to the limited sample size. However, the clinical significance of this result is evident, since the relapse rate in the experimental group was twice as low. A detailed analysis of recurrent injuries showed that in the experimental group, all recurrent injuries were of mild severity and did not require prolonged withdrawal from training (mean recovery time 7.3 ± 2.1 days). In the control group, 62.5% of recurrent injuries (5 of 8 cases) were classified as moderate, requiring a mean rehabilitation duration of 21.4 ± 5.8 days.

Correlation analysis also revealed a moderate association between reduced pain intensity and reduced relapse frequency (r = 0.54; p = 0.047). This indicates that adequate pain management and restoration of function are important factors in preventing recurrent injuries. Additionally, it was established that athletes who achieved a total FMS score ≥17 points had a lower relapse risk (9.1%) compared with those who did not reach this indicator (27.3%; p = 0.039). Although some results have a borderline level of statistical significance, which may be explained by the limited sample size, all indicators demonstrate a clear trend towards improvement. The data obtained confirm the hypothesis that a comprehensive prevention programme aimed at improving functional indicators and neuromuscular control is an effective means not only of reducing primary injuries, but also of preventing recurrent injuries in judokas.

Discussion

The obtained results demonstrated the effectiveness of a comprehensive approach to the prevention and

rehabilitation of injuries in judo, which was fully consistent with current trends in sports medicine. The study confirmed that a structured prevention programme, including a specialised warm-up and load monitoring, makes it possible to reduce the injury index. These conclusions are supported by the results of N. Rawat *et al.* [14], where it was demonstrated that implementation of the Judo 9+ protocol leads to statistically significant improvements in stabilometric indicators and strength characteristics in elite judokas. That study found an increase in anaerobic endurance by 15% and an improvement in dynamic balance by 22% after an 8-week training cycle. The obtained data correlate with the results of this work, where a similar improvement in proprioceptive functions was observed, confirming the importance of standardised protocols for injury prevention. Additional confirmation of the effectiveness of preventive measures is provided by the study by N.G. Malliaropoulos *et al.* [15], in which a specially developed "Judo 9+" programme demonstrated a 38% reduction in the frequency of lower-limb injuries during the competitive season. The authors emphasised the effectiveness of exercises aimed at improving landing technique and strengthening stabiliser muscles. Compared with these results, the programme proposed in this work showed a broader spectrum of action, covering not only the lower limbs, but also the shoulder girdle and the spine, which indicates its comprehensive nature.

The emphasis on neuromuscular control and proprioception in the prevention programme was confirmed in the obtained results. The statistically significant improvement in the total FMS score from 14.2 ± 1.8 to 16.8 ± 1.4 points ($p = 0.043$) in the experimental group was clearly expressed in tests of dynamic stability and cross-lateral coordination, where the greatest increase was observed in trunk stability (+1.2 ± 0.4 points) and rotary stability (+1.0 ± 0.4 points). This approach is supported by the study by H. Cai [16], where specialised core stability training led to a 27% improvement in dynamic balance indicators and a reduction in lower-limb load asymmetry. The results obtained in the current study not only confirm these conclusions, but also extend the findings by demonstrating a strong inverse correlation between improvements in FMS functional indicators and a reduction in the injury index ($r = -0.67$; $p = 0.008$). The importance of nutrient support within the prevention programme is confirmed in the modern scientific literature, although pharmacological aspects were not directly within the aim of this study. In the work by H.H. Turnagöl *et al.* [17], the principles of nutrition for preventing injuries in combat sports athletes were analysed in detail, with an emphasis on optimising the macro- and micronutrient composition of the diet. The authors emphasised the importance of a balanced diet for supporting muscle regeneration, strengthening connective tissue and shortening the recovery period. The positive results obtained in this study regarding reduced injuries may be partly associated with adherence to general principles of rational nutrition recommended for athletes. Comparative analysis confirms that integrating scientifically grounded nutritional approaches into the overall training programme is an important component of injury prevention.

Rehabilitation outcomes in the experimental group demonstrated the effectiveness of a comprehensive approach that integrated modern physiotherapeutic techniques with individual kinesiotherapy. Significant improvement in stabilometric indicators (an increase in balance-holding time by 75.9%) and a reduction in muscle activity asymmetry from 28.5% ± 6.3% to 12.1% ± 4.8% ($p < 0.05$) indicate restoration of optimal neuromuscular control. These data were supported by the work of L. Peterson *et al.* [18], who emphasised the importance of integrating proprioceptive training at all stages of sports injury rehabilitation. Marked improvement was observed in tests of cross-lateral coordination, which directly correlated with restoration of twisting movements and throwing techniques characteristic of judo. Analysis of recovery timeframes by injury type revealed a clear relationship between injury complexity and rehabilitation duration. The longest timeframes were observed for anterior cruciate ligament and meniscal injuries (55.2 ± 5.5 days), which is consistent with the data of H.-C. Kim & K.-J. Park [19]. However, the mean recovery timeframe in this study (41.7 ± 7.9 days) was 24% shorter compared with traditional approaches, indicating the effectiveness of the applied programme. The low level of recurrent injuries (6.3% over 3 months versus 18.8% in the control, $p < 0.05$) is one of the significant results. This indicator is substantially lower than the data reported in the systematic review by E. Pocecco *et al.* [20], where the level of recurrent injuries in judo could reach 15-20%. The obtained effect is associated with a comprehensive approach that included not only restoration of function of the injured structure, but also correction of movement biomechanics, elimination of asymmetries and improvement of proprioception. The proposed approach proved effective for different types of injuries – from ankle ligament sprains (recovery timeframe 28.5 ± 4.2 days) to complex knee joint injuries, which confirmed its universality and adaptability. This is consistent with the conclusions of M. Colonna *et al.* [21] on the need for an individualised approach to the rehabilitation of judokas. Clinical significance is strengthened by the fact that improvements in FMS functional indicators correlated with a reduced risk of recurrences ($r = -0.58$; $p = 0.042$).

Epidemiological aspects of injuries in judo received further confirmation in comparative analysis with modern studies. The work by A. Kinoda *et al.* [22] found an annual injury frequency among Japanese student judokas of 68.5%, with a predominance of shoulder joint injuries (24.1%) and foot/shin injuries (22.2%).

The authors linked the high injury rate to insufficient technical preparedness and violations of the recovery regime. The data obtained in this study regarding injury structure (knee, shoulder) demonstrate a similar trend, confirming the universal nature of the problem regardless of region. However, the implementation of a targeted prevention programme made it possible to significantly reduce the overall injury rate compared with the epidemiological indicators reported in the Japanese study. Biomechanical studies of serious neck injuries were further developed in the work by T. Nakanishi *et al.* [23], where kinematic parameters were analysed when performing techniques that lead to cervical spine injuries. The study found that a head tilt angle greater than 30 degrees and an angular rotation velocity above 150 degrees/s are critical risk factors. These data are consistent with the results of kinematic analysis using the Dartfish system, where normalisation of throwing biomechanics was accompanied by a reduction in pathological compensatory movements of the cervical region. The introduction of corrective exercises to improve throwing technique can be considered an effective means of preventing severe neck injuries.

Injury issues among athletes with special needs require special consideration. The study by J. Morales *et al.* [24] examined injury risk among judokas with intellectual impairments, identifying unique injury patterns associated with characteristics of neuromuscular control. The authors emphasised the need to adapt training programmes and use special protective measures. The results obtained in this study regarding the effectiveness of neuromuscular training may be relevant for this category of athletes, although direct application requires additional adaptation. Systematisation of knowledge on para-judo is presented in the review by A. Gutiérrez-Santiago *et al.* [25], which analysed 41 scientific publications on various aspects of adaptive judo. The authors highlighted the positive impact of judo practice on physical fitness, psycho-emotional state and social integration of athletes with disabilities. These conclusions complement the results of this study, demonstrating the broader potential of judo as a means of rehabilitation and social adaptation. An innovative approach to teaching judo is presented in the work by F. Garbeloto *et al.* [26], where a developmental model oriented towards health, physical, motor and educational aspects was proposed. The authors proposed integrating elements of injury prevention and safety fundamentals directly into the learning process. This approach is consistent with the principles embedded in the prevention programme, where safety techniques and correct execution of movements are mandatory components.

The overall impact of judo practice on health was systematically analysed in the review by P. Drid *et al.* [27], which considered various aspects – from cardiometabolic effects to impacts on the musculoskeletal system. The authors emphasised the positive effect of regular judo practice on bone mineral density, muscle strength and functional mobility. These data confirm the appropriateness of using judo as a means of physical rehabilitation and health maintenance. The specifics of adaptive judo for individuals with neuropathy were studied by E. Nerozzi *et al.* [28], where improvements in motor skills, balance, and quality of life after a course of training were demonstrated. The authors emphasised the importance of proprioceptive training and balance exercises. These results are consistent with the data on the effectiveness of proprioceptive training in the rehabilitation of injured judokas.

A comparative analysis of the results of this study with the works by A. Frey *et al.* [29] and K.J. Park and D.N. Jeong [30] revealed both points of convergence and certain differences. The obtained data on the structure of injuries, with a predominance of knee and shoulder joint injuries, fully correspond to the epidemiological data of both studies, confirming the universal nature of injury patterns in judo regardless of region. However, the 52.4% reduction in the injury index identified in this study exceeds the effectiveness indicators of prevention programmes described in the mentioned works. The comprehensive rehabilitation approach, which included proprioceptive training, demonstrates more pronounced effectiveness compared with the traditional methods described by K.J. Park and D.N. Jeong. The low level of recurrent injuries (6.3%) in the experimental group also differs substantially from the indicators reported in the study by A. Frey *et al.* The obtained results confirm the need to integrate modern neuromuscular approaches into prevention programmes in judo.

The biomechanics of falling techniques were studied by S. Koshida *et al.* [31] with the aim of preventing head injuries. The authors found that correct falling technique during osoto-gari is characterised by lower angular rotation velocity of the head and a more even distribution of impact energy. These conclusions confirm the importance of falling technique, to which significant attention was paid in the prevention programme. The systematic review by M. Colonna *et al.* [21] analysed 27 studies on injuries in judo, identifying a predominance of knee joint injuries (25.8%) and shoulder girdle injuries (20.3%). The authors emphasised the need to develop specialised prevention programmes, which fully aligns with the aim of this study. Psychosocial aspects of judo practice were studied by D. Lindell-Postigo *et al.* [32], who identified a positive effect of an intervention programme on social skills, self-esteem and the emotional state of schoolchildren. These results complement the data on the comprehensive positive impact of judo that goes beyond physical preparation.

Conclusions

The conducted study proved the effectiveness of a comprehensive programme for the prevention and rehabilitation of injuries in judo, implemented over

12 months. The introduction of a specialised programme that included a targeted 20-minute warm-up with an emphasis on proprioception, correction of movement technique based on FMS functional screening, individually selected corrective exercises, and kinesiotaping methods, ensured a statistically significant reduction in the injury index by 52.4%. Specific indicators demonstrate a decrease from 0.84 ± 0.21 to 0.40 ± 0.13 cases per 1,000 hours of training, which is a clinically significant result for sports practice.

A detailed analysis of the effectiveness of the programme by injury type revealed the most pronounced positive dynamics for ankle joint injuries (48.6%) and shoulder girdle injuries (43.2%). This indicates the targeted effect of the proposed measures specifically on the most vulnerable segments of the musculoskeletal system of judokas, which is associated with the biomechanics of movements in this sport. The statistically significant improvement in FMS functional indicators by 18.3% (from 14.2 ± 1.8 to 16.8 ± 1.4 points) and the identified inverse correlation between improved FMS and reduced injuries ($r = -0.67$; $p = 0.008$) confirm the study hypothesis regarding the relationship between athletes' functional status and injury risk. The clinical effectiveness of the rehabilitation programme is confirmed by a substantial reduction in pain intensity by 45.9% (from 34.2 ± 8.7 mm to 18.5 ± 6.9 mm on the VAS) and a shortening of mean recovery timeframes by 17.2% (from 51.6 ± 9.2 to 42.7 ± 7.9 days). The moderate correlation identified between reduced pain syndrome and shorter recovery timeframes ($r = 0.62$; $p = 0.009$) indicates the comprehensive positive effect of the implemented measures.

The study resulted in a reduction in the frequency of recurrent injuries in the experimental group to 12.5% versus 25.0% in the control, confirming the long-term effect of the proposed approach. Correlation analysis revealed an association between achieving optimal functional indicators (FMS ≥ 17 points) and a reduction in recurrence risk to 9.1%, which is an important argument for implementing regular functional testing in the training process. The study had certain limitations, in particular the limited sample size (64 participants), which could have affected the power of statistical analysis, and the absence of stratification by age groups, which does not allow differentiation of the programme's effectiveness for young and adult athletes. Promising directions for further research include the development of differentiated programmes for different age groups and levels of training, studying the effectiveness of the proposed approach among judokas with special needs, investigating the influence of psychological factors on the recovery process, as well as conducting multicentre studies with a larger number of participants to confirm the reproducibility of the results and develop standardised national protocols for injury prevention in judo.

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Conflict of Interest

None.

References

[1] Kons RL, Athayde MSDS, Antunes L, Lopes JSS, Detanico D. Injuries in judo athletes with disabilities: Prevalence, magnitude, and sport-related mechanisms. J Sport Rehabil. 2022;31(7):904–10. DOI: 10.1123/jsr.2021-0352

[2] Palavani LB, Nogueira BV, Costa M, Mitre LP, Frediani MK, Rielo G, et al. Cervical spine injuries in professional judo: A cross-sectional analysis of prevalence, risk factors, and preventive measures. Neurosurg Rev. 2024;47:899. DOI: 10.1007/s10143-024-03146-w

[3] von Gerhardt AL, Vriend I, Verhagen E, Tol JL, Kerkhoffs GM, Reurink G. Systematic development of an injury prevention programme for judo athletes: The IPPON intervention. BMJ Open Sport Exerc Med. 2020;6:e000791. DOI: 10.1136/bmjsem-2020-000791

[4] von Gerhardt AL, Reurink G, Kerkhoffs GM, Verhagen E, Krabben K, Mooren J, et al. Effectiveness of a judo-specific injury prevention programme: A randomised controlled trial in recreational judo athletes. Br J Sports Med. 2023;57(8):450–6. DOI: 10.1136/bjsports-2022-105869

[5] Mahmoudkhani MR, Shakibaee A, Minoonejad H, Rajabi R, Barati AH. Effect of an injury prevention program in judo athletes: MSSLSTS intervention. Trauma Mon. 2021;26(1):25–31.

[6] Blach W, Smolders P, Simenko J, Mackala K. Diagnostics of tissue-involved injury occurrence of top-level judokas during the competition: Suggestion for prevention. PeerJ. 2022;10:e13074. DOI: 10.7717/PEERJ.13074

[7] Blach W, Dobosz D, Gasienica-Walczak B, Grants J, Litwiniuk A. Falls are the leading cause of injuries among farmers – limitations of practicing judo in preventing these incidents. Appl Sci. 2021;11(16):7324. DOI: 10.3390/app11167324

[8] Nakazawa R, Sakamoto M, Dambadarjaa B, Khuyagbaatar E, Khadbaatar A. Fact-finding survey regarding judo-related injuries of judokas in developing country. J Phys Ther Sci. 2020;32(2):161–5. DOI: 10.1589/jpts.32.161

[9] Arkkukangas M, Bååthe KS, Ekholm A, Tonkonogi M. Health promotion and prevention: The impact of specifically adapted judo-inspired training program on risk factors for falls among adults. Prev Med Rep. 2020;19:101126. DOI: 10.1016/j.pmedr.2020.101126
[10] Boychenko N, Tropin Y, Romanenko V, Holokha V. Analysis of publications on adaptive judo: Bibliometric analysis. Phys Rehabil Recreat Health Technol. 2025;10(3):173–84. DOI: 10.15391/prrht.2025-10(3).04
[11] National Center for Rehabilitation and Health [Internet]. [cited 2025 November 14]. Available from: https://ncro.com.ua/
[12] Bahr R, Engebretsen L, editors. Handbook of sports medicine and science: Sports injury prevention. Chichester: John Wiley & Sons, Ltd.; 2009. 250 P.
[13] WMA Declaration of Helsinki – Ethical principles for medical research involving human participants [Internet]. 2024 October 19 [cited 2025 November 14]. Available from: https://surl.lt/ppmerg
[14] Rawat N, Agarwal S, Anwar U. Judo 9+ injury prevention protocol (J9+IPP) on balance, strength, and anaerobic fitness in elite judokas: A one-group pretest-post-test, quasi-experimental trial. Comp Exerc Physiol. 2024;20(3):257–62. DOI: 10.1163/17552559-00001035
[15] Malliaropoulos NG, Callan M, Johnson J. Comprehensive training programme for judo players nine plus 9+: Possible lower limb primary injury prevention. Muscles Ligaments Tendons J. 2014;4(2):262–8.
[16] Cai H. Core stability training effects on lower limb rehabilitation of judokas. Braz J Sports Med. 2022; 28(6):647–50. DOI: 10.1590/1517-8692202228062022_0081
[17] Turnagöl HH, Koşar ŞN, Güzel Y, Aktitiz S, Atakan MM. Nutritional considerations for injury prevention and recovery in combat sports. Nutrients. 2021;14(1):53. DOI: 10.3390/nu14010053
[18] Peterson L, Renstrom PAFH, Lynch S. Sports injuries: Prevention, treatment and rehabilitation. London: Routledge; 2024. 700 P. DOI: 10.4324/9781003056898
[19] Kim HC, Park KJ. Type of injury and recovery time in elite adolescent Korean judo athletes: An epidemiological study. Int J Sports Sci Coach. 2021;16(3):682–9. DOI: 10.1177/1747954121990951
[20] Pocecco E, Ruedl G, Stankovic N, Sterkowicz S, Del Vecchio FB, Gutiérrez-García C, et al. Injuries in judo: A systematic literature review including suggestions for prevention. Br J Sports Med. 2013;47(18):1139–43. DOI: 10.1136/bjsports-2013-092886
[21] Colonna M, Rolim Y, Vale RGDS, de Castro JBP, Nunes RDAM, Lima VP, et al. Analysis of injuries in Judo athletes: A systematic review. Retos. 2022;43:560–6. DOI: 10.47197/RETOS.V43I0.84524
[22] Kinoda A, Mącznik A, Kimura T, Muramoto Y, Katsumata Y, Sato K. 1-year prevalence and factors related to injuries and illnesses in Japanese Judo collegiate athletes. J Funct Morphol Kinesiol. 2024;9(3):148. DOI: 10.3390/jfmk9030148
[23] Nakanishi T, Hitosugi M, Murayama H, Takeda A, Motozawa Y, Ogino M, et al. Biomechanical analysis of serious neck injuries resulting from judo. Healthcare. 2021;9(2):214. DOI: 10.3390/healthcare9020214
[24] Morales J, Iteya M, Mulroy J, Kons R, Simenko J, Fukuda DH, et al. Injury risk in judo athletes with intellectual disabilities. Int J Sports Med. 2024;45(7):511–8. DOI: 10.1055/a-2280-4963
[25] Gutiérrez-Santiago A, Gutiérrez-Santiago JA, Prieto-Lage I, Paramés-González A, Suárez-Iglesias D, Ayán C. A scoping review on para judo. Am J Phys Med Rehabil. 2023;102(10):931–8. DOI: 10.1097/PHM.0000000000002136
[26] Garbeloto F, Miarka B, Guimarães E, Gomes FRF, Tagusari FI, Tani G. A new developmental approach for Judo focusing on health, physical, motor, and educational attributes. Int J Environ Res Public Health. 2023;20(3):2260. DOI: 10.3390/ijerph20032260
[27] Drid P, Franchini E, Lopes-Silva JP, Fukuda DH, Wells AJ, Lakicevic N, et al. Health implications of judo training. Sustainability. 2021;13(20):11403. DOI: 10.3390/su132011403
[28] Nerozzi E, Prada V, Pegreffi F, Grandis M, Schenone A, Pierantozzi E. Adaptive Judo and neuropathy: A mini review on motor skills, balance, and quality of life improvement. Front Psychol. 2025;15:1545358. DOI: 10.3389/fpsyg.2024.1545358
[29] Frey A, Lambert C, Vesselle B, Rousseau R, Dor F, Marquet LA, et al. Epidemiology of judo-related injuries in 21 seasons of competitions in France: A prospective study of relevant traumatic injuries. Orthop J Sports Med. 2019;7(5). DOI: 10.1177/2325967119847470
[30] Park KJ, Jeong DN. Injuries pattern and heart rate variation in elite judo athletes: A Korean prospective cohort study. Sci Sports. 2022;37(5–6):496.e1–7. DOI: 10.1016/j.scispo.2022.03.001
[31] Koshida S, Ishii T, Matsuda T, Hashimoto T. Kinematics of judo breakfall for osoto-gari: Considerations for head injury prevention. J Sports Sci. 2017;35(11):1059–65. DOI: 10.1080/02640414.2016.1210194
[32] Lindell-Postigo D, Zurita-Ortega F, Melguizo-Ibáñez E, González-Valero G, Ortiz-Franco M, Ubago-Jiménez JL. Effectiveness of a Judo intervention programme on the psychosocial area in secondary school education students. Sports. 2023;11(8):140. DOI: 10.3390/sports11080140

Дзюдодо жаракаттардын алдын алуу жана медициналык реабилитациялоо: клиникалык жана практикалык сунуштар

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Аннотация. Изилдөөнүн актуалдуулугу дзюдодо таяныч-кыймыл аппаратынын жаракаттары менен жаракат алуунун жогорку деңгээли менен байланыштуу, бул анын алдын алуу жана калыбына келтирүү үчүн натыйжалуу комплекстүү ыкмаларды иштеп чыгууну талап кылат. Изилдөөнүн максаты дзюдо спортчуларынын жаракаттарынын алдын алуу жана медициналык реабилитациялоо боюнча комплекстүү программаны иштеп чыгуу жана натыйжалуулугун баалоо болгон. Максатка жетүү үчүн жаракаттардын жыштыгы жана түзүлүшү, жаракаттардан кийин калыбына келүү ылдамдыгы, таяныч-кыймыл аппаратынын функционалдык абалы, проприоцептивдик көзөмөл жана булчуң симметриясынын көрсөткүчтөрү талданды. Комплекстүү диагностика, функционалдык тестирлөө жана калыбына келтирүү ыкмаларын колдонуу менен 64 дзюдо спортчусунун катышуусунда перспективдүү квазиэкспериментердик интервенциялык изилдөө жүргүзүлдү. 12 айлык алдын алуу программасын ишке ашыруу жаракат индексинин 1 000 сааттык машыгуу жүктөмүнө 0,84 ± 0,21ден 0,40 ± 0,13 учурга чейин статистикалык жактан маанилүү төмөндөшүнө өбөлгө түздү ($p < 0,01$). Эң чоң төмөндөө жумшак ткандардын жаракаттарында, томуктун чоюлушунда (-48,6 %) жана ийин курунун булчуң жаракаттарында (-43,2 %) байкалган. Реабилитациялык комплекс калыбына келүү убактысын 24 %га кыскартууну (41,7 ± 7,9 күнгө чейин) жана визуалдык аналогдук шкала боюнча оору синдромунун интенсивдүүлүгүн 7,4 ± 1,2ден 1,6 ± 0,8 пунктка чейин ($p < 0,001$) төмөндөтүүнү камсыз кылды. Машыгуу процессине кайтып келгенден кийинки алгачкы үч айда кайталануу көрсөткүчү 6,3 % түздү. Жыйынтыктар сунушталган комплекстүү ыкма дзюдодо жаракаттарды азайтууда, калыбына келүүнү тездетүүдө жана кайталануулардын минималдаштырууда абдан натыйжалуу экенин тастыктады. Иштелип чыккан сунуштар жаракаттарды азайтуу жана дзюдочулардын спорттук карьерасын узартуу үчүн машыгуу процессине киргизилиши мүмкүн

Негизги сөздөр: кинезиотерапия; проприоцепция; таяныч-кыймыл системасы; функционалдык калыбына келтирүү; кинематикалык анализ

Профилактика и медицинская реабилитация травм в дзюдо: клинико-практические рекомендации

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Аннотация. Актуальность работы обусловлена высоким уровнем травматизма в дзюдо с повреждениями опорно-двигательного аппарата, что требует разработки эффективных комплексных подходов к его профилактике и реабилитации. Цель исследования заключалась в разработке и оценке эффективности комплексной программы профилактики и медицинской реабилитации травм у спортсменов-дзюдоистов. Для достижения цели проанализированы показатели частоты и структуры травматизма, скорость восстановления после повреждений, функциональное состояние опорно-двигательного аппарата, проприоцептивный контроль и мышечную симметрию. Проведено проспективное квазиэкспериментальное интервенционное исследование с участием 64 дзюдоистов с применением комплексной диагностики, функционального тестирования и реабилитационных методик. Внедрение 12-месячной программы профилактики способствовало статистически значимому снижению индекса травматизма с 0,84 ± 0,21 до 0,40 ± 0,13 случаев на 1 000 часов тренировочной нагрузки ($p < 0,01$). Наибольшее уменьшение отмечалось для травм мягких тканей, растяжений связок голеностопного сустава (-48,6 %) и повреждений мышц плечевого пояса (-43,2 %). Реабилитационный комплекс обеспечил сокращение продолжительности восстановления на 24 % (до 41,7 ± 7,9 дней) и снижение интенсивности болевого синдрома по визуально-аналоговой шкале с 7,4 ± 1,2 до 1,6 ± 0,8 балла ($p < 0,001$). Частота рецидивов составляла 6,3 % в течение первых трех месяцев после возвращения в тренировочный процесс. Выводы подтвердили, что предложенный комплексный подход является высокоэффективным для снижения травматизма, ускорения восстановления и минимизации рецидивов в дзюдо. Разработанные рекомендации могут быть интегрированы в тренировочный процесс для снижения травматизма и продления спортивной карьеры дзюдоистов

Ключевые слова: кинезиотерапия; проприоцепция; опорно-двигательный аппарат; функциональное обновление; кинематический анализ

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Justification of diagnostic methods for haemangiomas of the external coverings in children

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Abstract. The absence of unified approaches to the diagnosis of skin haemangiomas in children, along with the need for their differentiation from other vascular anomalies, necessitates the creation of a structured diagnostic algorithm capable of ensuring objectivity in evaluation and reducing the risk of diagnostic errors. The aim of this study was to provide a theoretical justification and analytical clarification of the diagnostic criteria for haemangiomas in children based on a systematic analysis of modern instrumental and laboratory methods, followed by the development of an integrated diagnostic algorithm. An analysis of 23 scientific publications was conducted, which allowed for the determination of the informativeness of individual methods and the sequence of their optimal application in clinical practice. It was established that ultrasound imaging had the highest diagnostic agreement with morphological confirmation, while thermographic assessment and auscultation were characterised by lower accuracy and are only useful in the preliminary orientation stage. It was determined that age-specific interpretation of laboratory markers is necessary: the leukocyte intoxication index (LII) had different reference values in infants and older children due to the physiological features of the leukocyte formula. The diagnostic thresholds for coagulation parameters for the early detection of Kasabach-Merritt syndrome were identified: platelets <50 × 103/μL, fibrinogen <100 mg/dL, D-dimers >5-20 mg/L. Coagulation monitoring is indicated in large or rapidly growing haemangiomas due to the risk of consumptive coagulopathy. Based on the obtained results, a

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hierarchical diagnostic algorithm was formulated, which involves the stepwise application of clinical examination, ultrasound imaging, laboratory testing of systemic markers, and morphological confirmation in cases of atypical progression or insufficient non-invasive data. The proposed approach enhances diagnostic accuracy, standardises the sequence of examinations, and minimises the need for invasive interventions in paediatric practice

Keywords: vascular anomaly; instrumental method; laboratory marker; pathomorphological study; systemic response; peripheral blood

Introduction

Haemangiomas of the external coverings in children are benign vascular tumours that can lead to functional disorders, cosmetic defects, and life-threatening complications. The lack of a unified diagnostic algorithm and the need for differentiation from other vascular anomalies make it essential to comprehensively justify the informativeness of laboratory, instrumental, and morphological diagnostic methods for accurate verification of the diagnosis and optimisation of therapeutic tactics.

In clinical practice, there are cases when skin haemangiomas take forms similar to other vascular lesions, creating diagnostic difficulties. For instance, K. Djawad [1] reported the clinical similarity between cavernous haemangiomas and circumscript lymphangiomas, where the diagnosis was corrected only after histopathological analysis, indicating the limitations of visual inspection and the need for morphological verification for accurate differentiation. A. AbouZeid *et al*. [2] described cases of internal haemangiomas associated with skin manifestations in infants with posterior mediastinal involvement, which manifested as respiratory distress. The authors used magnetic resonance imaging (MRI) and ultrasound for diagnosis but did not propose systematic patient selection criteria for extended examination of internal organs. Neonatal forms of multiple haemangiomas were discussed by W. Meireles *et al*. [3], where the diagnosis was made mainly based on physical examination with ultrasound and computed tomography (CT) confirmation, but the study was limited to a single clinical case without validating the diagnostic approach on a larger cohort.

Systematised clinical experience regarding the evaluation and management of patients with infantile haemangiomas was summarised in M. Park's [4] publication, which particularly emphasised the need for early recognition of the proliferative phase of the tumour and timely initiation of therapy. The author provided a clinical observation algorithm based on localisation type, lesion size, and growth rate, mentioning dermatoscopy, ultrasound, and MRI, but restricted the discussion to expert recommendations without quantitative assessment of diagnostic accuracy and sensitivity for each method. A retrospective study by Z. Bayramoğlu *et al*. [5] on 296 cases of skin haemangiomas demonstrated the importance of histopathological subtyping for choosing therapeutic tactics, but the work was limited to describing histological variants without in-depth analysis of the diagnostic methods of imaging and their effectiveness for each type of lesion. S. Toktosunova [6] analysed the clinical-morphological characteristics of external haemangiomas in children, establishing the necessity of morphological confirmation for accurate treatment assignment and dynamic observation, but the study did not include a systematic comparative analysis of the informativeness of non-invasive diagnostic approaches relative to the pathomorphological standard.

Another study by S. Naeem *et al*. [7] focused on liver tumour classification, including haemangiomas, based on fused CT and MRI images using machine learning, where a multilayer perceptron achieved 99% accuracy after combining data. However, the authors noted limitations related to the heterogeneity of modalities and the absence of analysis on the impact of deep neural networks in paediatric practice. In a clinical case description, D. Safin *et al*. [8] explored the differential diagnosis of infantile haemangioma, which was mistakenly perceived as an arteriovenous malformation, emphasising the importance of Doppler sonography and a multidisciplinary approach. However, they did not provide systematic criteria for avoiding similar diagnostic errors in clinical practice. In the case of aggressive forms of haemangiomas, D. Sahajwalla *et al*. [9] described a vertebral haemangioma in a child that manifested with neurological deficits and resembled a malignant process on imaging, highlighting the need for awareness of characteristic MRI signs to avoid misdiagnosis and plan safe surgical intervention, but without a systematic comparison of the sensitivity and specificity of various imaging methods. Mobile imaging technologies were the subject of study by M. Guerrero *et al*. [10], who used thermography via a smartphone to monitor the regression of haemangiomas during sclerotherapy. However, they acknowledged the method's limitations as an auxiliary tool without the potential for primary diagnosis and low specificity for differentiating various types of vascular lesions.

Despite numerous publications on the clinical and therapeutic aspects of haemangiomas in children, the comparative diagnostic value of different imaging methods and their correlation with pathomorphological data remains insufficiently studied, which has led to the necessity for the current study. The aim of this research was to develop a scientifically substantiated diagnostic algorithm for children with external covering haemangiomas based on a systematic analysis of the informativeness of instrumental and laboratory diagnostic methods. The objectives of the study were to analyse instrumental

imaging methods for haemangiomas based on their diagnostic informativeness relative to pathomorphological examination as the reference standard; determine the diagnostic significance of laboratory markers of systemic response in children, taking into account age-specific reference values; and justify the principles of rational selection of diagnostic methods depending on the clinical situation and characteristics of the tumour process.

Materials and Methods

The study was conducted as a mixed descriptive-analytical approach with two components: a systematic review of scientific literature to substantiate diagnostic approaches and a retrospective analysis of clinical data to illustrate the diagnostic hierarchy of methods. Scientific sources were searched in international databases PubMed, Scopus, Web of Science, and Google Scholar for the period 2019-2025 using key terms: "infantile hemangioma", "vascular anomalies", "diagnostic methods", "pediatric diagnosis", "ultrasound", "doppler", "computed tomography", "magnetic resonance imaging", "laboratory markers", "Kasabach-Merritt syndrome" in combination with "children" and "pediatric". Inclusion criteria were original studies focused on the diagnosis of vascular tumours in the paediatric population; systematic reviews and meta-analyses on imaging methods; clinical guidelines from international societies. Exclusion criteria were: studies on adult populations; publications without full-text access; conference abstracts without methodological details. Based on screening of titles and abstracts, relevant publications were selected, directly related to the diagnosis of haemangiomas in the paediatric population that met the criteria for methodological quality and relevance were included for further analysis.

The methodology for systematising the literary data was based on a structured approach to information extraction from selected sources. For each publication, the following was determined: the type of study (original study, clinical case, review), the sample size, the age characteristics of the patients, the diagnostic methods used, the main results, and conclusions. Special attention was paid to sources containing quantitative data on the diagnostic accuracy of methods, sensitivity, specificity, or comparative characteristics of different approaches. The literature analysis included three thematic areas: classification systems of vascular anomalies, including the International Society for the Study of Vascular Anomalies classification [11], morphological classification by vessel architecture type and depth of location, phase classification (proliferative, stabilisation, involution); physical principles and diagnostic accuracy of instrumental methods of verification (ultrasound with Doppler mapping, contrast-enhanced ultrasound (CEUS), CT and MRI, thermographic diagnosis, pathomorphological examination); pathophysiological mechanisms of the systemic response to haemangiomas and corresponding laboratory biomarkers (morphological analysis of peripheral blood, leukocyte intoxication index (LII), coagulation profile, cortisol levels).

A comparative content analysis was applied, which included the classification of methods by the principle of action, analysis of diagnostic capabilities, evaluation of advantages and limitations, identification of indications and contraindications. Based on the systematised literature data, a hierarchical diagnostic algorithm was developed, integrating clinical, instrumental, and laboratory methods for verifying haemangiomas in children. At the final stage of the methodological approach, analytical integration of the obtained data was carried out. For this purpose, a step-by-step procedure for processing literature data was applied, which included ranking instrumental and laboratory methods by diagnostic informativeness, performed by comparing their sensitivity, specificity, diagnostic capabilities, and clinical indications as provided in the selected publications; integration of key features of various methods into an ordered logical structure that ensured the alignment of clinical, instrumental, and laboratory criteria in a unified diagnostic field; and the construction of a hierarchical diagnostic scheme, formed as a sequence of steps (clinical evaluation → ultrasound imaging → advanced imaging methods → laboratory markers → morphological verification), reflecting the algorithm for applying methods based on their informativeness and clinical relevance.

Results

Comparative analysis and diagnostic value of current imaging methods for haemangiomas

Infantile haemangiomas in children are characterised by a three-phase progression: the phase of active proliferation, which begins in the first weeks of life and peaks at 2-6 months of age; the stabilisation phase after 12-18 months; and the phase of spontaneous involution, which may last up to 5-10 years. Understanding the pathogenetic mechanisms of each phase has direct diagnostic significance for clinical practice, as these neoplasms arise from the abnormal persistence of embryonic precursor cells of the vascular tissue, which are activated in the postnatal period [12]. In the proliferation phase, haemangiomas demonstrate rapid growth, increasing in size 5-10 times over the first 3-6 months, clinically presenting as bright red formations with a warm surface and elastic consistency. Pathogenetically, this phase is characterised by active angiogenesis involving specific growth factors that stimulate endothelial cell proliferation and the formation of a new vascular network [13,14]. Intense vascularisation is visualised on ultrasound with colour Doppler mapping as a pronounced vascular pattern with high-speed arterial blood flow. M. McNab *et al.* [15] demonstrated that Doppler ultrasound evaluation of vascularisation allowed for the diagnosis of haemangiomas and the determination of their phase of development in an infant

with periorbital involvement. In proliferating haemangiomas, blood flow velocities range from 15-40 cm/s with a low resistance index, reflecting active arterial circulation and allowing prediction of tumour behaviour.

The stabilisation phase is characterised by the cessation of active tumour growth, with the tumour maintaining its size, as angiogenic activity decreases and the vascular network matures and stabilises [16]. On ultrasound, there is a reduction in blood flow intensity compared to the proliferation phase: velocities decrease to 10-20 cm/s, and the density of the vascular network decreases, indicating the transition to a homeostatic tissue state, thus allowing objective assessment of the onset of stabilisation. The phase of spontaneous involution is marked by a gradual reduction in tumour size, a colour change from bright red to pale pink, flattening, and a decrease in tissue elasticity, which pathogenetically correlates with the activation of programmed endothelial cell death and replacement of the vascular tissue with connective or fatty structures [17]. On ultrasound, involuting haemangiomas show a significant reduction or complete absence of Doppler signals, which correlates with the reduction in the vascular network and allows visualisation signs to be interpreted as markers of natural tumour regression.

In some cases, haemangiomas can induce a systemic response in the child's body, especially when the tumour is large or rapidly proliferating. Immune cells in the tumour microenvironment can influence the haemangioma's activity and induce systemic changes [18], which can be accompanied by changes in the morphological composition of peripheral blood in children with actively proliferating haemangiomas [19]. Therapeutic interventions can influence the differentiation of haemangioma progenitor cells, which is associated with the transition to the involution phase [20], and the use of modern therapeutic approaches may induce stress changes in tumour cells, accompanied by the intensification of oxidative processes and systemic responses in the body [21]. Thus, a haemangioma acts not only as a localised tumour but also as a potential source of systemic changes, indirectly affecting the general condition of the child and reflecting in the haematological profile.

Ultrasound with colour Doppler mapping is based on the reflection of sound waves from tissues of different densities and the analysis of blood flow parameters, which allows visualisation of the tumour structure, assessment of its vascularisation, and differentiation of the proliferation phase from involution. M. McNab *et al*. [15] demonstrated the detection of subclinical signs of haemangiomas (hypoechoic zones, structural heterogeneity, increased vascularisation), which were not evident during clinical examination and influenced the prediction of disease progression. Three-dimensional ultrasound with energy Doppler provides volumetric reconstruction of the vascular architecture and a quantitative assessment of therapy effectiveness. J. Zhang *et al*. [22] used this approach for monitoring the local administration of bleomycin in resistant haemangiomas in children, where the tumour volume decreased by 70%, with a corresponding reduction in vascular density.

Thermographic diagnosis records the tissue temperature profile, with a decrease in temperature correlating with haemangioma involution, while stability or an increase indicates active growth [23]. M. Liao *et al*. [24] demonstrated the possibilities of prenatal ultrasound for haemangiomas of the fetal skin coverings, evaluating morphology, size, and identifying complications (heart failure, hydrops), which allowed for the adjustment of pregnancy management. CEUS uses microbubble contrast to provide detailed visualisation of tumour perfusion in real-time. G. Cericola *et al*. [25] used CEUS to evaluate liver haemangiomas in infants with multiple skin manifestations, where the method demonstrated diagnostic accuracy comparable to MRI for detecting lesions up to 4 mm without the need for sedation or radiation, making it optimal for repeat monitoring in paediatric practice.

X-ray CT is used to assess the depth of infiltration, tumour topography relative to bony structures, and to plan surgical interventions in large or complicated haemangiomas. Histological examination is the gold standard for diagnosing and differentiating haemangiomas from other vascular anomalies. L. Mariani *et al*. [27] and L. Belani *et al*. [28] described clinical cases in children where imaging methods detected only vascularised formations but could not determine their cellular composition. Histological examination of biopsy material with immunohistochemical analysis allowed for the diagnosis of Kaposi-like haemangioendothelioma instead of infantile haemangioma, leading to a change in therapy from propranolol to sirolimus, with subsequent normalisation of coagulation parameters and tumour regression. For effective haemangioma diagnosis in clinical practice, it is important to focus on current imaging approaches. Given the technical development of ultrasound methods, particularly CEUS, it is appropriate to summarise their diagnostic capabilities in Table 1.

Table 1. Comparative characteristics of instrumental methods for diagnosing haemangiomas

Method	Principle of action	Diagnostic capabilities	Advantages	Disadvantages and risks
Auscultation	Listening for vascular murmurs over the tumour	Primary assessment of arterial blood flow (shunts)	Simplicity, non-invasive	Very low specificity, subjectivity
Thermographic diagnosis	Recording infrared radiation	Detecting hyperthermia in the zone of active blood flow (often atypical application)	Non-invasive, rapid	Does not provide structural information, limited clinical application

Table 1. Continued

Method	Principle of action	Diagnostic capabilities	Advantages	Disadvantages and risks
Ultrasound with doppler/CEUS	Analysing ultrasound wave reflection and Doppler effect; in CEUS, contrast is injected to evaluate microvascular blood flow	Determining size, structure, vascularisation; CEUS can distinguish haemangiomas from malignant formations in 85% of cases	High informativeness, non-invasive, no radiation exposure. CEUS is quick and accurate (30 mins)	Operator-dependent; CEUS less available; sometimes requires further confirmation
CT with contrast	Layered X-ray scanning with iodine contrast	Assessing topography, relationships with organs, bony structures. Often used for atypical haemangiomas	High spatial anatomical resolution, especially useful in intra-organ lesions	Radiation exposure, risk of contrast allergy, need for sedation in children
Fine-needle biopsy/EUS-core biopsy	Tissue sampling under ultrasound or endoscopic control for histology	Final diagnosis confirmation. Rarely used due to risks, mostly for atypical visualisation	Highest accuracy, possible immunohistochemical verification	Invasiveness, bleeding risk, potential false-negative results without histological analysis

Source: compiled by the authors based on A. Rešić *et al*. [29], F. Esposito *et al*. [30]

In analysing the presented spectrum of instrumental methods for diagnosing haemangiomas in children, it should be noted that their effectiveness largely depends on the clinical context, the localisation of the lesion, the age of the patient, and the presence of complications. Auscultation and thermographic diagnosis have a supplementary role in the diagnostic strategy due to their low specificity. Methods based on blood flow visualisation, particularly ultrasound with colour or spectral Doppler, as well as CEUS, showed high sensitivity and allowed for non-invasive assessment of the tumour's vascular profile. These approaches are especially valuable in paediatric practice due to minimising radiation exposure and avoiding sedation.

There are specific clinical situations that require expanding the diagnostic algorithm. The detection of multiple skin haemangiomas (five or more) requires mandatory liver screening, as a significant proportion of such patients show hepatic involvement. G. Cericola *et al*. [25] demonstrated that CEUS is the optimal method, combining high sensitivity for detecting small formations (up to 4 mm) with the absence of the need for sedation and radiation exposure. In haemangiomas of deep localisation or those spreading to critical anatomical areas, CT with contrast or MRI is required. CT is the method of choice when evaluating relationships with bony structures and for quickly obtaining topographic information when planning surgical interventions, while MRI provides the best differentiation of the type of vascular formation and characterisation of soft tissue components.

The systematic analysis demonstrated that the highest diagnostic accuracy and agreement with the morphological conclusion were observed when using ultrasound with Doppler and contrast-enhanced ultrasonography, while auscultation and thermographic diagnosis had the lowest specificity and served as supplementary screening methods. CT and MRI occupied an intermediate position, demonstrating high informativeness for specific indications (deep localisations, syndromic forms), but requiring justified use due to radiation exposure or the need for sedation in paediatric practice. Histological examination remains the only method for final morphological verification of the diagnosis in complex cases. Therefore, the optimal diagnostic strategy is based on a hierarchical approach, taking into account the clinical characteristics of the tumour, the patient's age, and the balance of the method's diagnostic value relative to the potential risks of intervention.

Clinical and laboratory markers as indicators of systemic response to haemangioma

Haemangiomas, as localised vascular neoplasms, can in some cases induce a systemic response in the child's body, especially with large tumours or rapid proliferation. During growth or involution, there is active remodelling of tumour tissue with the release of cellular breakdown products and biologically active substances into the systemic circulation, which can lead to an endogenous intoxication syndrome. The LII is an integral marker that reflects the child's systemic response to the tumour process. An increase in LII in patients with large or rapidly growing haemangiomas indicates the activation of the neutrophil branch of haematopoiesis in response to endogenous intoxication. This is especially relevant when destructive treatment methods are used, which lead to massive tumour tissue necrosis and intensified systemic response. Tumour cell interactions with the immune system are accompanied by changes in the morphological composition of peripheral blood: children with actively proliferating haemangiomas may show relative neutrophilia as a response to inflammation or relative lymphopenia due to immune cell redistribution [18,19]. Age-specific interpretation of the LII is important. The physiological predominance of lymphocytes in infants (up to 55% in children under 1 year old) results in significantly lower LII values compared to older children, where the neutrophil blood formula predominates. Therefore, using uniform reference values for all age groups is methodologically incorrect and may lead to false clinical interpretations. Establishing

age-specific normative values for LII allows for the correct identification of pathological deviations in patients with haemangiomas and an objective assessment of the degree of the systemic response to the tumour process. Coagulation parameters have diagnostic and prognostic significance in complicated haemangiomas in children. Pathophysiological disturbances in haemostasis form due to the cascade of platelet consumption and clotting factors caused by the pathological proliferation of endothelial cells in the vascular tumour. Kasabach-Merritt syndrome, which occurs with Kaposi-like haemangioendothelioma or tufted angioma, is characterised by the classical triad: thrombocytopenia, hypofibrinogenemia, and microangiopathic haemolytic anaemia. The primary pathogenetic mechanism remains the capture of platelets and activated clotting factors by tumour endothelial cells, followed by localised coagulation and systemic coagulopathy. High intratumour expression of tissue factor promotes the activation of the extrinsic clotting pathway, enhancing the consumption of fibrinogen and the formation of microthrombi within the tumour's vascular network [26].

L. Mariani *et al*. [27] described two cases of Kasabach-Merritt syndrome in infants with deep thrombocytopenia (down to $9 \times 10^3/\mu L$), decreased fibrinogen levels (less than 100 mg/dL), and high D-dimer concentrations (>20 mg/L), indicating active consumptive coagulopathy. Sirolimus treatment normalised the coagulation parameters within 2-6 weeks, confirming the role of laboratory markers as diagnostic and monitoring tools. L. Belani *et al*. [28] described a case of a 2-month-old child with Kasabach-Merritt syndrome (thrombocytopenia, hypofibrinogenemia, high D-dimers) resistant to steroids and vincristine. Sirolimus treatment led to normalisation of haemostasis within 12 days, confirming that dynamic monitoring of coagulation parameters is a reliable biomarker of treatment efficacy.

F. Kapp *et al*. [31] confirmed that children with vascular anomalies, including Kaposi-like haemangioendothelioma, experienced severe platelet dysfunction, impaired aggregation, and reduced levels of von Willebrand factor, which prevented adequate primary haemostasis. Haemostasis disturbances in vascular anomalies involve not only platelet consumption but also qualitative dysfunction of the platelet component, explaining the development of bleeding even with moderate thrombocytopenia ($50\text{-}100 \times 10^3/\mu L$). These data expand the understanding of coagulopathy pathophysiology in vascular anomalies, demonstrating that haemostasis disturbances are not limited to simple platelet consumption. In suspected Kasabach-Merritt syndrome, extended coagulation tests should assess platelet functional activity and von Willebrand factor levels, even in the absence of active bleeding. Repeatedly elevated D-dimer levels serve as a marker of active fibrinolysis and allow stratification of patients by the risk of coagulopathy decompensation.

In the study by B. Massara *et al*. [32], a clinical case of Kaposi-like haemangioendothelioma with a fatal outcome in a child was demonstrated, where coagulopathy was accompanied by persistent hypercalcaemia due to paraneoplastic synthesis of parathyroid hormone-related protein. This fatal case emphasised the importance of comprehensive laboratory diagnostics in Kaposi-like haemangioendothelioma in children. Hypercalcaemia, caused by paraneoplastic secretion of PTHrP (parathyroid hormone-related protein), served as an additional unfavourable prognostic marker. In severe forms, extended biochemical testing (electrolytes, kidney and liver function) is required for the timely detection of paraneoplastic complications. The appearance of atypical laboratory changes against the backdrop of no response to standard therapy requires escalation in treatment intensity.

Summarising the findings of studies [27-30], diagnostic threshold values include a platelet count of less than $50 \times 10^3/\mu L$ (critical $<10 \times 10^3/\mu L$), fibrinogen concentration below 100 mg/dL, and D-dimer levels above 5-20 mg/L, reflecting active consumptive coagulopathy. Based on these indicators, stratification of the severity of Kasabach-Merritt syndrome is possible: mild (platelets $50\text{-}100 \times 10^3/\mu L$, monitoring without immediate therapy), moderate (platelets $20\text{-}50 \times 10^3/\mu L$, indications for pathogenetic treatment), and severe (platelets $<20 \times 10^3/\mu L$, life-threatening condition requiring intensive therapy). When detecting a rapidly growing vascular formation in children, a basic coagulation test is mandatory, and in the case of thrombocytopenia below $100 \times 10^3/\mu L$, extended testing of platelet function and von Willebrand factor is necessary. Regular monitoring of coagulation profile indicators is a pathophysiologically justified tool for the early detection of Kasabach-Merritt syndrome even in the absence of clinical signs of bleeding, evaluation of tumour activity, and monitoring the effectiveness of pathogenetic therapy. To systematise diagnostic criteria and optimise the interpretation of laboratory markers in paediatric practice, it is advisable to generalise reference values and pathological deviations of key markers of systemic response in children with haemangiomas (Table 2).

Table 2. Diagnostic value of laboratory markers of systemic response in children with haemangiomas

Laboratory marker	Reference values	Pathological deviations	Diagnostic value
LII in infants (<1 year)	<1.5 units	>2 units	Systemic intoxication in large/rapidly growing haemangiomas
LII in children (>1 year)	<2 units	>3 units	Systemic intoxication, especially after destructive treatments
Platelets	$150\text{-}450 \times 10^3/\mu L$	$<50 \times 10^3/\mu L$ (critical $<10 \times 10^3/\mu L$)	Kasabach-Merritt syndrome

Table 2. Continued

Laboratory marker	Reference values	Pathological deviations	Diagnostic value
Fibrinogen	200-400 mg/dL	<100 mg/dL	Consumptive coagulopathy
D-dimers	<0.5 mg/L	>5-20 mg/L	Active fibrinolysis and intravascular coagulation
Von Willebrand factor	50-150%	<50%	Qualitative platelet dysfunction
Calcium (total)	2.2-2.6 mmol/L	>2.7 mmol/L	Paraneoplastic hypercalcaemia (unfavourable prognostic marker)

Note: interpretation of LII must consider age-related features of the leukocyte formula (physiological predominance of lymphocytes in infants)
Source: compiled by the authors based on L. Mariani *et al.* [27], L. Belani *et al.* [28], F. Kapp *et al.* [31]

The diagnostic criteria presented in Table 2 allow for the stratification of patients based on the degree of systemic response and the risk of complications. It is mandatory to use age-specific reference values for the LII, as the physiological characteristics of the leukocyte formula in infants (lymphocyte predominance up to 55%) significantly affect the calculation of this indicator. Comprehensive evaluation of coagulation parameters (platelets, fibrinogen, D-dimers, von Willebrand factor) is critical for the early detection of Kasabach-Merritt syndrome, stratification of coagulopathy severity, assessment of complication risks, and monitoring the effectiveness of pathogenetic therapy.

In addition to coagulation and haematological markers, monitoring the stress response markers in children with large or complicated haemangiomas is advisable. As shown by S. Lawrence & R. Scofield [33], chronic dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis in response to prolonged stress, particularly in post-traumatic stress disorder, led to immune homeostasis disruption, increased risk of autoimmune disorders, and reduced anti-infective immunity. In children with somatic stressors, such as large or complicated haemangiomas, a similar model of dysregulation could develop: prolonged elevated serum cortisol levels indicated chronic activation of the HPA axis, which affected not only immune mechanisms but also the overall hormonal balance. Research by N. Mbiydzenyuy & L. Qulu [34] indicated a close relationship between the HPA axis and other neuroendocrine systems, including the hypothalamic-pituitary-gonadal axis. It was shown that excessive or prolonged elevated cortisol levels disrupted the secretion of gonadotropins and sex steroids, which, in turn, influenced behavioural reactions, development of secondary sexual characteristics, and immune response. In the clinical context, this interaction could be particularly significant for children with congenital or acquired vascular malformations, which caused not only physiological but also psycho-emotional stress.

Thus, laboratory markers supplement instrumental diagnostics and allow for objective evaluation of the systemic component of the disease in children with haemangiomas. The LII reflects the degree of the body's systemic response to the tumour process and endogenous intoxication, especially in large or rapidly growing lesions. Coagulation parameters (platelets, fibrinogen, D-dimers) are critically important for early detection of Kasabach-Merritt syndrome, stratification of coagulopathy severity, assessment of complication risks, and monitoring the effectiveness of pathogenetic therapy. Markers of HPA axis activity characterise the integrative neuroendocrine response of the child's body to chronic somatic stress. It is essential to use age-specific reference values for the correct interpretation of haematological indicators in paediatric practice, ensuring accurate diagnosis and a personalised approach to patient management.

Integrated diagnostic algorithm for verifying haemangiomas in children

Based on a systematic analysis of the informativeness of diagnostic methods, an integrated diagnostic algorithm for verifying haemangiomas in children has been developed, which is based on a hierarchical application of visual and laboratory methods, considering their diagnostic value, safety, and accessibility.

Stage 1: Primary clinical assessment. The diagnostic process begins with a detailed clinical examination of the vascular formation, determining its location, size, colour, consistency, and growth dynamics based on anamnesis. When characteristic signs of infantile haemangioma (bright red or bluish colour, soft consistency, increase with straining or crying, appearance in the first weeks of life) are detected, the patient proceeds to instrumental verification. The clinical examination also helps identify patients at risk: children with multiple skin haemangiomas (five or more), large lesions (over 5 cm), or those located in functionally significant areas (periorbital region, respiratory tracts) require more intensive diagnostic evaluation.

Stage 2: Ultrasound with colour doppler mapping. Ultrasound is the first-line imaging method that allows the determination of three key diagnostic parameters: the depth of the tumour's location relative to the skin surface (superficial, deep, or mixed localisation), structural tissue characteristics (homogeneous hypoechoic structure in typical haemangiomas or heterogeneous in atypical forms), and vascularisation pattern (intense vascular pattern with high-speed blood flow indicates the proliferative phase, while a decrease or absence of Doppler signals is characteristic of the involution phase). In cases of typical ultrasound images corresponding to infantile haemangiomas, the diagnosis is considered clinically verified, and the

patient proceeds to laboratory assessment or directly to therapeutic strategy selection. The advantages of ultrasound in paediatric practice include non-invasiveness, absence of radiation exposure, the possibility of repeated studies for dynamic monitoring, and high tolerance by young patients.

Transition to extended imaging. Indications for using CT or MRI arise when atypical ultrasound signs cause diagnostic doubts: deep localisation with extension to muscle fascia or internal organs, proximity to bone structures where adequate ultrasound imaging is not possible, pronounced structural heterogeneity that may indicate an alternative type of vascular formation, or imaging signs suggesting a malignant process. An absolute indication for extended examination is the detection of five or more skin haemangiomas, which necessitates mandatory liver screening using CEUS or MRI to exclude hepatic lesions, as a significant number of such patients show multiple internal organ haemangiomas.

Stage 3: Laboratory evaluation of systemic response. All patients with a verified haemangioma undergo a clinical blood test to calculate the LII using the Calf-Kalifa formula, which allows for objective assessment of the degree of systemic response to the tumour process. It is critically important to interpret the results based on age-specific reference values for the morphological indicators of peripheral blood, as the absolute number of leukocytes, neutrophils, and lymphocytes varies by age, influencing the calculation of LII. For haemangiomas larger than five centimetres or rapidly growing tumours, it is mandatory to assess coagulation parameters (platelet count, fibrinogen concentration, D-dimer levels) for early detection of Kasabach-Merritt syndrome, even in the absence of clinical signs of bleeding. The diagnostic threshold values indicating the development of consumptive coagulopathy are platelet levels below $50 \times 10^3/\mu L$ (critical level $<10 \times 10^3/\mu L$), fibrinogen concentration below 100 mg/dL, and D-dimer levels above 5 mg/L. If thrombocytopenia below $100 \times 10^3/\mu L$ is detected, extended coagulation testing is indicated, including functional activity of platelets and von Willebrand factor, for complete characterisation of the haemostatic state.

Stage 4: Morphological verification by biopsy. Indications for biopsy are clearly defined and limited to specific clinical situations where non-invasive methods do not allow for a reliable diagnosis. Such situations include: atypical clinical presentations that do not match the classical course of infantile haemangioma (unusual location, rapid aggressive growth, appearance after six months of age); resistance to standard propranolol therapy for four to six weeks, which may indicate an alternative type of vascular formation; laboratory signs of Kasabach-Merritt syndrome (thrombocytopenia, hypofibrinogenemia, elevated D-dimers), which requires differentiating infantile haemangioma from Kaposi-like haemangioendothelioma or tufted angioma for appropriate pathogenetic therapy selection; imaging signs suggesting a malignant process (invasive growth, destruction of adjacent tissues, regional lymphadenopathy). In all other cases, biopsy is not indicated, as the diagnosis can be established based on the clinical picture and non-invasive imaging methods, in line with the bioethical principles of paediatric practice and the concept of minimising invasive interventions in young children.

The proposed algorithm, based on the hierarchical application of methods with varying informativeness from primary clinical examination to non-invasive imaging and laboratory assessment, and finally to morphological verification in exceptional cases, improves diagnostic accuracy, standardises the sequence of examinations, and minimises the need for invasive interventions. The key feature of the algorithm is a personalised approach to choosing diagnostic methods based on clinical tumour characteristics (location, size, number of lesions), patient age, and response to initial therapy, allowing for maximum diagnostic accuracy with minimal risks to the patient and rational use of diagnostic resources in the healthcare system.

Discussion

A review of the literature demonstrated that ultrasound with Doppler mapping was recognised as the first-line method for diagnosing haemangiomas in paediatric practice. Ultrasound enabled the detection of subclinical signs, such as the deep component of haemangiomas, which were not visible during routine clinical examination, and this was critical for predicting disease progression and selecting the optimal therapeutic strategy. Colour Doppler mapping defined three key parameters: the depth of tumour location relative to the skin surface, structural heterogeneity of the tissue, and the nature of vascularisation, all of which directly influenced the choice of therapeutic strategy. These conclusions were consistent with the findings of F. Bellinato *et al*. [35], who, in their comprehensive review, highlighted that ultrasound with Doppler is the first-line method for assessing the depth and size of haemangiomas in children. The authors recommended the use of high-frequency ultrasound for differential diagnosis of deep, mixed-type, and proliferative haemangiomas, emphasising the importance of standardising examination protocols to ensure reproducibility across different medical institutions. F. Bellinato *et al*. [35] detailed ultrasound characteristics of haemangiomas at various stages of development: in the proliferative phase, haemangiomas were characterised by well-defined hypoechoic hypervascular formations with rapid blood flow and a low resistance index, while in the involution phase, there was a reduction in size, increased echogenicity due to fibrous and fatty replacement of the vascular tissue, and decreased vascular density with reduced Doppler signals. The

advantages of ultrasound in paediatric practice include non-invasiveness, absence of radiation exposure, the ability to conduct repeated studies for dynamic monitoring without risk to the child, high patient tolerance, and relative availability of equipment in most healthcare settings. However, it should be noted that in some cases, deep haemangiomas or those with complex anatomical localisations might require advanced imaging methods like CT or MRI.

CT was primarily used for haemangiomas extending to internal organs or when evaluating relationships with bone structures, demonstrating sufficient informativeness for these specific clinical situations. S. Cerbu *et al*. [36] concluded in their five-year study on the diagnosis of vascular anomalies in children that CT, despite the risk of radiation exposure, remained a useful method for paediatric patients with deep haemangiomas requiring detailed topographic assessment, particularly when planning surgical interventions. The authors noted that CT typically demonstrated well-defined lesions with a lobular architecture and intense homogeneous contrast enhancement, enabling differentiation of haemangiomas from other vascular formations and solid tumours. X. Liang *et al*. [37] demonstrated that contrast-enhanced CT revealed enhanced lesions of the respiratory tract but that the most specific results came from a combined diagnostic approach including flexible fibre-optic laryngoscopy for direct visualisation of the lesion and evaluation of the degree of airway obstruction.

MRI was mainly used in cases of suspected syndromic haemangiomas – PHACE (Posterior fossa malformations, Hemangiomas, Arterial anomalies, Cardiac defects, Eye abnormalities), LUMBAR (Lower body haemangiomas and other cutaneous defects, Urogenital anomalies, Ulceration, Myelopathy, Bony deformities, Anorectal malformations, Arterial anomalies, Renal anomalies) – to assess associated developmental anomalies of the heart, vascular, and central nervous systems in children. L.B. Gil *et al*. [38] expanded the understanding of MRI characteristics of haemangiomas in different locations in paediatric patients, including orbital haemangiomas with a risk of visual impairment, respiratory tract haemangiomas with obstructive manifestations, parotid haemangiomas with potential cosmetic defects, and liver haemangiomas requiring evaluation of the number and size of lesions.

The study confirmed the importance of age-specific interpretation of laboratory indicators in children for the objective assessment of the systemic response to haemangiomas. The physiological predominance of lymphocytes in infants led to much lower values of the LII compared to older children, so using uniform reference values for all age groups was deemed methodologically incorrect. P. Sharan & C. Vellapandian [39] supported the theoretical basis for considering age-specific endocrine and immune system functioning in interpreting laboratory markers in children, highlighting the dynamic nature of normative indicators in the development of the child's body. F. Bellinato *et al*. [35] also emphasised the need for monitoring coagulation parameters in paediatric patients with large haemangiomas and pointed to the potential development of consumptive coagulopathy in aggressive forms of the disease, which required regular monitoring of platelets, fibrinogen, and D-dimers for early detection of potentially life-threatening complications.

Clinical cases presented in the works of M. Oweidat *et al*. [40], R. Monreal-Robles *et al*. [41], and E. Graff *et al*. [42] described haemangiomas with atypical or complicated courses in children, including unusual locations with technical difficulties in visualisation, recurrent bleeding as a complication of mucosal damage, and diagnostic challenges due to discordant morphological data across different diagnostic methods. This highlighted the necessity of a comprehensive multidisciplinary diagnostic approach in such cases involving paediatricians, surgeons, dermatologists, and pathomorphologists. A. Dong *et al*. [43] demonstrated that haemangiomas could imitate metastatic lesions on functional imaging using positron emission tomography, which confirmed the significant limitations of functional imaging techniques in differentiating benign from malignant processes without histological confirmation, especially in cases of atypical locations or unusual progression. This was consistent with the fundamental concept that morphological verification remained the gold standard in complex cases where clinical and imaging data did not allow for a definitive diagnosis with sufficient reliability.

The work of F. Wang *et al*. [44] demonstrated the high diagnostic potential of multimodal ultrasound, combining B-mode, colour Doppler, and elastography, in the evaluation of sclerosed liver haemangiomas in children, emphasising the value of non-invasive imaging as the foundation of primary diagnosis in paediatric practice and the potential reduction in the need for biopsy with typical imaging characteristics. The "one-stop shop" model proposed by L. Sandulescu *et al*. [45], which involved the simultaneous use of various imaging methods (ultrasound, CT, MRI) during a single visit for fast and efficient haemangioma diagnosis, could be justified in specialised paediatric centres to optimise diagnostic and treatment times, minimise the number of visits to medical institutions, and reduce the psycho-emotional burden on the child and their family. However, the generally accepted approach remained a gradual hierarchical strategy with reserving more invasive or resource-intensive methods for complex and atypical cases in children, optimising the balance between diagnostic value and economic efficiency of the examination.

Conclusions

Based on a systematic analysis of current scientific sources, a hierarchy of diagnostic informativeness of

instrumental methods was identified, considering the balance between accuracy and potential risks: morphological studies remain the reference standard, while ultrasound with Doppler is the first-line method with high clinical value; basic clinical approaches (auscultation, thermographic evaluation) may be used only as auxiliary methods. The pathogenetic justification for including the LII in the diagnostic algorithm as an integral marker of endogenous intoxication caused by the resorption of vascular tissue breakdown products, particularly after destructive treatment methods, has been established. The necessity of mandatory coagulation monitoring (platelets, fibrinogen, D-dimers) for early detection of Kasabach-Merritt syndrome in patients with large or rapidly growing haemangiomas has been confirmed, while the observed insufficient frequency of such studies in clinical practice (35.64% of the required volume) indicates the need for standardisation of diagnostic protocols.

The developed integrated diagnostic algorithm is based on a hierarchical application of methods of varying informativeness: primary clinical diagnosis → ultrasound with Doppler as the first-line method → laboratory assessment of the systemic response → morphological verification in cases of atypical clinical presentation, resistance to therapy, or suspected complications. This approach allows for diagnosis in most clinical cases based on non-invasive methods, reserving biopsy for complex diagnostic situations, in line with the bioethical principles of paediatric practice and the concept of minimising invasive interventions. Study limitations included the descriptive-analytical design with a focus on systematic literature review from 2019-2025, without conducting a prospective clinical study, which may limit the generalisability of empirical observations to other populations. Future research directions include the prospective validation of the proposed diagnostic algorithm in larger multicentre cohorts, assessing its impact on clinical outcomes, sensitivity and specificity at each stage of the algorithm, as well as the development of automated clinical decision support systems integrating imaging and laboratory data using machine learning techniques.

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Conflict of Interest

None.

References

[1] Djawad K. Cavernous hemangioma resembling lymphangioma circumscriptum: The central role of dermoscope in diagnosis. J Dermatol Dermatol Surg. 2022;26(1):54–6. DOI: 10.4103/jdds.jdds_144_20

[2] AbouZeid A, Mohammad S, Aly H, Ragab I. Posterior mediastinal and cutaneous back hemangiomas in infants: A new association. Eur J Pediatr Surg Rep. 2021;9(1):e37–40. DOI: 10.1055/s-0040-1721408

[3] Meireles W, Rangel J, Antonialli G, Medina C, Silva R. Clinical diagnosis of disseminated neonatal hemangiomatosis: A case report. Resid Pediatr. 2024;14(1). DOI: 10.25060/residpediatr-2024.v14n1-862

[4] Park M. Infantile hemangioma: timely diagnosis and treatment. Clin Exp Pediatr. 2021;64(11):573–4. DOI: 10.3345/cep.2021.00752

[5] Bayramoğlu Z, Kılınç A, Unlu Y. Cutaneous hemangioma: Our experience over 8 years and literature review. Int J Acad Med Pharm. 2020;2(3):291–5. DOI: 10.29228/jamp.45811.

[6] Toktosunova S. Clinical and morphological characteristics and diagnosis of external haemangiomas in children. Child Health. 2023;18(7):1645–52. DOI: 10.22141/2224-0551.18.7.2023.1645

[7] Naeem S, Ali A, Qadri S, Khan Mashwani W, Tairan N, Shah H, et al. Machine-learning based hybrid-feature analysis for liver cancer classification using fused MR and CT images. Appl Sci. 2020;10(9):3134. DOI: 10.3390/app10093134

[8] Safin D, Onlasynov A, Amatov D. Missed diagnosis: Infantile hemangioma or arteriovenous malformation? Clinical case. Fortune J. 2023;6:517–20. DOI: 10.26502/fjhs.155

[9] Sahajwalla D, Vorona G, Tye G, Harper A, Richard H, Sisler I, et al. Aggressive vertebral hemangioma masquerading as neurological disease in a pediatric patient. Radiol Case Rep. 2021;16:1107–12. DOI: 10.1016/j.radcr.2021.02.023

[10] Guerrero M, Lacouture N, Ayala R. Thermal imaging for monitoring the treatment of hemangioma in a pediatric patient: Case report. J Surg Case Rep. 2024;8:rjae536. DOI: 10.1093/jscr/rjae536

[11] International Society for the Study of Vascular Anomalies. ISSVA classification of vascular anomalies [Internet]. [cited 2025 December 12]. Available from: https://www.issva.org/UserFiles/file/ISSVA-Classification-2018.pdf

[12] Zhang H, Wei T, Johnson A, Sun R, Richter G, Strub G. NOTCH pathway activation in infantile hemangiomas. J Vasc Surg Venous Lymphat Disord. 2020;9(2):489–96. DOI: 10.1016/j.jvsv.2020.07.010

[13] Cimmino I, Margheri F, Prisco F, Perruolo G, D'Esposito V, Laurenzana A, et al. Prep1 regulates angiogenesis through a PGC-1α-mediated mechanism. FASEB J. 2019;33:13893–904. DOI: 10.1096/fj.201901230RR

[14] Xie F, Zhang X, Luo W, Ge H, Sun D, Liu P. Notch signaling pathway is involved in bFGF-induced corneal lymphangiogenesis and hemangiogenesis. J Ophthalmol. 2019;1:9613923. DOI: 10.1155/2019/9613923
[15] McNab M, García C, Tabak D, Aranibar L, Castro A, Wortsman X. Subclinical ultrasound characteristics of infantile hemangiomas that may potentially affect involution. J Ultrasound Med. 2020;40(6):1125–30. DOI: 10.1002/jum.15489
[16] Xu X, Wu Y, Li H, Xie J, Cao D, Huang X. Notch pathway inhibitor DAPT accelerates in vitro proliferation and adipogenesis in infantile hemangioma stem cells. Oncol Lett. 2021;22(6):854. DOI: 10.3892/ol.2021.13115
[17] Li M, Wang X, Yang E, Li Y, Geng Y, Chen Z, et al. OTUB1 catalytic-independently deubiquitinates TGFBI and mediates angiogenesis in infantile hemangioma by regulating glycolysis. Arterioscler Thromb Vasc Biol. 2023;43(5):654–73. DOI: 10.1161/ATVBAHA.123.319177
[18] Liu C, Zhao Z, Guo S, Zhang L, Fan X, Zheng J. Exosomal miR-27a-3p derived from tumor-associated macrophage suppresses propranolol sensitivity in infantile hemangioma. Cell Immunol. 2021;370:104442. DOI: 10.1016/j.cellimm.2021.104442
[19] Liu J, Zhong W, Wang R, Wang P, Tong G, Chai M, et al. Macrophage ferroptotic resistance is required for the progression of infantile hemangioma. J Am Heart Assoc. 2024;14(1):e034261. DOI: 10.1161/JAHA.124.034261
[20] Wang Y, Kong L, Sun B, Cui J, Shen W. Celecoxib induces adipogenic differentiation of hemangioma-derived mesenchymal stem cells through the PPAR-γ pathway in vitro and in vivo. Exp Ther Med. 2022;23(6):375. DOI: 10.3892/etm.2022.11303
[21] Wu H, Wang X, Liang H, Zheng J, Huang S, Zhang D. Enhanced efficacy of propranolol therapy for infantile hemangiomas based on a mesoporous silica nanoplatform through mediating autophagy dysfunction. Acta Biomater. 2020;107:272–85. DOI: 10.1016/j.actbio.2020.02.033
[22] Zhang J, Yin S, Zhou D, Wen J, Gao H, Chen L, et al. Quantitative evaluation of percutaneous local drug perfusion against refractory infantile hemangioma via 3-D power Doppler angiography. Ultrasound Med Biol. 2019;46(3):610-9. DOI: 10.1016/j.ultrasmedbio.2019.11.002
[23] Leñero-Bardallo J, Acha B, Serrano C, Pérez-Carrasco J, Ortiz-Álvarez J, Bernabéu-Wittel J. Thermography as a method for bedside monitoring of infantile hemangiomas. Cancers. 2022;14(21):5392. DOI: 10.3390/cancers14215392
[24] Liao M, He B, Xiao Z, Wang L, Chen Y, Liu X, et al. Prenatal ultrasound evaluation of fetal cutaneous hemangioma and related complications. J Matern Fetal Neonatal Med. 2022;36(1):2157257. DOI: 10.1080/14767058.2022.2157257
[25] Cericola G, Gunst L, Bel H, Jrad H, Sahlmann J, Puzik A, et al. Assessment of CEUS for evaluation of hepatic infantile hemangiomas. medRxiv. 2025. DOI: 10.1101/2025.05.08.25327084
[26] Li K, Peng YG, Yan RH, Song WQ, Peng XX, Ni X. Age-dependent changes of total and differential white blood cell counts in children. Chin Med J. 2020;133(16):1900–7. DOI: 10.1097/CM9.0000000000000854
[27] Mariani L, Schmitt I, Garcia C, Kiszewski A. Low dose sirolimus treatment for refractory tufted angioma and congenital kaposiform hemangioendothelioma, both with Kasabach-Merritt phenomenon. Pediatr Blood Cancer. 2019;66(8):e27810. DOI: 10.1002/pbc.27810
[28] Belani L, Sapuan J, Abdullah S, Hing E, Loh C, Alias H. Kaposi hemangioendothelioma of the right upper limb with the Kasabach-Merritt phenomenon: A potentially lethal diagnostic challenge. Front Pediatr. 2022;10:995399. DOI: 10.3389/fped.2022.995399
[29] Rešić A, Barčot Z, Habek D, Pogorelić Z, Bašković M. The evaluation, diagnosis, and management of infantile hemangiomas – a comprehensive review. J Clin Med. 2025;14(2):425. DOI: 10.3390/jcm14020425
[30] Esposito F, D'Auria D, Ferrara D, Esposito P, Gaglione G, Zeccolini M, et al. Hepatic hemangiomas in childhood: The spectrum of radiologic findings. A pictorial essay. J Ultrasound. 2022;26(1):261–76. DOI: 10.1007/s40477-022-00714-y
[31] Kapp F, Schneider C, Holm A, Glonnegger H, Niemeyer C, Rössler J, et al. Comprehensive analyses of coagulation parameters in patients with vascular anomalies. Biomolecules. 2022;12(12):1840. DOI: 10.3390/biom12121840
[32] Massara B, Mariem R, Emna B, Meriam T, Faiza S, Sonia B, et al. Kaposiform hemangioendothelioma with fatal income: Kasabach-Merritt phenomenon and hypercalcemia. Clin Case Rep. 2022;10(2):e5458. DOI: 10.1002/ccr3.5458
[33] Lawrence S, Scofield R. Post traumatic stress disorder associated hypothalamic-pituitary-adrenal axis dysregulation and physical illness. Brain Behav Immun Health. 2024;41:100849. DOI: 10.1016/j.bbih.2024.100849
[34] Mbiydzenyuy N, Qulu L. Stress, hypothalamic-pituitary-adrenal axis, hypothalamic-pituitary-gonadal axis, and aggression. Metab Brain Dis. 2024;39:1613–36. DOI: 10.1007/s11011-024-01393-w

[35] Bellinato F, Marocchi M, Pecoraro L, Zaffanello M, Del Giglio M, Girolomoni G, et al. Diagnosis and treatment of infantile hemangioma from the primary care paediatricians to the specialist: A narrative review. Children. 2024;11(11):1397. DOI: 10.3390/children11111397
[36] Cerbu S, Arghirescu TS, Stănciulescu MC, Timofte CE, Mussuto E, Heredea ER, et al. Role of imagistic techniques in diagnosing soft-tissue vascular anomalies in pediatric population – a 5-year experience. Rom J Morphol Embryol. 2019;60(2):495–500.
[37] Liang X, Xu B, Xu Q, Chen X, Li Y. Diagnosis of infantile subglottic hemangioma: A 10-year experience of 25 cases. Front Pediatr. 2025;13:1499656. DOI: 10.3389/fped.2025.1499656
[38] Gil LB, Nedel CE, Silveira JG, Sperb AP, Barros MC, Nedel BL. Imaging of infantile hemangiomas: A pictorial review. Radiol Bras. 2025;58:e20250041. DOI: 10.1590/0100-3984.2025.0041
[39] Sharan P, Vellapandian C. Hypothalamic-pituitary-adrenal axis: Unveiling the potential mechanisms involved in stress-induced Alzheimer's disease and depression. Cureus. 2024;16(8):e67595. DOI: 10.7759/cureus.67595
[40] Oweidat M, Alra'e M, Anati M, Hassouneh A, Juneidi S. Hemangioma of the abdominal wall in infancy. J Surg Case Rep. 2025;(4)rjaf238. DOI: 10.1093/jscr/rjaf238
[41] Monreal-Robles R, Del Cueto Aguilera A, García-Compeán D, González J, Borjas-Almaguer O, Jáquez-Quintana J, et al. Cavernous hemangioma: uncommon cause of obscure gastrointestinal bleeding diagnosed by video capsule endoscopy and contrast-enhanced CT. Arch Clin Med Case Rep. 2020;4(3):512–9. DOI: 10.26502/acmcr.96550224
[42] Graff E, Keihanian T, Shergill U, Girotra M. S3038 peri-gastric venous hemangioma: A tale of discordant cytology and histology on EUS-core biopsy. Am J Gastroenterol. 2020;115:S1600. DOI: 10.14309/01.ajg.0000714200.73838.4d
[43] Dong A, Nian S, Bai Y, Zuo C. Hemangioma of the ilium simulating bone metastasis on 18F-PSMA-1007 PET/CT. Clin Nucl Med. 2024;49:e304–6. DOI: 10.1097/RLU.0000000000005076
[44] Wang F, Numata K, Nihonmatsu H, Chuma M, Ideno N, Nozaki A, et al. Added value of ultrasound-based multimodal imaging to diagnose hepatic sclerosed hemangioma before biopsy and resection. Diagnostics. 2022;12:2818. DOI: 10.3390/diagnostics12112818
[45] Sandulescu L, Urhuț C, Săndulescu S, Ciurea A, Cazacu S, Iordache S. One stop shop approach for the diagnosis of liver hemangioma. World J Hepatol. 2021;13(12):1892–908. DOI: 10.4254/wjh.v13.i12.1892

Балдардын тышкы терисинин гемангиомаларын диагностикалоо ыкмаларын негиздөө

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Аннотация. Балдарда теринин гемангиомаларын диагностикалоодо бирдиктүү ыкманын жоктугу жана аларды башка кан тамыр аномалияларынан айырмалоо зарылдыгы объективдүү баалоону камсыз кылган жана диагностикалык каталардын тобокелдигин азайтууга мүмкүндүк берген структураланган диагностикалык алгоритмди түзүүнү талап кылат. Бул изилдөөнүн максаты – заманбап инструменталдык жана лабораториялык ыкмаларды системалуу талдоого негизделген балдардагы гемангиомаларды диагностикалоо критерийлерин теориялык жактан негиздеп, аналитикалык жактан тактоо жана андан соң интеграцияланган диагностикалык алгоритмди иштеп чыгуу болду. 23 илимий басылманы талдоо ар бир ыкманын маалыматтуулугун жана клиникалык практикада аларды оптималдуу колдонуу тартибин аныктоого мүмкүндүк берди. Ультраүн сүрөттөлүшүнүн морфологиялык тастыктоо менен эң жогорку диагностикалык дал келүүсү аныкталды, ал эми термографиялык баалоо жана аускультация төмөн тактыкка ээ болуп, алгачкы багыттоо этабында гана пайдалуу экени белгилүү болду. Лабораториялык маркерлерди куракка жараша талдоо зарыл экени аныкталды: лейкоциттердин интоксикация индексинин эталондук маанилери наристелерде жана улуу балдарда лейкоцит формуласынын физиологиялык өзгөчөлүктөрүнө байланыштуу айырмаланат. Касабах-Меррит синдромун эрте диагностикалоо үчүн коагуляция параметрлеринин диагностикалык чектери аныкталды: тромбоциттер <50 × 103/мкл, фибриноген <100 мг/дл, D-димерлер >5-20 мг/л. Чоң же ылдам өсүп жаткан гемангиомаларда сарптоо коагулопатиясынын тобокелдигине байланыштуу коагуляцияны мониторингдөө көрсөтүлөт. Алынган натыйжаларга негизделип, клиникалык текшерүү, УЗИ, системалуу маркерлердин лабораториялык анализдери жана атипикалык жүрүш же инвазивдик эмес маалыматтар жетишсиз болгондо морфологиялык тастыктоону баскычтап колдонууну камтыган иерархиялык диагностикалык алгоритм иштелип чыкты. Сунушталган ыкма диагностикалык тактыкты жакшыртат, текшерүүлөрдүн тартибин стандартизациялайт жана педиатриялык практикада инвазивдүү кийлигишүүлөргө болгон муктаждыкты минималдаштырат

Негизги сөздөр: кан тамыр аномалиясы; аспаптык ыкма; лабораториялык маркер; патоморфологиялык изилдөө; системалуу реакция; перифериялык кан

Обоснование методов диагностики гемангиом наружных покровов у детей

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Аннотация. Отсутствие единых подходов к диагностике кожных гемангиом у детей, а также необходимость их дифференциации от других сосудистых аномалий требуют создания структурированного диагностического алгоритма, способного обеспечить объективность оценки и снизить риск диагностических ошибок. Целью данного исследования было теоретическое обоснование и аналитическое уточнение диагностических критериев гемангиом у детей на основе систематического анализа современных инструментальных и лабораторных методов с последующей разработкой интегрированного диагностического алгоритма. Был проведен анализ 23 научных публикаций, что позволило определить информативность отдельных методов и последовательность их оптимального применения в клинической практике. Было установлено, что ультразвуковая визуализация имеет наибольшее диагностическое согласие с морфологическим подтверждением, в то время как термографическая оценка и аускультация характеризуются более низкой точностью и полезны только на этапе предварительной ориентации. Было установлено, что необходима возрастная интерпретация лабораторных маркеров: индекс интоксикации лейкоцитами имел разные референтные значения у младенцев и детей старшего возраста в связи с физиологическими особенностями лейкоцитарного формуляра. Определены диагностические пороги коагуляционных параметров для ранней диагностики синдрома Касабаха-Мерритта: тромбоциты <50 × 103/мкл, фибриноген <100 мг/дл, D-димеры >5-20 мг/л. Мониторинг коагуляции показан при крупных или быстро растущих гемангиомах из-за риска консуматорной коагулопатии. На основании полученных результатов был сформулирован иерархический диагностический алгоритм, который предполагает поэтапное применение клинического обследования, ультразвуковой визуализации, лабораторного тестирования системных маркеров и морфологического подтверждения в случаях атипичного течения или недостаточности неинвазивных данных. Предлагаемый подход повышает точность диагностики, стандартизирует последовательность обследований и сводит к минимуму необходимость инвазивных вмешательств в педиатрической практике

Ключевые слова: сосудистая аномалия; инструментальный метод; лабораторный маркер; патоморфологическое исследование; системная реакция; периферическая кровь

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State of phosphorus-calcium metabolism in young and old rats under conditions of experimental vitamin D hypervitaminosis at different altitudes and ways of its correction

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Abstract. This study aimed to systematically analyse and synthesise current scientific data on the mechanisms of Ca-P metabolism disorders under the combined influence of hypervitaminosis D, altitude hypoxia and age, as well as to justify effective corrective approaches. Scientific sources were analysed using comparative analysis, data synthesis, and information generalisation methods. The analysis conducted that the Ca-P metabolism regulation system is a complex network with vitamin D metabolism being central, where the balance between parathyroid hormone and FGF23 determines the stability of Ca and P levels in plasma. Analysis of scientific sources revealed characteristic age-related features of metabolic disorders. The data showed that in young organisms with high levels of bone remodelling, Ca/P imbalance can lead to a significant decrease in bone mineral density (by 12-18%), while in older organisms, data on the development of progressive osteomalacia and renal failure in the context of a decrease in functional reserves predominate. A review of studies on the effects of high-altitude hypoxia showed that it can cause a complex of disorders, including renal dysfunction (increase in creatinine to 0.81 ± 0.04 mg/dL), electrolyte imbalance (decrease in calcium to 8.1 ± 0.6 mg/dL with an increase in phosphorus to 7.1 ± 0.4 mg/dL) and adaptation of vitamin D metabolism, in particular through increased CYP27B1 expression. The conclusions obtained as a result of the analysis are of theoretical importance for the further development of scientifically based recommendations for the safe supplementation of vitamin D in patients of different age groups living in high-altitude regions

Keywords: parathyroid hormone; osteomalacia; high altitude hypoxia; age-related characteristics; renal failure

Introduction

Phosphorus-calcium metabolism is a central mechanism for ensuring the structural integrity of bone tissue, regulating neuromuscular conduction, and maintaining systemic metabolic balance. Blood calcium

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and phosphorus levels are controlled by a complex network of hormonal, enzymatic, and cellular mechanisms, among which the activity of vitamin D and its metabolites is substantial. Disruption of these mechanisms can lead to soft tissue calcification, nephropathy, cardiovascular dysfunction, osteoporosis and other pathological conditions, which makes the study of Ca-P homeostasis highly relevant from a medical and biological point of view. The analysis of age differences and the influence of external factors, such as hypoxia, which can modify the biological effects of vitamin D and change the course of hypervitaminosis depending on the altitude above sea level, is becoming increasingly relevant.

A contribution to the relationship between vitamin D, calcium and phosphates was made in a study by I.V. Kolosovych & I.V. Hanol [1], which showed that an imbalance of these components affects the course of acute pathological conditions. The study emphasised that changes in the levels of calcium, phosphates and active metabolites of vitamin D can be predictors of the severity of the inflammatory process. A comprehensive review by M. Sun *et al*. [2] showed that calcium-phosphate metabolism disorders are multifactorial in nature and are accompanied by profound changes in the cellular proteome and metabolome. The study emphasised that the changes identified affect signalling pathways, energy metabolism and stress responses. Their conclusions underscored the complexity of the body's systemic responses to Ca-P imbalance and the need for multifaceted analysis models. The importance of studying phosphorus-calcium metabolism disorders is also due to its key role in maintaining the structural integrity of bone tissue and systemic metabolic balance. As noted by B. Çaykara *et al*. [3], the relationship between vitamin D, calcium and phosphorus levels is fundamental to homeostasis, and any imbalance can have serious pathophysiological consequences.

D.D. Bikle [4] highlighted the latest insights into the metabolism and functions of vitamin D, particularly its role in regulating immune response, cell cycle, and intercellular interactions. The study emphasised that even small deviations in the levels of 25(OH)D and $1.25(OH)_2D$ can cause a systemic effect. The study by D. Bikle & S. Christakos [5] revealed new aspects of the skin's involvement in vitamin D metabolism, contributing to the research the role in overall mineral homeostasis. The study demonstrated that skin tissue can act as an autonomous endocrine organ capable of altering systemic calcium and phosphate concentrations. F. Saponaro *et al*. [6] emphasised enzymatic pathways of vitamin D metabolism, including the variability of Cytochrome P450 family 24 subfamily A member 1 (CYP24A1) and Cytochrome P450 family 27 subfamily B member 1 (CYP27B1) activity in different age groups. The article emphasises that changes in the enzymatic profile with age or under stressful conditions can contribute to the development of hypervitaminosis.

A. Papadopoulou *et al*. [7] detail the genetic mechanisms of hereditary disorders of calcium-phosphate metabolism. The study emphasised that mutations in transporters and enzymes can cause severe forms of metabolic disorders with early onset. Vitamin D is central in this regulatory network. According to N.A. Shaikh *et al*. [8], vitamin D has a complex effect not only on mineral absorption but also on the function of cell populations, particularly intestinal stem cells. However, the mechanisms by which vitamin D modulates the processes of proliferation, differentiation, and homeostasis in target organs remain unclear, especially in conditions of excess. The dissertation by A. Hossain [9] emphasised the role of vitamin D deficiency and excess as modified risk factors for the development of non-communicable diseases, including metabolic syndrome and cardiovascular pathologies. The study analysed in detail the mechanisms of Ca-P metabolism disorders in the context of the systemic inflammatory response. The final link in the calcium-phosphate metabolism regulation system was highlighted by M.L. Noonan [10] in an analysis of the role of Fibroblast growth factor 23 (FGF23) in the mechanisms of osteocyte oxygenation and biomineralization, especially in the context of chronic kidney disease. The study demonstrated that changes in the oxygen supply to bone tissue can radically alter the hormonal regulation of phosphate.

Thus, analysis of the accumulated data clearly demonstrates the complexity of the Ca-P homeostasis regulation system and its dependence on age and environmental factors. However, there are gaps in the research on this problem. There is conflicting and incomplete data on the characteristics of hypervitaminosis D in organisms of different ages. In addition, there are virtually no studies devoted to the effect of chronic hypoxia on the development and consequences of vitamin D toxicity. These shortcomings in existing works necessitate a targeted study of these aspects and form a specific scientific basis for conducting new experimental studies. The study aimed to analyse current theoretical data on changes in phosphorus-calcium metabolism in young and old rats under conditions of experimental vitamin D hypervitaminosis at different altitudes and to identify possible ways to correct these disorders. The study goals included: establishment of age-specific features of phosphorus-calcium metabolism under normoxic and hypoxic conditions, in particular, description of differences between young and old organisms, determination of variations in basic biochemical parameters, and characterisation of changes occurring in response to vitamin D excess; analysis of the complex of biochemical, hormonal and metabolic disorders induced by hypervitaminosis D in animals of different ages; assessment of the effectiveness of approaches to the correction of calcium-phosphate metabolism disorders.

As part of the preparation of the review, a multi-stage literature search was conducted in PubMed,

Scopus, Web of Science, and Google Scholar databases. At the initial stage, 512 publications were identified that matched a broad set of keywords related to phosphorus-calcium metabolism, vitamin D hypervitaminosis, age differences, and the effects of hypoxia. After removing duplicates, the number was reduced to 426 sources, which were screened by title and abstract. Further filtering based on inclusion criteria – the presence of primary experimental or generalised data on Ca-P metabolism regulation; analysis of the effects of hypervitaminosis D; comparison of young and old organisms; availability of data on hypoxia and high-altitude conditions; clear description of methodology – reduced the sample to 148 sources. Thirty-six publications that met the methodological quality requirements, contained transparently described statistical procedures, and had practical or theoretical significance for the formation of a conceptual model of Ca-P metabolism disorders were selected for the final stage.

The final selection included both experimental studies on rodents and animal models of different age groups, as well as systematic clinical observations of patients with Ca-P metabolism disorders, chronic kidney diseases, conditions associated with vitamin D deficiency or excess, as well as studies devoted to the adaptation of the body to mid-mountain and high-mountain conditions. The sample size in clinical and experimental studies ranged from 15-30 experimental animals to 250-600 individuals in population and cross-sectional studies. The main results included the assessment of hormonal markers (parathyroid hormone, calcitonin, FGF23), active metabolites of vitamin D, indicators of bone remodelling, functional state of the kidneys, and calcium and phosphorus levels. This systematic characterisation of sources ensured the representativeness of the review and formed a comprehensive theoretical basis for further analysis of the pathophysiological mechanisms and age-specific responses to vitamin D hypervitaminosis in normoxic and hypoxic conditions. The analysis had certain limitations, mainly due to the lack of experimental studies that simultaneously studied the combined effect of all three factors – hypervitaminosis D, altitude hypoxia, and age – on a single model. Most of the sources cited examined individual aspects of this problem, which complicates direct comparison of results and requires logical extrapolation of data.

Theoretical basis of Ca–P metabolism regulation

A systematic analysis of scientific literature synthesised a comprehensive overview of the mechanisms regulating phosphorus-calcium metabolism, including age-related characteristics, the effects of vitamin D toxicity, and conditions of altitude hypoxia. B. Zhang *et al*. [11] provided a fundamental concept of the systemic nature of changes, demonstrating profound age-related remodelling of ion profiles, including calcium and phosphorus, in various organs of mice. The "ion clocks of ageing" indicate a close relationship between mineral homeostasis disorders and general ageing processes. The specific mechanisms of these changes are revealed in studies devoted to individual organs. V.A. Areco *et al*. [12] described in detail the molecular architecture of intestinal calcium absorption, in which the transporters Transient Receptor Potential Vanilloid 6 (TRPV6), calbindin-D9k and PMCA1b is central, the expression of which is strictly controlled by calcitriol via the Vitamin D receptor (VDR). With age, the efficiency of this system may decrease, contributing to the development of hypocalcaemia.

W.L. Miller & E.A. Imel [13] described in detail in their review the two-stage process of vitamin D metabolism, which is the basis for the regulation of calcium-phosphorus homeostasis. The authors emphasised that the first stage of 25-hydroxylation occurs in the liver with the formation of 25(OH)D, the main circulating marker of the body's supply. The second key stage, according to their data, occurs in the kidneys, where the enzyme CYP27B1 (1α-hydroxylase) converts 25(OH)D into the biologically active hormone calcitriol ($1.25(OH)_2D$), whose activity is hundreds of times higher. D. Bellavia *et al*. [14] investigated the molecular mechanisms of calcitriol action through its nuclear receptor (VDR). The study described how the calcitriol-VDR complex, forming a heterodimer with the retinoic acid receptor (RXR), binds to vitamin D response elements (VDRE) in deoxyribonucleic acid (DNA), regulating gene transcription. The study outlined the effects in target organs in detail: in the intestine, the genes for calcium channels TRPV6, calbindin-D9k and calcium-magnesium ATPase (PMCA1b) are induced, ensuring active calcium transport; calcium reabsorption increases in the kidneys; a dual role is noted in the bones, from being necessary for mineralisation to promoting resorption with the participation of parathyroid hormone (PTH) in calcium deficiency.

O.M. Gutiérrez *et al*. [15] investigated the feedback mechanisms in the regulation of calcitriol levels on the example of mice. The study determined that PTH is a potent stimulator of CYP27B1 expression in response to hypocalcaemia. In contrast, fibroblast growth factor-23 (FGF23), which is produced in bone during hyperphosphataemia, inhibits CYP27B1 and induces the expression of the inactivation enzyme CYP24A1. Thus, the PTH/FGF23 balance determines the rate of vitamin D metabolism and the stability of Ca and P levels. S. De Vincentis *et al*. [16], in a clinical study, substantiated the importance of the calcium-to-phosphorus ratio (Ca/P) in plasma as an integral indicator of the state of the mineral homeostasis system. The study demonstrated that changes in this ratio may be early markers of profound disturbances in the complex regulatory network involving vitamin D, PTH and FGF23, even before the onset of clinical symptoms. Thus, the results of these

studies have shaped the concept of the Ca-P metabolism regulation system as a complex network with a central integrated role of vitamin D metabolism.

Effects of hypervitaminosis D at the molecular and systemic levels

Hypervitaminosis D causes a rapid disruption of this finely tuned system. Experimental data from M. El-Boshy *et al*. [17] on rats documented the development of severe hypercalcaemia (12.4 ± 0.5 mg/dL) and hyperphosphataemia (7.9 ± 0.3 mg/dL) in the context of severe oxidative stress and inflammation. According to the analysis by M. Gurudatta [18], the endocrine profile of this condition includes a sharp suppression of parathyroid hormone secretion due to the activation of calcium-sensitive receptors (CaSR) and a compensatory increase in FGF23 levels aimed at reducing toxicity. However, as described by A. Nowacka *et al*. [19], the enzyme CYP24A1, which catalyses the inactivation of both calcitriol and 25(OH)D, are substantial in protecting against intoxication. Its activity increases sharply in hypervitaminosis in an attempt to restore balance. The biochemical consequence is not only calcification of soft tissues, but also a paradoxical disturbance of bone mineralisation, similar to osteomalacia, observed by D. Durup *et al*. [20] in female rats under conditions of deficiency (Table 1).

Table 1. Biochemical and molecular effects of hypervitaminosis D in rats (according to literature data)

Parameter	Control group (normal vitamin D levels)	Group with hypervitaminosis D	Effect
Serum calcium (mg/dL)	9.8 ± 0.3	12.4 ± 0.5	Hypercalcaemia
Serum phosphorus (mg/dL)	6.2 ± 0.2	7.9 ± 0.3	Hyperphosphataemia
Malondialdehyde in the liver (nmol/mg prot.)	1.8 ± 0.2	4.5 ± 0.3	Oxidative stress
TNF-α in the liver (pg/mL)	25.6 ± 2.1	68.3 ± 4.5	Systemic inflammation
Serum creatinine (mg/dL)*	0.52 ± 0.03	0.81 ± 0.04	Kidney dysfunction

Note: * – creatinine data are taken from a study of the effects of hypoxia, which also demonstrates similar mechanisms of renal damage during metabolic stress, which is relevant for the hypervitaminosis D model
Source: compiled by the authors based on M. El-Boshy et al. [17], M. Gurudatta [18], A. Nowacka *et al*. [19], D. Durup *et al*. [20]

At the molecular level, hypervitaminosis D initiates a cascade of pathological events, the central links of which are powerful oxidative stress and systemic inflammation. Experimental data from M. El-Boshy *et al*. [17] in rats document a sharp increase in malondialdehyde (MDA) levels, a key marker of lipid peroxidation, from 1.8 ± 0.2 to 4.5 ± 0.3 nmol/mg protein in the liver. At the same time, there was a significant increase in the concentration of the pro-inflammatory cytokine tumour necrosis factor-alpha (TNF-α) from 25.6 ± 2.1 to 68.3 ± 4.5 pg/mL. These processes directly damage cell membranes and structures, initiating apoptosis, which confirms the close relationship between vitamin D toxicity, oxidative damage and immune dysregulation, as described in detail by C. Argano *et al*. [21]. A key pathophysiological consequence is soft tissue calcification, as excess $Ca^{2+}$and PO_4^{3-} ions in plasma lead to the formation of hydroxyapatite microcrystals in the walls of blood vessels, kidneys, heart and lungs, accompanied by structural and functional disorders. Renal damage is particularly pronounced, manifested by elevated urea and creatinine levels, as well as histological signs of tubular necrosis and interstitial fibrosis. The endocrine profile of this condition is characterised by a profound imbalance: a sharp suppression of parathyroid hormone secretion due to the activation of calcium-sensitive receptors (CaSR) is combined with a compensatory increase in fibroblast growth factor-23 (FGF23) levels aimed at reducing toxicity, as described by M. Gurudatta [18]. However, the effectiveness of this protective mechanism may be limited, especially in the context of a possible decrease in the expression of the Klotho co-receptor. The enzyme CYP24A1, which catalyses the inactivation of vitamin D metabolites, is substantial in the body's response to intoxication. A. Nowacka *et al*. [19] emphasise that its activity increases sharply in hypervitaminosis D, attempting to restore homeostasis by accelerating the breakdown of both calcitriol ($1,25(OH)_2D$) and its precursor 25(OH)D. A paradoxical but natural consequence is a negative effect on bone tissue. Excess vitamin D can lead to excessive stimulation of osteoclast differentiation and activity through a change in the Receptor Activator of Nuclear factor Kappa-B Ligand/Osteoprotegerin (RANKL/OPG) ratio, enhancing bone resorption, which can contribute to osteopenia. This is consistent with the data of D. Durup *et al*. [20], who observed the development of osteomalacia in female rats under conditions of hypophosphatemic hypovitaminosis, emphasising the critical significance of balanced levels of both vitamin D and phosphorus for maintaining healthy bone remodelling. Thus, hypervitaminosis D is a complex pathological condition that exceeds the scope of simple hypercalcaemia and includes the mutual reinforcement of hormonal imbalance, oxidative stress, systemic inflammation, calcification and functional damage to key organs.

Age-related features of Ca-P metabolism disorders

The most fundamental and systemic age-related changes in the regulation of phosphorus-calcium metabolism occur in the FGF23-Klotho axis, as confirmed by an

in-depth analysis in a review by S. Devi [22]. The study described in detail how Klotho, being an essential co-receptor for fibroblast growth factor-23 (FGF23), performs a key anti-ageing function. Its decreased expression with age is not only a marker but also a central driver of ageing, leading to the development of renal resistance to FGF23. S. Wang *et al*. [23] further contributed to the topic by demonstrating how a defective FGF23-Klotho axis directly contributes to chronic microinflammation and the progression of renal fibrosis, creating a cycle of damage. The study highlighted the renal link in this mechanism, clearly describing that the main physiological task of FGF23, which is produced by osteocytes, is to inhibit phosphate reabsorption in the proximal tubules of the kidneys by modulating sodium-phosphate cotransporters. Thus, age-related Klotho deficiency disrupts this negative feedback, promoting the accumulation of phosphate in the blood and the progression of hyperphosphatemia (Table 2).

Table 2. Synthesised age differences in the regulation of Ca-P metabolism

Parameter/System	Young organisms	Old organisms
Axis FGF23-Klotho	Adequate renal sensitivity to FGF23, high Klotho levels	Resistance to FGF23, a sharp decrease in Klotho, and hyperphosphataemia
Kidney function	High clearance, effective phosphaturia	Decreased glomerular filtration rate (GFR), impaired phosphate excretion
Intestinal absorption of Ca	Effective due to high expression of TRPV6 and calbindin	Possible reduction due to decreased expression of VDR and transport proteins
Systemic mineral balance	Stable ion profile	Deep remodelling of Ca and P content in organs
Musculoskeletal cross-flow	Synchronised remodelling, synergism	Imbalance, development of osteoporosis and sarcopenia

Source: compiled by the authors based on B. Zhang *et al*. [11], S. Devi [22], D.-X. Huang *et al.* [24], B. Kirk *et al*. [25]

This process is significantly exacerbated by the parallel age-related decline in renal functional reserve. Experimental data from D.-X. Huang *et al*. [24] on rats simulate this condition, demonstrating that under conditions of metabolic stress (readaptation after hypoxia), creatinine clearance drops sharply by 27%, reflecting a deterioration in glomerular filtration. The systemic nature of age-related remodelling of mineral homeostasis was demonstrated by B. Zhang *et al*. [11] in a study of ion mice. The study identified specific, organ-associated changes in the content of calcium, phosphorus and other ions, which made it possible to construct accurate "ion clocks of ageing". This indicates that Ca-P metabolism disorders are not an isolated phenomenon, but part of a profound systemic metabolic restructuring of the entire organism.

The bone manifestations of this complex of disorders were analysed from a different perspective in the context of bone-muscle cross-talk, analysed in detail by B. Kirk *et al*. [25]. The study emphasised the inextricable link between the progression of osteoporosis and sarcopenia (loss of muscle mass) through common hormonal and metabolic pathways, such as the Insulin like growth factor (IGF-1), vitamin D and chronic inflammation, which simultaneously affect bone mineral density and skeletal muscle function. This concept complements the traditional view of age-related changes in bone, which is based on a comparison of different models. A study by T. Li *et al*. [26] on growing broiler chickens demonstrates that a young organism dependent on intensive bone formation is extremely sensitive to Ca/P imbalance in the diet. Calcium or phosphorus deficiency led to sharp fluctuations in alkaline phosphatase (ALP) activity and a significant decrease in bone mineral density (by 12-18%) and bone strength (by 15-22%). In contrast, the model of hypophosphatemic hypovitaminosis D in sexually mature female rats, created by D. Durup *et al*. [20], caused the development of true osteomalacia and disruption of the mineralisation of already formed osteoid. This indicates that in adult and elderly organisms, the main problem is not the speed as the quality of remodelling, which deteriorates due to resource deficiency and hormonal resistance. A clinical study by S. Jiampochaman *et al*. [27] among elderly patients with renal insufficiency confirms the practical aspect of these changes, demonstrating the need for individual vitamin D dosing due to the reduced effectiveness of standard regimens associated with decreased renal conversion and tissue sensitivity.

Thus, the most significant age-related difference is not simply a different rate of remodelling, but a fundamental change in the state of regulatory systems. In young organisms, Ca/P imbalance mainly affects the kinetics of active bone mineralisation. In older organisms, the progression of osteomalacia and osteoporosis in the context of resistance syndrome caused by a decrease in Klotho, renal dysfunction and systemic metabolic remodelling, which creates a pathophysiological basis for a more severe course of conditions associated with hypervitaminosis D or hypoxia.

The effect of high-altitude hypoxia on oxygenation, renal function and metabolism

The effects of altitude hypoxia exert a complex and potent modulatory influence on phosphorus-calcium homeostasis, often acting as a catalyst or amplifier of disturbances initiated by other factors,

notably hypervitaminosis D. Systematic reviews by L.M. Palubiski *et al*. [28] and S.-Y. Wang *et al*. [29] described this effect, classifying it according to duration and severity. They emphasised that although acute hypoxia can cause transient changes in renal haemodynamics, chronic hypoxia leads to persistent and often irreversible disorders such as renal vascular remodelling, hyperfiltration with subsequent decline in glomerular function, and tubulointerstitial damage. These changes directly affect the ability of the kidneys to perform their role in mineral homeostasis to effectively filter and reabsorb electrolytes, particularly phosphates.

Experimental data from C. Yan *et al*. [30] on rats exposed to chronic hypoxia quantitatively confirm the specific nature of these disorders. They recorded the development of a characteristic electrolyte imbalance: stable hypocalcaemia (decrease in serum calcium to 8.1 ± 0.6 mg/dL) and hyperphosphataemia (increase in phosphorus to 7.1 ± 0.4 mg/dL). This profile (low Ca, high P) is a key pathogenetic factor, as it creates favourable conditions for FGF23 secretion by osteocytes and leads to further imbalance in the regulatory system. The adaptation of vitamin D metabolism to oxygen-deficient conditions demonstrates a compensatory response. A study by X. Chen *et al*. [31] on high-altitude rodents revealed increased expression of the CYP27B1 (1α-hydroxylase) gene in the kidneys. This was interpreted as an attempt by the body to increase the synthesis of active calcitriol ($1.25(OH)_2D$) to counteract hypocalcaemia by enhancing intestinal calcium absorption. However, in the case of excessive doses of vitamin D, this adaptation can become pathological, leading to uncontrolled generation of calcitriol and an increase in its toxic effects.

The key intracellular integrator of all responses to hypoxia is the hypoxia-inducible factor (HIF) system. G. Almanzar *et al*. [32] described in detail how the stabilisation of HIF-1α under conditions of oxygen deficiency triggers a large-scale reorganisation of cellular metabolism, directing it towards anaerobic glycolysis, and modulates numerous signalling pathways associated with angiogenesis, inflammation and cell survival. Regarding Ca-P metabolism, HIF can directly interact with the signalling pathways involved in its regulation. It is believed that there is cross-regulation between HIF and vitamin D receptor signalling. HIF can influence the transcription of VDR target genes or modulate the stability of the receptor. In addition, hypoxia through HIF activation can suppress the expression of NaPi-IIa and NaPi-IIc, the main transporters responsible for phosphate reabsorption in the renal tubules. This mechanism may explain hyperphosphataemia regardless of FGF23 levels. Studies also show that hypoxia can exacerbate oxidative stress and systemic inflammation, which in turn suppresses Klotho expression in the kidneys, as described by S.-Y. Wang *et al*. [29]. Thus, hypoxia creates a triple blow to phosphate homeostasis: through direct renal effects (inhibition of transporters), through increased resistance to FGF23 (decreased Klotho), and through modulation of vitamin D metabolism (increased CYP27B1). This complex interaction significantly increases the risk of developing severe Ca-P metabolism disorders, especially in combination with other pathological conditions, such as hypervitaminosis D, and necessitates the development of special corrective strategies for high-altitude conditions.

A structured analysis of the literature identified promising corrective approaches that act at different levels of pathogenesis. The fundamental strategy is to optimise the dietary calcium-to-phosphorus ratio, the effectiveness of which in supporting bone mineralisation has been demonstrated by T. Li *et al*. [26]. Among pharmacological methods, substances aimed at restoring the balance of the FGF23-Klotho axis stand out. B.-H. Liu *et al*. [33] demonstrated that fucoidan improves Ca-P metabolism disorders and bone abnormalities in rats with a model of chronic kidney disease, precisely through modulation of this axis. Another approach is to combat oxidative stress with antioxidants, the effectiveness of which is substantiated by data from M. El-Boshy *et al*. [17] on a significant increase in lipid peroxidation markers in hypervitaminosis D. Non-pharmacological interventions are substantial. J. Zhang & Z.-B. Cao [34] provided convincing evidence that regular exercise is an effective way to improve vitamin D status and tissue sensitivity to it. The general principles of renoprotection and gradual adaptation to hypoxic conditions, described in the reviews by S.-Y. Wang *et al*. [29], form the basis for a physiological approach to the prevention of mineral metabolism disorders in high altitude conditions.

The obtained results can be used to analyse the complex nature of phosphorus-calcium metabolism disorders under the combined effects of hypervitaminosis D and altitude hypoxia, considering the age factor. The synergistic effect between these factors requires in-depth consideration of molecular and physiological mechanisms. The study by W.R. Beck *et al*. [35] demonstrates the complex effect of hypoxia on bone tissue, which is consistent with the data obtained on mineralisation disorders. The use of network analysis revealed specific changes in bone microarchitecture under conditions of simulated altitude training, confirming the significance of structural changes in bone when analysing Ca-P metabolism disorders. It has been established that hypoxia can modulate bone remodelling processes by altering the balance between mineralisation and resorption, which explains the age-related differences in susceptibility to Ca-P homeostasis disorders. O. Melnyk *et al*. [36] revealed the integral nature of the body's responses to hypoxic stress, confirming the data obtained on the systemic effects of hypoxia. A close relationship between the state of the neuro-endocrine-immune complex and metabolomic

indicators under conditions of acute stress has been proven, which is consistent with the identified disturbances in hormonal regulation. Specific markers of metabolic disorders that correlate with individual resistance to hypoxia were identified, emphasising the need for an individual approach to assessing the effects of hypoxic exposure. E. Sivertsson *et al*. [37] demonstrated a new mechanism of intrarenal hypoxia development, which complements the data obtained on renal disorders. The study demonstrated that thyroid hormones can induce intrarenal hypoxia by enhancing oxygen metabolism, which may be an additional factor in kidney damage in conditions of endocrine regulation disorders. This mechanism is substantial for research on the relationship between different hormonal systems in hypoxia.

The study by Y. Du *et al*. [38] reveals the molecular mechanisms of renal damage under hypoxia, confirming the data obtained on renal function disorders. Impaired uric acid excretion and changes in desmin expression in podocytes have been established, which is consistent with the identified signs of renal dysfunction. A decrease in Na+-K+-ATPase activity was detected, indicating impaired energy metabolism in renal cells and explaining the development of renal dysfunction under conditions of high-altitude hypoxia. D. Chang *et al*. [39] demonstrate the effectiveness of corrective interventions under conditions of hypoxia, confirming the promise of the developed corrective approaches. The protective role of L-carnitine in the reproductive system under hypoxic stress has been proven, indicating the promise of using metabolic correctors. A positive effect on the hormonal profile and spermatogenesis indicators has been found, confirming the possibility of correcting hypoxic damage. The study by M.M. Soliman *et al*. [40] provides substantial data on oxidative stress in high altitude conditions, which is consistent with the results obtained on oxidative stress in hypervitaminosis D. An increase in lipid peroxidation markers and changes in antioxidant protection were found, confirming the role of oxidative stress in the pathogenesis of hypoxic lesions. Histochemical studies have confirmed the presence of structural changes in various organs, which explains the systemic nature of lesions when hypoxia and hypervitaminosis D are combined. A.E. Ahmed *et al*. [41] demonstrated peculiarities of metabolic disorders in high-altitude populations, which complements the data obtained on age characteristics. The prevalence of metabolic syndrome and its components among high-altitude residents was analysed, confirming the relevance of considering the age factor. Age and gender characteristics of lipid metabolism disorders and cardiometabolic risks were established, which is relevant for the development of prevention strategies.

A study by L. Jie *et al*. [42] on a rat model with comorbid osteoarthritis and osteoporosis demonstrated that the alkaloid palmatine can effectively influence bone tissue metabolism disorders by modulating the intestinal microflora and host metabolism. This highlights the potential role of prebiotics, probiotics, or metabolically active compounds in correcting Ca-P metabolism disorders, especially when they are associated with systemic inflammation and metabolic syndrome, which often accompany ageing. Similar approaches that aim to restore intestinal homeostasis may improve mineral absorption and tissue sensitivity to vitamin D. Insulin-like growth factor-1 can be integral in restoring renal function and bone metabolism. As noted by J.M.D. Tocados *et al*. [43], IGF-1 has pleiotropic effects in renal diseases, including anti-fibrotic and anti-apoptotic actions and involvement in the regulation of phosphate homeostasis. Therefore, strategies aimed at supporting or modulating the IGF-1 pathway are useful for protecting the kidneys from damage caused by both hypercalcaemia in hypervitaminosis D and ischaemia under conditions of hypoxia, thereby indirectly improving the regulation of Ca-P metabolism. When considering correction of the FGF23-Klotho axis, it is necessary to address the latest insights into the regulation of FGF23. S. Dastghaib *et al*. [44] emphasised the complex regulation of FGF23 expression and secretion, which depends not only on phosphate levels, but also on inflammatory cytokines, iron and oxidative stress. This creates opportunities for indirect influence on FGF23 through control of these factors, for example, with antioxidants or anti-cytokine therapy, which is relevant in hypervitaminosis D, accompanied by powerful oxidative stress. A fundamental aspect of any vitamin D-related correction remains its receptor (VDR). The molecular mechanisms of vitamin D3 action via VDR in different tissues are described in detail by V. Morsanuto [45]. Determination of the tissue-specific modulation of VDR-dependent pathways contributes to the development of selective vitamin D receptor modulators that would have protective effects on bones and kidneys, minimising the risk of soft tissue calcification during the correction of hypovitaminosis or excess. The potential role of vitamin D3 as a protector against hypoxic damage is noteworthy, as it can be substantial for patients in high altitudes. A study by C. Dai *et al*. [46] showed that vitamin D3 reduces hypoxia-induced lung damage by suppressing the complement system, coagulation, and autophagy pathways. This suggests that adequate (but not excessive) vitamin D levels are a substantial factor in resistance to hypoxic stress, particularly for protecting the vascular endothelium and preventing microvascular complications that exacerbate Ca-P metabolism disorders. Integrating the results of these studies formed a comprehensive pathogenetic model. The combination of hypervitaminosis D and hypoxia leads to a synergistic increase in Ca-P metabolism disorders through several interrelated mechanisms. Hypoxia-induced renal dysfunction limits phosphate excretion, exacerbating hyperphosphataemia.

Adaptation of vitamin D metabolism in the form of increased CYP27B1 expression under conditions of substrate excess leads to hypercalcitriolaemia. Age-related features determine the direction of organ damage – from calcification to osteomalacia.

Conclusions

Based on a systematic analysis of the literature, Ca-P metabolism is defined as a complex integrated network in which vitamin D metabolism is central. The key mechanism for maintaining homeostasis is the dynamic balance between parathyroid hormone (a stimulator of calcitriol synthesis) and FGF23 (its inhibitor), and the Ca/P ratio in blood plasma can serve as an integral indicator of the state of the system. A review of experimental data shows that hypervitaminosis D leads to a complex pathological condition characterised not only by pronounced hypercalcaemia and hyperphosphataemia, but also by severe oxidative stress, systemic inflammation, suppression of PTH secretion, compensatory increase in FGF23, and activation of the CYP24A1 inactivation enzyme. This leads to a high risk of soft tissue calcification and paradoxical bone mineralisation disorders.

The age factor determines fundamental changes in the reactivity of the Ca-P exchange system. The most substantial link is the age-related decrease in the expression of the Klotho co-receptor, which leads to renal resistance to FGF23, progression of hyperphosphataemia, renal dysfunction and impaired bone-muscle cross-flow. In young organisms, disorders prevail in the kinetics of bone formation, while in older organisms, they prevail in remodelling, leading to osteomalacia and osteoporosis. Altitude hypoxia acts as a substantial modulator that exacerbates Ca-P homeostasis disorders through a range of mechanisms: it causes a characteristic electrolyte imbalance (hypocalcaemia and hyperphosphataemia), contributes to renal dysfunction, inhibits Klotho expression, modulates the activity of renal phosphate transporters, and increases CYP27B1 expression. The latter, in conditions of excess vitamin D intake, can contribute to uncontrolled calcitriol synthesis. This synthesis suggests a synergistic effect between hypervitaminosis D, hypoxia, and ageing. This synergy may be realised through the mutual reinforcement of the following links: renal dysfunction under hypoxia limits phosphate excretion, exacerbating hyperphosphataemia from vitamin D, and increased CYP27B1 expression under hypoxia contributes to excessive calcitriol formation. Age-related Klotho deficiency and decreased functional reserves create the basis for a more severe course of such combined lesions.

A review of the literature indicates the promise of multi-level approaches to correction, including optimisation of the dietary Ca/P ratio, use of substances to modulate the FGF23-Klotho axis and combat oxidative stress, use of non-pharmacological methods (physical exercise), as well as strategies for renoprotection and adaptation to hypoxia. Some studies also highlight the potential role of modulation of the microbiome, the IGF-1 pathway, selective VDR modulators, and adequate vitamin D levels in protecting against hypoxic damage. Prospects for further research include experimental verification of the synergy of factors in a single model, study of the molecular mechanisms of cross-interaction between HIF and VDR pathways, as well as preclinical and clinical evaluation of comprehensive corrective approaches.

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Conflict of Interest

None.

References

[1] Kolosovych IV, Hanol IV. The role of phosphorus-calcium homeostasis and vitamin D in the pathogenesis of acute pancreatitis and assessment of its severity. Physiol J. 2022;68(3):61–7. DOI: 10.15407/fz68.03.061
[2] Sun M, Wu X, Yu Y, Wang L, Xie D, Zhang Z, et al. Disorders of calcium and phosphorus metabolism and the proteomics/Metabolomics-based research. Front Cell Dev Biol. 2020;8:576110. DOI: 10.3389/fcell.2020.576110
[3] Çaykara B, Öztürk G, Mutlu HH, Arslan E. Relationship between vitamin D, calcium, and phosphorus levels. J Acad Res Med. 2020;10(3):252–7. DOI: 10.4274/jarem.galenos.2020.3351
[4] Bikle DD. Vitamin D: Newer concepts of its metabolism and function at the basic and clinical level. J Endocr Soc. 2020;4(2):bvz038. DOI: 10.1210/jendso/bvz038
[5] Bikle D, Christakos S. New aspects of vitamin D metabolism and action – addressing the skin as source and target. Nat Rev Endocrinol. 2020;16:234–52. DOI: 10.1038/s41574-019-0312-5
[6] Saponaro F, Saba A, Zucchi R. An update on vitamin D metabolism. Int J Mol Sci. 2020;21(18):6573. DOI: 10.3390/ijms21186573
[7] Papadopoulou A, Bountouvi E, Karachaliou FE. The molecular basis of calcium and phosphorus inherited metabolic disorders. Genes. 2021;12(5):734. DOI: 10.3390/genes12050734
[8] Shaikh NA, Chen JR, Baylink DJ, Tang X. Vitamin D-mediated regulation of intestinal stem cells 2297. J Immunol. 2025;214(1):vkaf283.232. DOI: 10.1093/jimmun/vkaf283.232

[9] Hossain A. Hypovitaminosis D: A modifiable risk factor for noncommunicable diseases [Master's thesis]. Dhaka: BRAC University; 2022.
[10] Noonan ML. Linking osteocyte oxygen sensing and biomineralization via FGF23: Implications for chronic kidney disease [Doctoral dissertation]. Indianapolis: Indiana University-Purdue University Indianapolis; 2022.
[11] Zhang B, Podolskiy DI, Mariotti M, Seravalli J, Gladyshev VN. Systematic age-, organ-, and diet-associated ionome remodeling and the development of ionomic aging clocks. Aging Cell. 2020;19(5):e13119. DOI: 10.1111/acel.13119
[12] Areco VA, Kohan R, Talamoni G, de Talamoni NGT, López MEP. Intestinal Ca^{2+} absorption revisited: A molecular and clinical approach. World J Gastroenterol. 2020;26(24):3344–64. DOI: 10.3748/wjg.v26.i24.3344
[13] Miller WL, Imel EA. Rickets, vitamin D, and Ca/P metabolism. Horm Res Paediatr. 2022;95(6):579–92. DOI: 10.1159/000527011
[14] Bellavia D, Costa V, De Luca A, Maglio M, Pagani S, Fini M, et al. Vitamin D level between calcium-phosphorus homeostasis and immune system: New perspective in osteoporosis. Curr Osteoporos Rep. 2024;22(6):599–610. DOI: 10.1007/s11914-016-0331-2
[15] Gutiérrez OM, Porter AK, Viggeswarapu M, Roberts JL, Beck GR. Effects of phosphorus and calcium to phosphorus consumption ratio on mineral metabolism and cardiometabolic health. J Nutr Biochem. 2020;80:108374. DOI: 10.1016/j.jnutbio.2020.108374
[16] De Vincentis S, Del Sindaco G, Pagnano A, Brigante G, Moretti A, Zirilli L, et al. Application of calcium-to-phosphorus (Ca/P) ratio in the diagnosis of pseudohypoparathyroidism: Another piece in the puzzle of diagnosis of Ca-P metabolism disorders. Front Endocrinol. 2023;14:1268704. DOI: 10.3389/fendo.2023.1268704
[17] El-Boshy M, Refaat B, Almaimani RA, Abdelghany AH, Ahmad J, Idris S, et al. Vitamin D3 and calcium cosupplementation alleviates cadmium hepatotoxicity in the rat: Enhanced antioxidative and anti-inflammatory actions by remodeling cellular calcium pathways. J Biochem Mol Toxicol. 2020;34(3):e22440. DOI: 10.1002/jbt.22440.
[18] Gurudatta M. An evaluation of role of Vitamin D in the pathophysiology of streptozotocin induced type-ii diabetes mellitus in rats and its impact on oral hypoglycemic/antidiabetic agents [Doctoral thesis]. Vijayapur: BLDE; 2022.
[19] Nowacka A, Śniegocki M, Bożiłow D, Ziółkowska EA. CYP24A1 in small intestinal Vitamin D metabolism and clinical implications. Nutrients. 2025;17(21):3348. DOI: 10.3390/nu17213348
[20] Durup D, Diaz-delCastillo M, Morgenlykke J, Jensen LT, Frandsen E, Abelson KS, et al. Hypophosphatemic hypovitaminosis D Induces osteomalacia in the adult female rat. Endocrinology. 2020;161(8):bqaa100. DOI: 10.1210/endocr/bqaa100
[21] Argano C, Torres A, Orlando V, Cangialosi V, Maggio D, Pollicino C, et al. Molecular insight into the role of vitamin D in immune-mediated inflammatory diseases. Int J Mol Sci. 2025;26(10):4798. DOI: 10.3390/ijms26104798
[22] Devi S. A review on Klotho: FGF23 mediated pathway integration and aging. J Gerontol Geriatr. 2025;73(3):92–108. DOI: 10.36150/2499-6564-n819
[23] Wang S, Xu Q, Zhang Y, Jiang X, Wang N, Hu Y, et al. The FGF23-Klotho axis promotes microinflammation in chronic kidney disease. Cytokine. 2024;184:156781. DOI: 10.1016/j.cyto.2024.156781
[24] Huang DX, Kang X, Jiang LJ, Zhu DL, Yang L, Luo JY, et al. Exploring the impact of high-altitude de-acclimatization on renal function: The roles of oxidative and endoplasmic reticulum stress in rat models. Biochem Biophys Res Commun. 2024;708:149770. DOI: 10.1016/j.bbrc.2024.149770
[25] Kirk B, Lombardi G, Duque G. Bone and muscle crosstalk in ageing and disease. Nat Rev Endocrinol. 2025;21:375–90. DOI: 10.1038/s41574-025-01088-X
[26] Li T, Xing G, Shao Y, Zhang L, Li S, Lu L, et al. Dietary calcium or phosphorus deficiency impairs the bone development by regulating related calcium or phosphorus metabolic utilization parameters of broilers. Poult Sci. 2020;99(6):3207–14. DOI: 10.1016/j.psj.2020.01.028
[27] Jiampochaman S, Chuengsaman P, Kanjanabuch T, Susantitaphong P, Sriudom K, Katesomboon S, *et al*. A comparison between severity-dependent protocol and fixed-dose regimen of oral vitamin D supplementation on correction of hypovitaminosis D among dialysis patients. J Ren Nutr. 2025;35(2):353–63. DOI: 10.1053/j.jrn.2024.11.002
[28] Palubiski LM, O'Halloran KD, O'Neill J. Renal physiological adaptation to high altitude: A systematic review. Front Physiol. 2020;11:756. DOI: 10.3389/fphys.2020.00756
[29] Wang SY, Gao J, Zhao JH. Effects of high altitude on renal physiology and kidney diseases. Front Physiol. 2022;13:969456. DOI: 10.3389/fphys.2022.969456
[30] Yan C, Tian D, Zhang C, Zhang Q, Sun Y. Evaluation of blood cellular and biochemical parameters in rats under a chronic hypoxic environment at high altitude. Ann Med. 2023;55(1):898–907. DOI: 10.1080/07853890.2023.2184859

[31] Chen X, An Z, Wei L, Zhang J, Li J, Wang Z, et al. Vitamin D3 metabolic enzymes in plateau Zokor (Myospalax baileyi) and plateau Pika (Ochotona curzoniae): Expression and response to hypoxia. Animals. 2022;12(18):2371. DOI: 10.3390/ani12182371
[32] Almanzar G, Alarcon JC, Garzon R, Navarro AM, Ondo-Méndez A, Prelog M. Hypoxia and activation of hypoxia inducible factor alpha as influencers of inflammatory helper T cells in autoimmune disease – a link between cancer and autoimmunity. Front Immunol. 2025;16:1633845. DOI: 10.3389/fimmu.2025.1633845
[33] Liu BH, Chong FL, Yuan CC, Liu YL, Yang HM, Wang WW, et al. Fucoidan ameliorates renal injury-related calcium-phosphorus metabolic disorder and bone abnormality in the CKD-MBD model rats by targeting FGF23-klotho signaling axis. Front Pharmacol. 2021;11:586725. DOI: 10.3389/fphar.2020.586725
[34] Zhang J, Cao ZB. Exercise: A possibly effective way to improve vitamin D nutritional status. Nutrients. 2022;14(13):2652. DOI: 10.3390/nu14132652
[35] Beck WR, Scariot PP, Papoti M, Pejon TM, Polisel EEC, Manchado-Gobatto FB, et al. Living high-training low on mice bone parameters analyzed through complex network approach. Int J Sports Med. 2025;46(1):32–40. DOI: 10.1055/a-2361-2840
[36] Melnyk O, Chendey I, Zukow W, Plyska O, Popovych I. The features of reactions to acute stress of neuro-endocrine-immune complex, metabolome, ECG and gastric mucosa in rats with various state of innate muscular endurance and resistance to hypoxia. J Educ Health Sport. 2023;38(1):96–128. DOI: 10.12775/jehs.2023.38.01.007
[37] Sivertsson E, Friederich-Persson M, Persson P, Nangaku M, Hansell P, Palm F. Thyroid hormone increases oxygen metabolism causing intrarenal tissue hypoxia; A pathway to kidney disease. PLoS One. 2022;17(3):e0264524. DOI: 10.1371/journal.pone.0264524
[38] Du Y, Qi M, Wang W, Chen B. Effect of high-altitude hypoxia environment on uric acid excretion, desmin protein level in podocytes, and Na+-K+-ATPase activity. Cell Mol Biol. 2022;68(6):84–91. DOI: 10.14715/cmb/2022.68.6.14
[39] Chang D, Kong F, Jiang W, Li F, Zhang C, Ding H, et al. Effects of L-carnitine administration on sperm and sex hormone levels in a male Wistar rat reproductive system injury model in a high-altitude hypobaric hypoxic environment. Reprod Sci. 2023;30(7):2231–47. DOI: 10.1007/s43032-022-00948-5
[40] Soliman MM, Aldhahrani A, Althobaiti F, Ahmed MM, Sayed S, Alotaibi S, et al. Characterization of the impacts of living at high altitude in Taif: Oxidative stress biomarker alterations and immunohistochemical changes. Curr Issues Mol Biol. 2022;44(4):1610–25. DOI: 10.3390/cimb44040110
[41] Ahmed AE, Alsamghan A, Momenah MA, Alqhtani HA, Aldawood NA, Alshehri MA, et al. Metabolic syndrome and cardiometabolic risk factors in the mixed hypercholesterolemic populations with respect to gender, age, and obesity in Asir, Saudi Arabia. Int J Environ Res Public Health. 2022;19(22):14985. DOI: 10.3390/ijerph192214985
[42] Jie L, Ma Z, Gao Y, Shi X, Yu L, Mao J, et al. The mechanism of palmatine-mediated intestinal flora and host metabolism intervention in OA-OP comorbidity rats. Front Med. 2023;10:1153360. DOI: 10.3389/fmed.2023.1153360
[43] Tocados JMD, Gómez AP, Coral JDD, Valdivielso JM. The multiple functions of insulin-like growth factor 1 in kidney disease. Nephrology. 2025;45(7):501337. DOI: 10.1016/j.nefro.2025.501337
[44] Dastghaib S, Koohpeyma F, Shams M, Saki F, Alizadeh A. New concepts in regulation and function of the FGF23. Clin Exp Med. 2023;23(4):1055–66. DOI: 10.1007/s10238-022-00844-X
[45] Morsanuto V. Biological effects of Vitamin D3 mediated by the interaction with VDR in different tissues [Doctoral thesis]. Vercelli: University of Eastern Piedmont; 2020. DOI: 10.20373/Uniupo/openthesis/115021
[46] Dai C, Lin X, Qi Y, Wang Y, Lv Z, Zhao F, et al. Vitamin D3 improved hypoxia-induced lung injury by inhibiting the complement and coagulation cascade and autophagy pathway. BMC Pulm Med. 2024;24:9. DOI: 10.1186/s12890-023-02784-Y

Эксперименталдык D витамини гипервитаминозу шартында ар кандай бийиктиктерде жана анын түзөтүү жолдору аркылуу жаш жана кары чычкандардагы фосфор-кальций метаболизминин абалы

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Аннотация. Бул изилдөөнүн максаты – гипервитаминоз D, бийиктиктеги гипоксия жана куракты айкалышкан таасири астында кальций-фосфор алмашуунун бузулуу механизмдери боюнча учурдагы илимий маалыматтарды системалуу талдоо жана синтездоо, ошондой эле натыйжалуу түзөтүү ыкмаларын негиздөө болду. Илимий булактар салыштырма талдоо, маалыматтарды синтездоо жана маалыматты жалпылоо ыкмалары менен талданды. Талдоо көрсөткөндөй, Ca-P метаболизмин жөнгө салуу системасы – бул татаал тармак, анын борборунда D витаминин метаболизми турат, ал эми паратирин гормону менен FGF23 ортосундагы тең салмактуулук плазмадагы Ca жана P деңгээлин туруктуу кармап турууга жооптуу. Илимий булактарды талдоо метаболикалык бузулуулардын куракка байланыштуу мүнөздүү өзгөчөлүктөрүн аныктады. Маалыматтар сөөк ремоделирлөө деңгээли жогору болгон жаш организмдерде Ca/P теңсиздиги сөөк минералдык тыгыздыгынын 12-18 %га кыскарышына алып келерин көрсөттү, ал эми карыган организмдерде функционалдык резервдердин азайышы шартында прогрессивдүү остеомаляция жана бөйрөк жетишсиздигинин өнүгүшү тууралуу маалыматтар үстөмдүк кылат. Жогорку бийиктиктеги гипоксиянын таасири боюнча жүргүзүлгөн изилдөөлөрдүн обзору анын бөйрөк функциясынын бузулушун (креатининдин 0,81 ± 0,04 мг/длге чейин жогорулашы), электролиттердин теңсиздиги (кальцийдин 8,1 ± 0,6 мг/длге чейин төмөндөшү жана фосфордун 7,1 ± 0,4 мг/длге чейин жогорулашы) жана D витаминин метаболизминин адаптациясы, өзгөчө CYP27B1 экспрессиясынын жогорулашы аркылуу. Анализдин жыйынтыгында алынган корутундулар жогорку тоолуу аймактарда жашаган ар кандай курактагы бейтаптарга D витаминин коопсуз кошумча берүү боюнча илимий негизделген сунуштарды мындан ары иштеп чыгууда теориялык мааниге ээ

Негизги сөздөр: паратирин гормон; остеомаляция; жогорку бийиктиктеги гипоксия; куракка байланыштуу өзгөчөлүктөр; бөйрөк жетишсиздиги

Состояние фосфоро-кальциевого обмена у молодых и старых крыс в условиях экспериментального гипервитаминоза витамина D на разных высотах и способы его коррекции

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Аннотация. Целью данного исследования было систематическое анализирование и обобщение современных научных данных о механизмах нарушений кальций-фосфорного обмена под комбинированным воздействием гипервитаминоза D, высотной гипоксии и возраста, а также обоснование эффективных корректирующих подходов. Научные источники были проанализированы с использованием методов сравнительного анализа, синтеза данных и обобщения информации. Проведенный анализ показал, что система регуляции метаболизма Ca-P представляет собой сложную сеть, в центре которой находится метаболизм витамина D, где баланс между паратиреоидным гормоном и FGF23 определяет стабильность уровней Ca и P в плазме. Анализ научных источников выявил характерные возрастные особенности нарушений метаболизма. Данные показали, что у молодых организмов с высоким уровнем ремоделирования костей дисбаланс Ca/P может привести к значительному снижению минеральной плотности костей (на 12-18 %), тогда как у пожилых организмов преобладают данные о развитии прогрессирующей остеомаляции и почечной недостаточности на фоне снижения функциональных резервов. Обзор исследований по влиянию высокогорной гипоксии показал, что она может вызывать комплекс нарушений, в том числе почечную дисфункцию (повышение креатинина до 0,81 ± 0,04 мг/дл), электролитного дисбаланса (снижение кальция до 8,1 ± 0,6 мг/дл при повышении фосфора до 7,1 ± 0,4 мг/дл) и адаптации метаболизма витамина D, в частности, за счет повышения экспрессии CYP27B1. Выводы, полученные в результате анализа, имеют теоретическое значение для дальнейшей разработки научно обоснованных рекомендаций по безопасному добавлению витамина D в рацион пациентов разных возрастных групп, проживающих в высокогорных регионах

Ключевые слова: паратиреоидный гормон; остеомаляция; высокогорная гипоксия; возрастные особенности; почечная недостаточность

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The air crisis: The escalating effects of climate change on the respiratory system

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Abstract. Climate change is increasingly recognised as a serious threat to respiratory health, making it essential to understand how changing environmental conditions affect lung function and the pattern of respiratory diseases. This review aimed to summarise current scientific evidence on the effects of rising temperatures, altered weather patterns, and deteriorating air quality on the global burden of respiratory diseases. A comprehensive analysis of the latest peer-reviewed literature, including epidemiological studies, systematic reviews, and reports from international health organisations, was conducted. Climate-related environmental factors were analysed in relation to observed trends in respiratory health indicators. The findings indicated that climate-driven environmental changes have a substantial impact on respiratory health. Elevated concentrations of ground-level ozone, wildfire smoke, and fine particulate matter are consistently associated with increased respiratory symptoms and exacerbations of asthma and chronic obstructive pulmonary disease (COPD). Rising atmospheric carbon dioxide levels and altered seasonal cycles contribute to longer and more intense pollen seasons, increasing exposure to aeroallergens. Extreme weather events, including heatwaves, heavy precipitation, and flooding, promote indoor mould growth and heighten the risk of respiratory infections. The most vulnerable populations – particularly children, the elderly, and socio-economically disadvantaged communities – bear a disproportionately higher disease burden due to greater exposure and limited adaptive capacity. The results of this review provide a scientific basis for public health planning and clinical decision-making, and may inform targeted mitigation and adaptation strategies aimed at reducing climate-related respiratory risks among vulnerable populations

Keywords: ground-level ozone; particulate matter; dust storms; aeroallergens; chronic obstructive pulmonary disease; mitigation; adaptation

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Introduction

Climate change is increasingly being recognised not just as an environmental problem, but as a major threat to human health – especially to respiratory health. The Earth is warming faster than ever before, weather patterns are becoming more unpredictable, and extreme events such as wildfires, dust storms, and floods are occurring more frequently. Because the lungs and airways represent the primary interface between the human body and the environment, any deterioration in air quality or climatic instability can have immediate and serious consequences for respiratory health. This subject is especially urgent now, given the latest surge in climate-driven air pollution episodes, wildfire smoke events, extended pollen seasons, and extreme weather across the globe – making it essential to examine how these changes affect breathing and lung disease rates.

A growing body of research from 2020 onward has started to document these connections in detail. For instance, a comprehensive review by the American Lung Association [1] explained that hotter, drier climates lead to more frequent and severe wildfires and dust storms, elevating levels of fine particulate matter ($PM_{2.5}$) and other pollutants which harm lung health. Similarly, a study by H. Bayram *et al*. [2] reported that rising temperatures and increased particulate matter and ozone levels exacerbate chronic respiratory diseases, extend pollen seasons, boost dust pollution in arid regions, and worsen risks from indoor mould after flooding – particularly affecting children and the elderly.

More specifically, J.-H. Chang *et al*. [3] argued that climate change not only increases the concentration of airborne particles, but may also alter the physicochemical properties (size, chemical composition, dispersion) in ways that facilitate deeper and more harmful deposition in the lungs – thereby raising the risk of developing or exacerbating respiratory diseases. Another systematic review by B. Rackow *et al*. [4] found that high temperatures combined with elevated levels of ozone (O_3), particulate matter (PM_{10}, $PM_{2.5}$), and nitrogen dioxide (NO_2) synergistically amplify mortality risk and worsen respiratory and cardiovascular conditions.

Moreover, the technical brief by the World Health Organisation [5] highlighted how climate change influences allergen dynamics – leading to earlier, longer, and more intense pollen seasons, increased mould proliferation after flooding, and greater exposure to airborne allergens, all of which contribute to rising incidence of allergic respiratory diseases such as asthma and allergic rhinitis. Complementing this, S.-Z. Deng *et al*. [6] emphasised the interactive, compounding effects of climate change, pollution, and aeroallergens on respiratory health – noting that extreme weather events and air pollution can intensify allergenicity and harm airway health.

Despite this growing evidence, important gaps remain. Most studies examined single factors – such as pollution, pollen, or weather extremes – in isolation. There is far less research that integrates multiple climate-related stressors (e.g., combined air pollution, allergen changes, extreme weather) into comprehensive models that reflect real-world exposure scenarios. Furthermore, very few of these studies focus on populations in Central Asia or other regions where rapid climate change is intersecting with social and economic vulnerabilities. As a result, there is limited region-specific data on how combined climate change impacts affect respiratory health in such contexts. This gap justifies the present research. The aim of this study was to systematically assess how the combined effects of climate-driven air pollution, changing allergen exposure (pollen, mould), and extreme weather events interact to influence the prevalence and severity of respiratory diseases – particularly among vulnerable populations in under-studied regions.

Materials and Methods

The present study was designed as a comparative systematic review of the scientific literature analysing the relationships between climatic factors, atmospheric air pollution, and the state of respiratory health in the population. The primary objective of the analysis was to identify the mechanisms through which climate-related environmental changes influence the concentrations of major atmospheric pollutants and the associated risks to the respiratory system. The search for scientific publications was conducted in international scientific databases. The review included studies published between 2010 and 2025, allowing the analysis to capture the most relevant research reflecting current trends in climate change and air quality.

The following keywords and the combinations were used for the search: "$PM_{2.5}$", "PM_{10}", "ozone", "air pollution", "climate change", "heat", "humidity", "dust storms", "stubble burning", "coal heating", "India", "Kyrgyzstan", "respiratory diseases", "vulnerable populations". The inclusion criteria involved selecting scientific articles that addressed the following aspects: the influence of climatic factors (temperature, humidity, precipitation, and extreme weather events) on the concentrations of atmospheric pollutants; the impact of air pollution on respiratory health in the population; as well as studies examining the main anthropogenic emission sources, including agricultural biomass burning, transport emissions, and the use of coal for heating. In addition, publications from international health organisations and environmental agencies containing statistical data on morbidity and mortality associated with air pollution were also considered. India and the Kyrgyz Republic were selected as regions for comparative analysis, which made it possible to examine the formation of air pollution under different climatic and socio-economic conditions [7,8].

During the analysis, data were extracted from the selected publications on pollutant concentrations ($PM_{2.5}$, PM_{10} and O_3), meteorological conditions, anthropogenic emission sources, and indicators of respiratory morbidity among different age and socio-economic population groups. Particular attention was paid to vulnerable groups, including children, older adults, and low-income populations. The collected data were systematised and analysed using a comparative descriptive approach. The results of studies conducted in India and the Kyrgyz Republic were considered separately, after which the identified trends and risk factors were compared. This approach made it possible to identify both general patterns in the influence of climate change on atmospheric air pollution and regional characteristics of its impact on respiratory health.

Results and Discussion

Influence of climatic factors on atmospheric pollutant composition

Climate change directly affects concentrations of particulate matter and ozone in the air, thereby increasing the risks of respiratory diseases. Sand and dust storms substantially elevate the levels of suspended particles, even at significant distances from the source. The World Health Organisation (WHO) [9] noted that such storm episodes directly impact air pollution, as the storms increase airborne particulate concentrations. In some regions, lifted dust constitutes the primary source of these particles. However, around 25% of dust emissions are linked to human activities, including deforestation, poor land management, and climate change. Expansion of arid areas under global warming leads to more frequent and intense storms, increasing dust suspension. This allows dust to penetrate deep into the respiratory tract, exacerbating asthma and chronic obstructive pulmonary disease (COPD) [10].

Higher temperatures and humidity accelerate chemical processes in the atmosphere, altering aerosol composition. For example, a study by Y. Park *et al*. [11] in Korea showed that nocturnal relative humidity increases aerosol liquid water content (ALWC), facilitating the conversion of nitrates into the condensed particle phase. This indicates that in India's hot and humid seasonal atmosphere, "wetter" $PM_{2.5}$ particles form, capable of absorbing more toxic components. Elevated temperatures also enhance the photochemical formation of ground-level ozone (O_3). As F. Rosser & J. Balmes [12] indicated, ozone is a highly toxic substance for the respiratory tract and is associated with multiple cases of childhood asthma. In South Asian countries, including India, ground-level O_3 rises during warm seasons; US data show that a third of the population experiences ozone concentrations exceeding standards, and climate change further increases O_3, reducing the effectiveness of existing control measures. The WHO emphasised that reducing greenhouse gas emissions can improve air quality, mitigating climate change impacts [10].

These findings demonstrated that climate change significantly alters air pollution dynamics, particularly fine particulate matter and ground-level ozone, with substantial respiratory health consequences. Rising ambient temperatures enhance photochemical reactions, increasing ozone formation, especially under stagnant atmospheric conditions. In India, heatwaves amplify ozone production in urban and suburban areas, leading to persistent smog episodes and increased exposure to respiratory irritants, as noted by X. Li *et al*. [13]. The authors' study reported links between elevated ozone levels and worsening asthma symptoms, breathlessness, and emergency healthcare visits. $PM_{2.5}$ particles become more chemically active and penetrate deeper into the lungs due to altered hygroscopic properties, increasing the incidence of respiratory inflammation. According to WHO data, particulate pollution is directly associated with cardiovascular and respiratory diseases, causing 4.2 million premature deaths in 2019 [10].

E.E. McDuffie *et al*. [14] also observed that a substantial proportion of global mortality related to $PM_{2.5}$ exposure arises from fossil fuel combustion, which forms a persistent background of aerosol pollution in the atmosphere. The authors estimated that these emissions are associated annually with over one million premature deaths, mainly from cardiovascular and respiratory diseases. The findings underline that reducing fossil fuel use could substantially lower the global disease burden due to air pollution. The authors also highlighted that low-income populations face increased risks because of being more frequently exposed to heavily polluted air and having limited protection. Consequently, assessing impacts requires considering not only emission levels but also the modifying influence of climate on particle behaviour in the atmosphere and respiratory tract.

Comparative analysis of anthropogenic emissions in India and Kyrgyzstan

India and Kyrgyzstan exhibit distinct local pollution sources, interacting with the respective climatic conditions. In India, average indoor $PM_{2.5}$ concentrations frequently exceed international health standards, reflecting combined exposure from ambient pollution, transport emissions, biomass burning, and seasonal agricultural residue combustion. Episodic $PM_{2.5}$ spikes during crop residue burning in the Indo-Gangetic Plain coincide with observed increases in bronchitis, asthma exacerbations, and hospital admissions. G. Govardhan *et al*. [15] analysed the impact of agricultural residue burning in northwestern India on Delhi's air quality using satellite data and atmospheric modelling. The model estimated that during peak fire periods, fires contributed approximately 30-35% of $PM_{2.5}$

concentrations in Delhi's atmosphere. Unfavourable meteorological conditions further enhance pollutant accumulation. The authors concluded that agricultural biomass burning is a significant regional source of seasonal air pollution and must be considered when developing air quality improvement measures. Under stagnant wind and inversion conditions, this contribution can rise sharply. G. Dipoppa & S. Gulzar [8] estimated that open stubble burning accounts for 40-60% of peak winter pollution, affecting not only farmers but millions of urban residents. The authors' study also noted that increased $PM_{2.5}$ exposure from fires correlates with reduced birth rates and infant mortality (30-36 cases per 1,000 live births).

In Kyrgyzstan and the surrounding mountains, the situation differs. Winter smog in Bishkek arises primarily from coal heating in homes and industries. Climatic factors interact with local emissions, producing severe seasonal pollution. According to a UNDP/UN report, approximately 70% of households use coal stoves [7]. Burning raw coal results in winter $PM_{2.5}$ concentrations of ~40-50 μg/m^3 in Bishkek [16], three to four times above safe limits. Monitoring confirms this: annual average $PM_{2.5}$ levels in industrial areas exceed standards by more than twofold. In Central Asia, K.O. Dzushupov *et al*. [17] applied spatial pollution modelling to study winter smog formation in Bishkek, showing that temperature inversions, expected to intensify with climate variability, lead to extreme $PM_{2.5}$ levels exceeding 200 μg/m^3. These findings align with the present study, confirming that meteorological factors play a dominant role in respiratory disease burden, in some cases outweighing industrial emissions alone. As noted by J. Xu *et al*. [18] and T. Li *et al*. [19], annual $PM_{2.5}$ levels remain above international standards, posing severe lung risks due to deep alveolar deposition. UNICEF [7] data report 112 deaths and 3,568 years of life lost due to pollution annually, primarily among the elderly and newborns.

Enhanced aeroallergens represent an additional climate-sensitive pathway. P.J. Beggs *et al*. [20] demonstrated through multinational pollen monitoring that elevated atmospheric CO_2 levels and longer warm seasons significantly increase pollen production and exposure duration. These results correspond with pollen-related findings in both India and Kyrgyzstan, confirming that aeroallergens constitute a rapidly growing climate risk to respiratory health. Similarly, N. Singh *et al*. [21] analysed mould prevalence in India post-monsoon and found that rainfall variability and prolonged indoor dampness are associated with worsened asthma symptoms in children. These observations align with the present review, particularly in flood-prone or poorly ventilated housing conditions.

The main distinction between Kyrgyzstan and India is that summer ozone levels in Kyrgyzstan remain close to standards, whereas the primary issue is winter smog. Comparison of India and Kyrgyzstan shows a common finding: local pollution sources (crop fires and coal heating) remain the main contributors, but the effects are amplified by climate conditions (dry air in India and mountain inversions in Kyrgyzstan). Notably, $PM_{2.5}$ remains the most frequently cited pollutant affecting respiratory health in both regions. Vulnerable populations are similarly affected: children, the elderly, low-income households, and residents of highly polluted areas. Consequently, both regions require simultaneous environmental and social interventions: technological measures (fuel cleaning, transition to safe heating) and targeted support for vulnerable families (subsidies, education).

Climate change is also consistently linked to altered aeroallergen dynamics, increasing respiratory disease incidence. Rising atmospheric CO_2 and warming extend and intensify flowering seasons. Data from both regions indicate earlier flowering, increased pollen production, and prolonged exposure periods, particularly affecting individuals with allergic rhinitis and asthma [22]. In India, climate change during the monsoon – characterised by irregular rainfall and prolonged humidity – creates favourable conditions for indoor mould growth. X. Li *et al*. [13] reported increased respiratory symptoms and infection risks in poorly ventilated homes, especially among children and low-income households. In Kyrgyzstan, earlier snowmelt and longer warm seasons similarly prolong pollen exposure in intermontane valleys, correlating with seasonal rises in allergic respiratory diseases.

Vulnerable populations and adaptation strategies

The literature showed that climate impacts disproportionately affect vulnerable populations. Children, the elderly, and socio-economically disadvantaged communities consistently experience higher exposure and greater susceptibility to adverse respiratory outcomes. In both India and Kyrgyzstan, limited access to clean indoor environments, healthcare, and adaptive resources exacerbates the health burden associated with climate change, pollution, and allergens [13].

J. Xu *et al*. [18] and D. Rattanaphra *et al*. [23] documented that young children, the elderly, and socio-economically vulnerable groups suffer most from combined pollution and climate exposures. Children are more sensitive to $PM_{2.5}$: breathe faster, have narrower airways, and particles deposit deeper. D. Rattanaphra *et al*. [23] estimated that children face higher risks than adults at equivalent $PM_{2.5}$ concentrations. Beyond physiological reasons, children and low-income families bear an additional "social risk": children and low-income households often live in damp, unventilated homes without air conditioning, heated with coal stoves. Low income increases proximity to pollution sources (e.g., coal-heavy outskirts) and limits the ability to relocate to cleaner areas, echoing the findings of J. Rentschler & N. Leonova [24].

The present study highlighted several recommendations. Risk mitigation should prioritise adaptive measures for vulnerable populations, particularly children. Technical recommendations include improving microclimates in schools and kindergartens. J. Bonan *et al*. [25] in Italy showed that portable HEPA air purifiers reduced classroom $PM_{2.5}$ concentrations by 32% and decreased school absenteeism due to illness by 12.5%. Implementing such measures in Indian and Kyrgyz preschools could substantially lower children's daily exposure during lessons. For residential areas, insulation and ventilation improvements are crucial. UNICEF in Kyrgyzstan is already working on enhancing school and home insulation and ventilation [26], enabling families to ventilate without heat loss in winter and reducing indoor smog accumulation. Another avenue is promoting alternative fuels and heating: subsidies for clean technologies (heat pumps, gas boilers, solar water heaters) have proven effective. The UNDP/UN [7] report recommended transitioning households from coal to clean energy to reduce peak winter pollution, which simultaneously benefits the climate by lowering greenhouse gas emissions.

Mitigation policy must be integrated: fuel standards should be tightened, and public transport promoted in major cities to reduce baseline pollution. Equally critical are information and protection for vulnerable groups: alerts during pollution peaks, healthcare access, and clear guidance for children and the elderly. All measures are supported by the study by J. Rentschler & N. Leonova [24], which showed that each large-scale adaptation measure (air purification, subsidies, etc.) saves thousands of lives and hundreds of millions in healthcare costs. The study demonstrated that climatic and anthropogenic factors act synergistically, creating environmental and social challenges. Effective population protection requires interdisciplinary strategies tailored to India and Kyrgyzstan and focused on vulnerable groups. Combining climate-oriented analyses with traditional environmental measures allows targeted adaptation programmes. Even simple technical interventions (air purifiers, insulation) alongside a clean energy transition can substantially reduce the adverse impact of pollution on residents' respiratory health. Overall, the reviewed literature aligns strongly with the findings presented in this study. Contemporary evidence consistently shows that climate change amplifies respiratory health risks through multiple interlinked mechanisms, including air pollution, aeroallergens, dust storms, and extreme weather events. While alternative interpretations exist, these interpretations do not undermine the core identified mechanisms. Collectively, data from India, Kyrgyzstan, and global literature confirmed that climate change accelerates respiratory disease incidence, particularly among vulnerable populations, highlighting the need for comprehensive measures to combat climate change and protect respiratory health.

Conclusions

This study demonstrated that climate change and respiratory health are closely interconnected through multiple, mutually reinforcing pathways. The findings indicated that rising global temperatures, increasing frequency of heatwaves, altered atmospheric circulation, and intensification of extreme weather events have significantly modified patterns of air pollution exposure. These environmental changes have increased the concentration and distribution of particulate matter, ozone, and other respiratory irritants, while also affecting the seasonal dynamics of aeroallergens, thereby extending the period during which vulnerable populations experience respiratory stress.

The results further highlighted that populations residing in regions with pre-existing air quality challenges – particularly areas affected by dust events, rapid urbanisation, or industrial emissions – bear a disproportionately high disease burden. Climate-related environmental stressors amplify pre-existing respiratory conditions, including asthma, chronic obstructive pulmonary disease, and allergic airway disorders. Socioeconomic factors, such as limited access to healthcare or protective infrastructure, exacerbate vulnerability and contribute to more severe outcomes. These patterns underscored the need for integrated, long-term mitigation and adaptation strategies at both community and policy levels. Strengthening early-warning systems, enhancing air quality surveillance, and improving public-health preparedness are essential. In addition, the consistent implementation of personal protective measures and community-level behavioural adaptations can substantially reduce exposure to climate-amplified respiratory hazards.

Overall, this study reinforced that climate change constitutes not only an environmental crisis but also a major determinant of respiratory health. Addressing this challenge requires coordinated action across public health, environmental regulation, and clinical care sectors. Despite advances in understanding the relationships between climate stressors and respiratory outcomes, important knowledge gaps remain. Future research should focus on three priority areas: developing precise regional models to predict respiratory disease trends under evolving climate scenarios; investigating biological mechanisms underlying individual susceptibility to climate-related pollutants; evaluating the effectiveness of community-level interventions and adaptive strategies in reducing long-term respiratory disease burden.

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Conflict of Interest

None.

References

[1] American Lung Association. Climate change and lung health [Internet]. [cited 2025 August 18]. Available from: https://www.lung.org/clean-air/climate-change/climate-change-lung-health
[2] Bayram H, Rice MB, Abdalati W, Elci MA, Mirsaeidi M, Annesi-Maesano I, et al. Impact of global climate change on pulmonary health: Susceptible and vulnerable populations. Ann Am Thorac Soc. 2023;20(8):1088–95. DOI: 10.1513/AnnalsATS.202212-996CME
[3] Chang JH, Lee YL, Chang LT, Chang TY, Hsiao TC, Chung KF, et al. Climate change, air quality, and respiratory health: A focus on particle deposition in the lungs. Ann Med. 2023;55(2):2264881. DOI: 10.1080/07853890.2023.2264881
[4] Rackow B, König HH, Wall M, Konnopka C. The interaction between air pollution, weather conditions, and health risks: A systematic review. Sci Total Environ. 2025;996:180080. DOI: 10.1016/j.scitotenv.2025.180080
[5] World Health Organization. Climate change, air pollution, pollen and health [Internet]. 2025 July 17 [cited 2025 August 18]. Available from: https://www.who.int/publications/i/item/B09412
[6] Deng SZ, Jalaludin BB, Antó JM, Hess JJ, Huang CR. Climate change, air pollution, and allergic respiratory diseases: A call to action for health professionals. Chin Med J (Engl). 2020;133(13):1552–60. DOI: 10.1097/CM9.0000000000000861
[7] UN Environment Programme. Ditch coal from homes to tackle air pollution in Bishkek – UN report [Internet]. 2022 October 31 [cited 2025 August 18]. Available from: https://www.unep.org/news-and-stories/press-release/ditch-coal-homes-tackle-air-pollution-bishkek-un-report
[8] Dipoppa G, Gulzar S. Bureaucrat incentives reduce crop burning and child mortality in South Asia. Nature. 2024;634(8036):1125–31. DOI: 10.1038/s41586-024-08046-z
[9] World Health Organization. Sand and dust storms [Internet]. 2025 April 23[cited 2025 August 18]. Available from: https://www.who.int/news-room/fact-sheets/detail/sand-and-dust-storms
[10] World Health Organization. Ambient (outdoor) air quality and health [Internet]. 2024 October 24 [cited 2025 August 18]. Available from: https://surl.li/tbagmc
[11] Park Y, Byun M, Park J, Han S, Kim JJ, Son YS, et al. The evolution of physical and chemical properties of PM2.5 in the developing stage of pollution events in a coastal megacity, South Korea. Atmos Environ. 2025;360:121435. DOI: 10.1016/j.atmosenv.2025.121435
[12] Rosser F, Balmes JR. Ozone and childhood respiratory health: A primer for US pediatric providers and a call for a more protective standard. Pediatr Pulmonol. 2023;58(5):1355–66. DOI: 10.1002/ppul.26368
[13] Li X, Zhou S, Xi X. Assessing short-term exposure risk and mortality burden of dust and fine aerosol PM2.5 in Central Asia. Sci Total Environ. 2025;991:179864. DOI: 10.1016/S0048-9697(25)01505-0
[14] McDuffie EE, Martin RV, Spadaro JV, Burnett R, Smith SJ, O'Rourke P, et al. Source sector and fuel contributions to ambient PM2.5 and attributable mortality across multiple spatial scales. Nat Commun. 2021;12:3594. DOI: 10.1038/s41467-021-23853-y
[15] Govardhan G, Ambulkar R, Kulkarni S, Vishnoi A, Yadav P, Choudhury BA, et al. Stubble-burning activities in north-western India in 2021: Contribution to air pollution in Delhi. Heliyon. 2023;9(6):e16939. DOI: 10.1016/j.heliyon.2023.e16939
[16] UNICEF. The impact of air pollution on the health and social aspects of the lives of women and children in Bishkek, Kyrgyzstan [Internet]. 2022 November [cited 2025 August 18]. Available from: https://www.unicef.org/kyrgyzstan/media/8126/file
[17] Dzushupov KO, Buban JMA, Aidaraliev AA, Ahmadi A, Chahal P, Ibrahim M, et al. Air pollution in Bishkek, Kyrgyzstan: driving factors and state response. Public Health Chall. 2022;1:e22. DOI: 10.1002/puh2.22
[18] Xu J, Su Z, Liu C, Nie Y, Cui L. Climate change, air pollution and chronic respiratory diseases: Understanding risk factors and the need for adaptive strategies. Environ Health Prev Med. 2025;30:7. DOI: 10.1265/ehpm.24-00243
[19] Li T, Cohen AJ, Krzyzanowski M, Zhang C, Gumy S, Mudu P, et al. Sand and dust storms: A growing global health threat calls for international health studies to support policy action. Lancet Planet Health. 2025;9(1):34–40. DOI: 10.1016/S2542-5196(24)00308-5
[20] Beggs PJ, Clot B, Sofiev M, Johnston FH. Climate change, airborne allergens, and three translational mitigation approaches. EBioMedicine. 2023;93:104478. DOI: 10.1016/j.ebiom.2023.104478
[21] Singh N, Singh S, Singh M, Salvi S, Mangal DK, Awasthi S, et al. Risk factors associated with symptoms of asthma in India. Eur Respir J. 2023;62(67):PA4434. DOI: 10.1183/13993003.congress-2023.PA4434
[22] World Health Organization. WHO ambient (outdoor) air quality database [Internet]. 2024 January 31 [cited 2025 August 18]. Available from: https://surl.li/lwoflo

[23] Rattanaphra D, Tawkaew S, Kingkam W, Nuchdang S, Kitpakornsanti K, Suwanmanee U. Health impacts and risk assessment of PM2.5 and PM10 at suburban site in Pathum Thani, Thailand. Toxicol Rep. 2025;15:102109. DOI: 10.1016/j.toxrep.2025.102109
[24] Rentschler J, Leonova N. Global air pollution exposure and poverty. Nat Commun. 2023;14:4432. DOI: 10.1038/s41467-023-39797-4
[25] Bonan J, Granella F, Renna S, Sarmiento L, Tavoni M. The effect of air purifiers in schools [Internet]. 2025 June 11 [cited 2025 August 18]. Available from: https://surl.li/thzdgz
[26] UNICEF. Air pollution in Kyrgyzstan causes major health impacts for children [Internet]. 2023 December 4 [cited 2025 August 18]. Available from: https://surl.li/rqircj

Аба кризиси: климаттын өзгөрүшүнүн дем алуу системасына күчөп жаткан таасирлери

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Аннотация. Климаттын өзгөрүшү дем алуу органдарынын ден соолугу үчүн олуттуу коркунуч катары көбүрөөк таанылып, өзгөрүлүп жаткан экологиялык шарттардын өпкөнүн функциясына жана дем алуу ооруларынын структурасына тийгизген таасирин түшүнүү зарыл экенин көрсөтөт. Бул обзордун максаты – температуранын жогорулашы, аба ырайынын өзгөрүшү жана абанын сапатынын начарлашы глобалдык дем алуу ооруларынын жүгүнө кандай таасир этерин көрсөтүүчү заманбап илимий маалыматтарды бириктирүү. Учурдагы рецензияланган илимий адабият, эпидемиологиялык изилдөөлөр, системалуу обзорлор жана эл аралык саламаттык сактоо уюмдарынын отчеттору кеңири талданды. Климаттык шарттарга байланыштуу экологиялык факторлор дем алуу ден соолуктун көрсөткүчтөрү менен салыштырылды. Талданган маалыматтар климаттык өзгөрүүлөрдүн дем алуу органдарына олуттуу таасир этерин көрсөттү. Жер бетиндеги озон, токой өрттөрүнүн түтүнү жана майда бөлүкчөлүү заттардын жогорку концентрациялары дем алуу белгилеринин күчөшү жана астма менен хроникалык обструктивдүү өпкө оорусунун (ХОБЛ) курчушуна туруктуу байланыштуу. Атмосферадагы көмүр кычкыл газдын деңгээлинин жогорулашы жана мезгилдик циклдердин өзгөрүшү гүлдөө мезгилдеринин узактыгын жана күчтүүлүгүн жогорулатып, аба аллергендерине экспозицияны көбөйтөт. Ысык толкундар, катуу жаан-чачындар жана суунун кирүүсү сыяктуу экстремалдык аба ырайы окуялары ички жердеги көгөрүү менен дем алуу инфекцияларынын тобокелчилигин жогорулатат. Эң назик топтор – айрыкча балдар, кары-картаңдар жана социалдык жактан экономикалык жагынан мүмкүнчүлүгү чектелген коомдор – көбүрөөк таасирге дуушар болуп, оорулардын жүгү пропорциялык эмес жогору. Бул обзордун жыйынтыктары коомдук саламаттык сактоо планын түзүү жана клиникалык чечимдерди кабыл алуу үчүн илимий негизди түзүп, уязвимый топтордун климаттык дем алуу тобокелчилигин азайтууга багытталган максаттуу адаптация жана жеңилдетүү стратегияларын иштеп чыгууга жардам бериши мүмкүн

Негизги сөздөр: жер бетиндеги озон; бөлүкчөлүү заттар; чаңдуу бороон; аба аллергендери; хроникалык обструктивдүү өпкө оорусу; жеңилдетүү; адаптация

Воздушный кризис: усиливающиеся последствия изменения климата для дыхательной системы

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Аннотация. Изменение климата все в большей степени признается серьезной угрозой для здоровья органов дыхания, что делает необходимым понимание того, как изменяющиеся условия окружающей среды влияют на функцию легких и структуру респираторных заболеваний. Целью данного обзора являлось обобщение современных научных данных о влиянии повышения температуры, изменения погодных условий и ухудшения качества воздуха на рост глобального бремени респираторных заболеваний. Был проведен всесторонний анализ современной рецензируемой научной литературы, включая эпидемиологические исследования, систематические обзоры и отчеты международных организаций здравоохранения. Данные о климатически обусловленных факторах окружающей среды анализировались в сопоставлении с зарегистрированными тенденциями показателей респираторного здоровья. Проанализированные данные засвидетельствовали о том, что климатически обусловленные изменения окружающей среды оказывают значительное влияние на здоровье органов дыхания. Повышенные концентрации приземного озона, дыма лесных пожаров и мелкодисперсных твердых частиц устойчиво ассоциированы с усилением респираторных симптомов и учащением обострений бронхиальной астмы и хронической обструктивной болезни легких (ХОБЛ). Повышение уровня углекислого газа в атмосфере и изменения сезонных циклов способствуют удлинению и усилению сезонов пыления, увеличивая воздействие аэроаллергенов. Экстремальные погодные явления, включая волны жары, интенсивные осадки и наводнения, способствуют росту плесени в помещениях и повышают риск респираторных инфекций. Наиболее уязвимые группы населения, особенно дети, пожилые люди и социально неблагополучные сообщества, несут непропорционально более высокое бремя заболеваний вследствие большей экспозиции и ограниченных адаптационных возможностей. Результаты данного обзора формируют научную основу для планирования мер общественного здравоохранения и клинического принятия решений, а также могут способствовать разработке целевых стратегий смягчения и адаптации, направленных на снижение климатически обусловленных респираторных рисков среди уязвимых групп населения

Ключевые слова: приземный озон; твёрдые частицы; пыльные бури; аэроаллергены; хроническая обструктивная болезнь лёгких; смягчение последствий; адаптация

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