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Osteopathic treatment of temporomandibular joint dysfunction

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Abstract. Temporomandibular joint dysfunction (TMD) is among the most prevalent disorders of the maxillofacial region and has a substantial negative impact on patients' quality of life. In recent years, growing interest has been directed toward non-pharmacological treatment strategies, including osteopathic manual therapy. The aim of this study was to assess the clinical effectiveness of osteopathic manipulative treatment and cranial osteopathy in patients diagnosed with TMD. The study cohort included individuals presenting with orofacial pain, restricted mandibular mobility, and signs of muscular hypertonicity and imbalance. The therapeutic protocol comprised a complex of osteopathic interventions, including soft tissue techniques, post-isometric relaxation, and cranial as well as visceral approaches. These methods were aimed at restoring the physiological mobility of cranial structures and improving the functional state of the masticatory muscles. Following the course of osteopathic treatment, a significant reduction in pain intensity in the mandibular region was observed, with mean scores decreasing from 6.1 to 3.1 points. The severity of painful clicking in the temporomandibular joint decreased from 7.4 to 2.8 points ($p = 0.022$). Functional improvement was also noted, reflected by increased maximal mouth opening and a reduction in headache frequency. Headache intensity declined from 6.7 to 3.5 points ($p = 0.044$). Overall, the findings demonstrate a statistically significant reduction in pain, improved mandibular mobility, and enhanced functional status of the temporomandibular joint after osteopathic treatment. A decrease in cephalgic symptoms and improvement in general well-being were also reported. These results support the integration of osteopathic manual therapy and cranial osteopathy into comprehensive, multidisciplinary rehabilitation programs for patients with temporomandibular joint dysfunction

Keywords: temporomandibular disorders (TMD); temporomandibular joint pathology; osteopathic manual therapy; cranial osteopathy; interdisciplinary rehabilitation

INTRODUCTION

Temporomandibular joint dysfunction (TMD) is one of the most common disorders of the maxillofacial region and ranks second in prevalence among musculoskeletal conditions after low back pain. According to epidemiological data, signs of temporomandibular joint (TMJ) dysfunction are observed in 30-50% of the general population, while clinically significant manifestations occur in approximately 10-25% of individuals, predominantly within the 20-40-year age group [1].

A.Y. Alqutaibi *et al.* [2] conducted a systematic review and meta-analysis examining the global prevalence of temporomandibular disorders, synthesising findings from multiple epidemiological studies across different regions worldwide. Their meta-analytical approach provided statistically robust estimates of TMD prevalence at the global level. Similarly, A.H. Alrizqi & B.M. Aleissa [3] performed a literature review assessing the prevalence of temporomandibular disorders between 2015 and 2021. The authors systematically

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analysed published data to identify trends and changes in the epidemiological landscape over a six-year period, thereby offering an updated perspective on the current scope and evolution of the condition. According to L.S. Vieira *et al.* [4], the pathogenesis of temporomandibular disorders is multifactorial, involving biomechanical, neuromuscular, psychoemotional, and postural components. Altered occlusal relationships, myofascial overstrain, psychological stress, and associated postural disturbances contribute to the development of pain syndrome, restricted mandibular mobility, and reduced quality of life.

Contemporary approaches to the management of temporomandibular joint dysfunction, as described by A. Herrera-Valencia *et al.* [5], include pharmacological therapy, occlusal splint therapy, physiotherapeutic interventions, psychotherapy, and surgical correction in severe cases. However, the effectiveness of conventional treatment modalities is not always satisfactory, particularly in patients with chronic forms of the disorder and a pronounced muscular-tonic component. In this context, increasing attention has been directed toward non-pharmacological, functionally oriented therapeutic strategies, among which osteopathic treatment occupies a prominent position. A. Pawlowski *et al.* [6] evaluated the effects of osteopathic techniques on pain reduction and functional improvement of the temporomandibular joint in young patients. Their study emphasized the potential of osteopathic interventions as an effective therapeutic option for adolescents with TMD, highlighting their safety profile and minimal invasiveness compared to conventional treatment approaches.

Osteopathy conceptualises the human body as an integrated functional system in which structure and function are inherently interrelated. Osteopathic techniques aim to restore physiological tissue mobility, optimise microcirculation, and re-establish neuromuscular balance. In the management of temporomandibular joint dysfunction, osteopathic interventions address not only local structural impairments but also systemic functional disturbances, contributing to improved cranial bone alignment, normalisation of masticatory muscle activity, and overall enhancement of temporomandibular joint function [7, 8]. A. Nahian & J.Jr. Mathew [9] examined several osteopathic approaches for the treatment of TMD, including muscle energy techniques for the facial musculature, direct myofascial release (MFR), and the balanced ligamentous tension (BLT) technique. The authors described the underlying mechanisms of these interventions and their clinical application in improving joint function, reducing pain intensity, and restoring normal mandibular mobility. The effectiveness and safety of these techniques were emphasised in the context of TMD management.

In a series of clinical studies, Y.A. Milutka [10] demonstrated that osteopathic manipulative treatment contributes to pain reduction, increased maximal mouth opening, decreased hypertonicity of the masticatory muscles, and improvement in patients' psychoemotional status. Nevertheless, despite the growing body of literature, important issues remain unresolved, particularly regarding the evaluation of osteopathic techniques within the framework of evidence-based medicine and the standardisation of rehabilitation protocols for patients with TMD.

Thus, the relevance of the present study is determined by the high prevalence of temporomandibular joint dysfunction, its substantial impact on patients' quality of life, and the need to develop and scientifically substantiate effective, safe, and minimally invasive treatment approaches, including osteopathic interventions. The aim of this study was to evaluate the clinical effectiveness of osteopathic manipulative treatment and cranial osteopathy in patients with temporomandibular joint dysfunction.

MATERIALS AND METHODS

A total of 30 patients were recruited from the Department of Maxillofacial Surgery at Osh Interregional United Clinical Hospital between January and June 2025. All potential participants were informed about the objectives and procedures of the study and provided written informed consent prior to enrollment. Inclusion criteria were as follows: age between 28 and 30 years; a confirmed diagnosis of TMD; and willingness to attend all scheduled treatment sessions and follow-up visits in accordance with the study protocol. Patients were excluded if they presented with any condition that could potentially confound the study outcomes or compromise participant safety. Exclusion criteria included acute inflammatory diseases, malignant neoplasms, and severe cardiovascular or neurological disorders. Individuals with absolute or relative contraindications to osteopathic manipulative treatment – such as acute fractures, recent maxillofacial trauma, or active infectious processes – were also excluded.

Additionally, patients receiving medications or undergoing therapeutic interventions that could significantly influence the assessed outcome measures were not included if safe discontinuation of such treatments was not feasible. Pregnancy and breastfeeding were considered exclusion criteria in cases where the proposed intervention might pose a potential risk to the mother or child. Participants who were unable or unwilling to adhere strictly to the study protocol, including regular attendance at all scheduled sessions and compliance with clinical recommendations, were withdrawn from the study.

Participant selection procedure. Participant recruitment was conducted in several stages. At the initial stage, eligibility according to the inclusion criteria was assessed based on a review of medical records and data obtained during a structured oral interview. A more comprehensive evaluation of compliance with all inclusion and exclusion criteria was performed by

the investigator immediately prior to obtaining written informed consent. If any risk factors, contraindications, or exclusion criteria were identified at this stage, the patient was excluded from participation. The specific reason for exclusion was documented in the study protocol to ensure transparency and methodological rigor.

Assessment of pain syndrome and functional status of the temporomandibular joint. Standardised methods and validated assessment tools were employed to ensure objective evaluation of pain intensity and TMJ function. Active maximal mouth opening was measured using a calibrated ruler or digital calliper and recorded in millimetres. Patients were instructed to open their mouths as widely as possible without provoking pain. The distance between the incisal edges of the upper and lower central incisors was measured. Each measurement was performed three times, and the mean value was calculated for statistical analysis. Pain intensity was assessed using a 10-cm visual analogy scale (VAS), where 0 indicated no pain and 10 represented the worst imaginable pain. Patients independently marked their perceived pain level on the scale, and the distance from the origin to the marked point was measured in millimetres to obtain a quantitative value. For comprehensive evaluation of TMJ functional status, the Temporomandibular Joint Symptom and Impact Scale (TMJ-SIS) was utilised. This instrument allowed quantitative assessment of mandibular mobility limitation, pain intensity at rest and during movement, as well as the impact of the disorder on quality of life and daily functioning. Individual item scores were summed to calculate an overall composite functional index of TMJ status.

Osteopathic intervention protocol. Osteopathic treatment was delivered by a certified practitioner with clinical expertise in the management of TMJ disorders. Each session followed a standardised structure and involved the sequential application of complementary techniques aimed at improving joint mobility, reducing muscular hypertonicity, and alleviating pain. The session commenced with a brief preparatory phase (2-3 minutes). The patient was positioned either seated or supine. Gentle palpatory assessment of the facial, cervical, and temporomandibular soft tissues was undertaken to evaluate muscle tone and to identify areas of increased tension or tenderness. This was followed by soft tissue techniques (5-7 minutes). Targeted manual therapy was applied to the masseter and temporalis muscles, incorporating gradual stretching and relaxation manoeuvres. Gentle passive mobilisation of the TMJ was performed to reduce muscle spasm and improve functional mobility. Each manoeuvre was executed slowly, with sustained engagement of areas of restriction for approximately 20-30 seconds, repeated two to three times bilaterally. Craniosacral techniques were subsequently applied (approximately 5 minutes). These included subtle manual balancing of the temporal bones and parietal region with the intention of optimising craniosacral dynamics. Gentle mandibular traction was also performed to facilitate decompression of the joint structures. The next phase involved structural mobilisation of the TMJ (5-10 minutes). Controlled mobilisation within a restricted, pain-free range was carried out to restore symmetry of mandibular movement. Rotational and lateral translational techniques were applied using precise, low-amplitude manual pressure. The session concluded with relaxation techniques targeting the cervical and shoulder girdle musculature (2-3 minutes). A post-treatment assessment was then conducted to reassess mandibular mobility and to document changes in the patient's subjective symptoms and overall comfort. Osteopathic treatment sessions were conducted twice weekly, with each session lasting 20-25 minutes. The total number of sessions ranged from 6 to 8 and was determined individually according to the baseline severity of symptoms and the patient's clinical progress. All techniques were applied gently and atraumatically, with continuous monitoring of the patient's response to the interventions.

Throughout the study, safety requirements and sanitary–hygienic standards were strictly observed. The study protocol was approved by the Local Ethics Committee of Osh State University (Protocol No. 136, dated December 11, 2024). The Osh Interregional United Clinical Hospital served as the clinical base of Osh State University. The study was conducted in full compliance with the principles of the Declaration of Helsinki [11]. Written informed consent was obtained from all participants prior to inclusion in the study.

All collected data were entered and analysed using SPSS statistical software (version 26.0). Descriptive statistics for quantitative variables were presented as mean values (M) and standard deviations (SD). The normality of distribution was assessed using the Shapiro-Wilk test. Pre- and post-treatment comparisons were performed using the paired Student's t-test for normally distributed data or the Wilcoxon signed-rank test for non-normally distributed variables. Differences were considered statistically significant at a p-value < 0.05.

RESULTS AND DISCUSSION

During the course of osteopathic treatment, a systematic analysis was conducted to evaluate the frequency of techniques applied to specific TMJ muscles and ligaments, as well as the incidence of pain reported during manual interventions. Techniques targeting the lateral and medial pterygoid muscles were used most frequently. These approaches were applied in 78% of treatment sessions and were associated with subjective pain responses in 62% of cases. In terms of frequency of application, interventions involving the masseter muscle were performed in 63% of sessions, followed by techniques addressing the temporalis muscle (55% of sessions) and the medial pterygoid muscle (33%). The distribution of the applied techniques is presented in Figure 1.

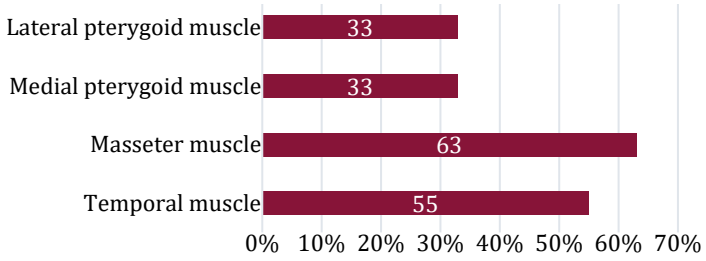

Figure 1. Distribution of pain symptoms elicited in the muscles during manual techniques
Source: developed by the authors

A pain response during manual intervention involving these muscles was observed in 48% and 40% of cases, respectively. When assessing pain manifestations associated with the ligamentous structures of the TMJ, the highest frequency of symptoms was recorded during work on the stylomandibular ligament, with pain reported in 58% of sessions. Less pronounced reactions were noted during interventions targeting the lateral ligament (37% of sessions). Figure 1 illustrates the distribution of pain symptoms elicited during manual techniques applied to muscular structures throughout the osteopathic sessions. Data analysis demonstrated that the highest frequency of pain responses occurred during interventions involving the lateral and medial pterygoid muscles, reflecting their key role in the pathogenesis of TMJ dysfunction and their substantial functional overload. The least frequently applied and least pain-provoking technique was that directed at the sphenomandibular ligament, which was used in only 22% of sessions and was associated with pain in 15% of cases, as shown in Figure 2.

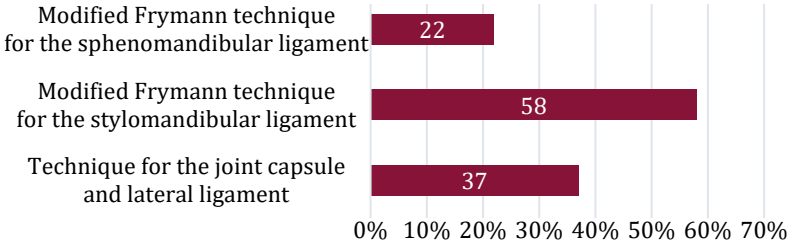

Figure 2. Distribution of pain symptoms elicited in the ligaments during manual techniques
Source: developed by the authors

The analysis of pain distribution patterns indicated that manual techniques applied to the primary masticatory muscles responsible for mandibular movement were more likely to provoke pain responses; however, this discomfort was generally transient and subsided within 1-2 minutes after the intervention. By contrast, interventions targeting the ligamentous structures of the TMJ were performed less frequently but tended to produce more distinct and localised tenderness. These findings suggest that both the frequency of technique application and the associated pain responses should be carefully considered when selecting osteopathic interventions for specific muscular and ligamentous structures. Particular attention should be given to the pterygoid muscles and the stylomandibular ligament due to their apparent clinical relevance. Figure 2 presents the distribution of pain symptoms observed during manual procedures involving the ligamentous apparatus of the TMJ. The highest incidence of pain was recorded during treatment of the stylomandibular ligament, underscoring its potential contribution to pain generation and functional restriction in TMJ disorders. In contrast, manual intervention involving the lateral ligament was associated with a less pronounced pain response, which may reflect its anatomical location and comparatively limited involvement in the pathological process among the study population. Statistical analysis was performed using data obtained from the TMJ SIS scale (Table 1).

Table 1. Statistical analysis of the TMJ SIS

Symptom	Severity type	Average value before treatment (X)	SD	Average value after treatment (X)	SD	p-value
Jaw pain	Typical	6.1	2.0	3.1	3.9	0.007
	Most severe	9.6	2.9	5.5	3.5	0.032
Painful TMJ clicking	Typical	7.4	2.2	2.8	2.8	0.022
	Most severe	8.6	2.2	3.3	1.9	0.07

Table 1, Continued

Symptom	Severity type	Average value before treatment (X)	SD	Average value after treatment (X)	SD	p-value
Mandibular lock	Typical	4.5	4.2	8.9	3.2	0.076
	Most severe	7.4	4.8	7.1	6.0	0.482
Headaches	Typical	6.7	4.9	3.5	4.4	0.044
	Most severe	6.5	4.2	6.4	4.9	0.336
Pain in the cervical-shoulder musculature	Typical	5.9	5.5	5.4	2.0	0.795
	Most severe	0.5	5.5	6.5	3.7	1.000
Dizziness	Typical	2.3	5.0	1.6	1.3	0.523
	Most severe	2.6	5.6	2.1	2.2	0.795
Tinnitus	Typical	5.9	5.5	1.4	5.0	0.795
	Most severe	6.5	5.5	1.5	5.7	1.000

Source: developed by the authors

As shown in Table 1, osteopathic therapy demonstrated the most pronounced effect on mandibular pain, moderate headaches, and joint clicking during mandibular movement. In contrast, symptoms related to secondary manifestations – such as pain in the cervical muscles and shoulder girdle, dizziness, and tinnitus – showed minimal or no clinically meaningful change. These findings support the targeted effect of osteopathic interventions on local TMJ structures and their functional manifestations. The results revealed a statistically significant reduction in pain intensity in the mandibular region, both for the most severe episodes ($p = 0.032$) and for typical pain manifestations ($p = 0.0007$). A significant decrease in the severity of painful joint clicking was also observed, both for maximum symptom intensity ($p = 0.0076$) and for routine manifestations ($p = 0.0220$). Although the daily frequency of jaw "locking" episodes remained unchanged, the maximum reported severity of this symptom decreased significantly ($p = 0.0077$). No statistically significant correlations were identified between osteopathic intervention and symptoms such as tinnitus, dizziness, or pain in the cervical and/or upper shoulder region. Additional analysis using data obtained from the TMJ Symptom Frequency Scale (SFS) scale (Table 2) further demonstrated a beneficial effect of osteopathic therapy on mandibular pain intensity ($p = 0.0207$), the severity of painful TMJ clicking ($p = 0.0011$), and the frequency of headaches ($p = 0.0122$). However, no significant changes were observed in parameters related to tinnitus, dizziness, or pain in the cervical-shoulder region.

Table 2. Statistical analysis of the TMJ SFS

Symptom	Average value before therapy ($\bar{X}$)	SD	Average value after therapy ($\bar{X}$)	SD	P
Jaw pain	7.71	2.01	4.34	2.35	0.0207
Painful TMJ clicking	8.04	4.09	6.64	2.74	0.0011
Headaches	6.68	0.69	3.71	3.23	0.0122
Pain in the cervical-shoulder musculature	5.04	4.09	5.64	2.74	0.7245
Dizziness	5.04	4.09	26.64	4.74	0.5211

Source: developed by the authors

Analysis of the data obtained using the TMJ SFS made it possible to assess the effectiveness of osteopathic therapy in terms of reducing the frequency of clinical symptom occurrence. After completion of the treatment course, a statistically significant reduction in the frequency of mandibular pain was observed: the mean score decreased from 7.71 ± 2.01 to 4.34 ± 2.35 ($p = 0.0207$). This finding indicates that osteopathic interventions contributed to a meaningful reduction in the recurrence of pain during mastication and mandibular movements. The frequency of painful clicking in the TMJ also declined significantly, from 8.04 ± 4.09 to 6.64 ± 2.74 ($p = 0.0011$). This suggests a positive therapeutic effect on functional impairment of the TMJ, particularly on joint complex dysfunction manifested by clicking phenomena. Osteopathic therapy was likewise associated with a statistically significant decrease in headache frequency, with the mean value decreasing from 6.68 ± 0.69 to 3.71 ± 3.23 ($p = 0.0122$). This improvement may be attributed to reduced muscular tension in the masticatory and cervical regions, as well as to improved biomechanical function of the TMJ.

Changes in the frequency of pain in the cervical and shoulder girdle muscles were not statistically significant (5.04 ± 4.09 vs. 5.64 ± 2.74; $p = 0.7245$). This suggests that the short-term course of osteopathic therapy had minimal impact on these secondary symptoms, or that their manifestation is influenced by more complex, multifactorial mechanisms. The mean dizziness scores changed from 5.04 ± 4.09 to 6.64 ± 4.74 ($p = 0.5211$).

However, these differences did not reach statistical significance, indicating that osteopathic therapy had no substantial effect on the frequency of this symptom and that its management may require a more comprehensive therapeutic approach. Overall, osteopathic therapy exerted its most pronounced effect on local TMJ-related symptoms, including mandibular pain, painful joint clicking, and headaches, with a significant reduction in their frequency. In contrast, secondary manifestations – such as cervical and shoulder girdle muscle pain, dizziness, and tinnitus – did not demonstrate statistically significant changes, underscoring the need for an integrated approach when addressing systemic or extra-articular symptoms. The findings indicate that a course of osteopathic treatment incorporating soft tissue techniques, craniosacral methods, and structural mobilisation procedures can significantly reduce pain intensity in the mandibular region, decrease both the frequency and severity of painful TMJ clicking, and alleviate associated headaches. Secondary symptoms, however, exhibited minimal clinical dynamics.

A comparison with findings reported in the literature supports the overall positive impact of manual and osteopathic approaches on the core clinical manifestations of temporomandibular disorders. The systematic review by G. Asquini *et al.* [12] concluded that manual therapy targeting craniomandibular structures contributes to meaningful pain reduction and functional improvement in patients with temporomandibular disorders. The outcomes of the present study are in line with these observations, particularly with regard to the decrease in pain intensity and painful joint symptoms. In addition, A. Herrera-Valencia *et al.* [5] reported that manual therapy leads to clinically significant and sustained reductions in pain, along with improvements in maximal mouth opening over the medium and long term. In our study, pain reduction was likewise statistically significant. However, maximal mouth opening was evaluated as a secondary parameter and was not defined as a primary endpoint of treatment efficacy.

J. Pawłowski *et al.* [13] investigated the effects of osteopathic treatment on TMJ dysfunction in adolescents and reported a marked reduction in pain along with improved functional outcomes. The findings of the present study are consistent with these results, although the current cohort included older participants. In a kinesiographic study, H. von Piekartz & K. Lüdtke [14] demonstrated that osteopathic manipulative techniques significantly improve mandibular kinematics. This aligns with the clinical improvements in mandibular mobility and the reduction of functional restrictions observed in our study. Russian researchers have also confirmed the effectiveness of osteopathic interventions for this condition. Y.A. Milutka & A.E. Fortin [15] highlighted the role of osteopathic therapy as part of a multidisciplinary treatment approach, emphasising its positive effects on pain and functional parameters – results that are largely consistent with those reported here.

M.V. Martyusheva *et al.* [16] described an interdisciplinary approach to diagnosing and managing patients with TMJ dysfunction, stressing the need to integrate the expertise of dentists, neurologists, and osteopaths to optimise therapeutic outcomes. The results of the present study support this perspective, as osteopathic intervention was implemented as part of a comprehensive rehabilitation program and produced significant improvements in key clinical measures. Finally, S. Easterbrook *et al.* [17] reviewed the potential of osteopathic manipulative treatment for temporomandibular disorders, emphasising the use of direct and indirect techniques to reduce pain and restore function. The findings of this pilot study are broadly in agreement with these conclusions, particularly regarding the significant reduction of pain and functional impairments (such as joint clicking and limited mouth opening), although in the current study the focus was on cranial and soft tissue techniques with quantitative assessment using standardised scales.

The results of this pilot study support the clinical effectiveness of osteopathic manipulative treatment and cranial osteopathy in TMJ dysfunction. A significant reduction was observed in mandibular pain intensity, the frequency of painful joint clicks, and associated headaches. In contrast, secondary symptoms such as tinnitus, dizziness, and cervical-shoulder pain showed minimal or no change. E. Schiffman *et al*. [18] developed and recommended the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD), which provide validated screening tools for identifying painful TMD subtypes and criteria for differentiating common intra-articular disorders. These recommendations align with the methodology of the present study, which utilised standardised assessment scales – including the TMJ SIS – allowing objective documentation of symptom improvement following osteopathic intervention.

A.A. Garstka *et al.* [19], in a literature review supplemented by clinical experience, emphasised the importance of accurate diagnosis of painful TMD forms and the use of comprehensive therapy, including physiotherapy, occlusal splints, and other conservative approaches. The findings of the current study complement these conclusions, demonstrating that osteopathic techniques – soft tissue, craniosacral, and structural mobilisation – can serve as an effective component of such integrated therapy, particularly for reducing local pain and improving functional limitations. D. Manfredini [20], in a systematic review, analysed the prevalence of tinnitus among patients with TMD and reported a higher incidence compared with the general population (median 42.3% vs. 12%), highlighting the comorbidity between TMD and tinnitus. In this study, tinnitus did not show significant change following osteopathic treatment, which aligns with D. Manfredini's

observations and underscores the need for further investigation into the pathophysiological links and treatment effectiveness for this symptom. Y.J. Liou *et al.* [21] identified bidirectional associations between TMD and severe depressive and anxiety disorders: the presence of TMD increased the risk of subsequent depression and anxiety by 3-7 times, while pre-existing psychiatric conditions increased the risk of TMD by 5-8 times. These findings emphasise the psychoemotional component of TMD pathogenesis and help explain why secondary symptoms, including potential psychosomatic manifestations, showed minimal change in the present study – likely requiring longer-term or combined interventions, including psychotherapeutic support.

Overall, these results demonstrate that osteopathic techniques are an effective and safe approach for reducing local pain, improving TMJ functional limitations, and enhancing patient quality of life. This pilot study supports the rationale for integrating osteopathic therapy into interdisciplinary rehabilitation programs and provides a basis for future randomised clinical trials with larger sample sizes aimed at clarifying mechanisms of action, long-term efficacy, and optimal application protocols for osteopathic interventions.

CONCLUSIONS

The study demonstrates the clinical effectiveness of osteopathic manipulative treatment and cranial osteopathy in patients with TMJ dysfunction. Application of osteopathic techniques led to a significant reduction in pain intensity, decreased frequency of functional joint disturbances, and a positive impact on associated headache symptoms. According to the TMJ Symptom Intensity Scale (SIS), average mandibular pain decreased from 6.1 ± 2.0 to 3.1 ± 3.9, representing a 49% reduction ($p = 0.007$), while the most severe pain decreased from 9.6 ± 2.9 to 5.5 ± 3.5 (-43%, $p = 0.032$). Painful mandibular clicking on the SIS decreased from 7.4 ± 2.2 to 2.8 ± 2.8 (-62%, $p = 0.022$) for typical manifestations, and the most severe clicks reduced by 62% (8.6 → 3.3, $p = 0.07$), indicating a clear trend toward improvement. Headache intensity decreased from 6.7 ± 4.9 to 3.5 ± 4.4 (-48%, $p = 0.044$). Less pronounced changes were observed for pain in the cervical and shoulder muscles, dizziness, and tinnitus ($p > 0.05$).

Analysis of symptom frequency using the SFS scale confirmed a reduction in the regularity of clinical signs of TMJ dysfunction. Mandibular pain frequency decreased from 7.71 ± 2.01 to 4.34 ± 2.35 (-44%, $p = 0.0207$), painful clicking from 8.04 ± 4.09 to 6.64 ± 2.74 (-17%, $p = 0.0011$), and headaches from 6.68 ± 0.69 to 3.71 ± 3.23 (-45%, $p = 0.0122$). No significant changes were observed in symptoms of cervical and shoulder muscle pain or dizziness ($p = 0.7245$ and $p = 0.5211$, respectively). These findings indicate that osteopathic interventions have a pronounced effect on local TMJ symptoms, reducing pain intensity, the frequency of clicks, and headaches by nearly half, while secondary symptoms appear to require a more comprehensive, multidisciplinary approach. The results support the integration of osteopathic manipulative treatment and cranial osteopathy into interdisciplinary rehabilitation programs for patients with temporomandibular disorders and provide a foundation for further randomised clinical trials. Future research should focus on multicenter, randomized controlled studies with longer follow-up periods to evaluate the long-term efficacy of osteopathic interventions, as well as exploring their combination with other rehabilitation approaches, including psychotherapeutic strategies aimed at managing secondary symptoms and improving overall quality of life in patients with TMJ dysfunction.

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CONFLICT OF INTEREST

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Чакалык-төмөнкү жаак муунунун дисфункциясын остеопатиялык дарылоо

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Аннотация. Чакалык-төмөнкү жаак муунунун (ЧТЖМ) дисфункциясы бейтаптардын жашоо сапатына олуттуу таасир тийгизген жаак-жүз аймагынын эң кеңири таралган патологияларынын бири болуп саналат. Акыркы жылдары бул патологияны дарылоодо дары-дармектүү эмес ыкмаларга, анын ичинде остеопатиялык мануалдык дарылоо ыкмаларына көбүрөөк көңүл бурулууда. Бул изилдөөнүн максаты ЧТЖМ дисфункциясы бар бейтаптарда остеопатиялык манипуляциялык дарылоонун жана краниалдык остеопатиянын натыйжалуулугун баалоо болду. Изилдөөгө оору синдрому, төмөнкү жаактын кыймылынын чектелиши жана булчуң-тондук дисбалансынын белгилери бар бейтаптар камтылды. Остеопатиялык кийлигишүүлөрдүн комплекси жумшак ткандарды коррекциялоо, постизометриялык релаксация, краниалдык жана висцералдык методикаларды камтыды, алар баш сөөктүн структураларынын физиологиялык кыймылдуулугун калыбына келтирүүгө жана жебе булчуңдарынын функциясын нормалдаштырууга багытталган. Изилдөөнүн жүрүшүндө остеопатиялык дарылоодон кийин төмөнкү жаак аймагындагы оору синдрому 6,1 баллдан 3,1 баллга чейин азайганы, ал эми ЧТЖМ дагы оорулуу чыкылдак 7,4 баллдан 2,8 баллга чейин азайганы аныкталды ($p = 0,022$). Ошондой эле ЧТЖМ дын функционалдык абалынын жакшырышы байкалды, оозду ачуунун амплитудасы жогорулады жана баш оорууларынын жыштыгы азайды, алардын интенсивдүүлүгү 6,7 баллдан 3,5 баллга чейин төмөндөдү ($p = 0,044$). Изилдөөнүн натыйжалары остеопатиялык дарылоо курсунан кийин оору синдромунун ишенимдүү азайышын, оозду ачуунун амплитудасынын жогорулашын жана ЧТЖМ дын функционалдык абалынын жакшырышын көрсөттү. Ошондой эле цефалгиялык көрүнүштөрдүн жыштыгынын азайышы жана бейтаптардын жалпы абалынын жакшырышы белгиленди. Аныкталган клиникалык эффекттер ЧТЖМ дисфункциясы бар бейтаптарды пландуу түрдө калыбына келтирүүнүн комплекстүү программасына остеопатиялык мануалдык дарылоону жана краниалдык остеопатияны киргизүүнүн максатка ылайыктуулугун тастыктайт

Негизги сөздөр: жаак муунунун функциясынын бузулушу; жаак муунунун патологиясы; мануалдык терапия; краниалдык остеопатия; реабилитация

Остеопатическое лечение дисфункции височно-нижнечелюстного сустава

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Аннотация. Дисфункция височно-нижнечелюстного сустава (ВНЧС) является одной из наиболее распространённых патологий челюстно-лицевой области, оказывающих значительное влияние на качество жизни пациентов. В последние годы всё большее внимание уделяется немедикаментозным подходам к терапии данной патологии, в том числе методам остеопатического мануального лечения. Целью настоящего исследования являлась оценка эффективности остеопатического манипулятивного лечения и краниальной остеопатии у пациентов с дисфункцией ВНЧС. В исследование были включены пациенты с болевым синдромом, ограничением движений нижней челюсти и признаками мышечно-тонического дисбаланса. Комплекс остеопатических вмешательств включал техники мягкотканой коррекции, постизометрической релаксации, краниальные и висцеральные методики, направленные на восстановление физиологической подвижности структур черепа и нормализацию функции жевательной мускулатуры. В ходе исследования было установлено, что после остеопатического лечения интенсивность болевого синдрома в области нижней челюсти снизилась с 6,1 до 3,1 балла, а болезненные щелчки в ВНЧС уменьшились с 7,4 до 2,8 балла ($p = 0,022$). Также наблюдалось улучшение функционального состояния ВНЧС, с увеличением амплитуды открывания рта и снижением частоты головных болей, где их интенсивность уменьшилась с 6,7 до 3,5 балла ($p = 0,044$). Результаты исследования показали достоверное уменьшение болевого синдрома, увеличение амплитуды открывания рта и улучшение функционального состояния ВНЧС после курса остеопатического лечения. Также отмечено снижение частоты цефалгических проявлений и улучшение общего самочувствия пациентов. Выявленные клинические эффекты подтверждают целесообразность включения остеопатического мануального лечения и краниальной остеопатии в комплексную программу междисциплинарной реабилитации пациентов с дисфункцией ВНЧС

Ключевые слова: нарушение функции челюстного сустава; патология челюстного сустава, мануальная терапия, краниальная остеопатия, реабилитация

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Current trends and epidemiological features of genitourinary diseases in the Osh region

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Abstract. Diseases of the genitourinary system represent a significant medical and social problem, substantially affecting quality of life, ability to work, and demographic indicators. The aim of this study was to examine overall morbidity and primary incidence of genitourinary diseases among the adult and paediatric population of the Osh region over the study period. The research was based on an analysis of official statistical data from regional medical institutions and the Ministry of Health. The findings indicated that overall morbidity and primary incidence showed a downward trend following a period of increase, which was associated with restrictions on preventive examinations and a rise in chronic infections. Significant gender differences were identified: women were more likely to suffer from inflammatory conditions, whereas men more frequently experienced prostate disorders and urolithiasis. It was concluded that systematic monitoring and analysis of urological morbidity are essential for improving preventive measures, increasing access to healthcare, and developing regional public health programmes. After reaching a peak in 2021 (45,870 per 100,000 population), overall morbidity decreased to 33,240 cases by 2024, while primary incidence declined from 22,480 to 17,210 per 100,000 population. Kidney and urinary tract diseases predominated (67.5%), with chronic pyelonephritis accounting for 26.9%. The incidence rate

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among women was, on average, 2.1 times higher than among men. The obtained results can be used to plan regional prevention programmes, optimise patient routing, and improve the effectiveness of urological care in medical institutions in the Osh region

Keywords: urological pathologies; urinary tract infections; nephrological disorders; prevalence structure; population analysis; dynamics of urological diseases; sanitary and demographic characteristics

INTRODUCTION

Diseases of the genitourinary system (DGS) occupy one of the key places in the structure of chronic non-infectious pathology in the world and in the Kyrgyz Republic. According to the World Health Organisation, about 7-10% of the adult population suffer from various forms of kidney and urinary tract diseases, and urinary tract infections (UTIs) are among the three most common bacterial diseases in women of reproductive age. Urological pathologies account for 9-15% of visits to outpatient clinics, which highlights their significance for the healthcare system. The incidence of UTIs increases by 2-3% annually, and the prevalence of chronic kidney disease (CKD) has increased by 15-18% between 2019 and 2024. Particularly high rates are recorded in regions with insufficient access to specialised medical care and low levels of prevention [1].

The trends observed in Central Asian countries, including Kyrgyzstan, are similar. According to statistics from the Kyrgyz Ministry of Health, the overall incidence of diseases of the genitourinary system for the period 2019-2024 ranges from 31 to 46 thousand cases per 100 thousand population, with higher rates characteristic of the southern regions of the country – Osh and Jalal-Abad. There has also been an increase in the incidence of urolithiasis and prostate diseases in men, which is associated with lifestyle changes, increased salt intake and delayed seeking of medical care [2].

Recent studies have examined various aspects of the epidemiology of urinary tract infections and kidney disease, but a number of important issues remain understudied. E. Broughton *et al*. [3] conducted a systematic review of the literature on the epidemiology of complicated urinary tract infections and showed an increase in their prevalence, as well as a link to comorbid conditions and antibiotic resistance. However, their work focused mainly on generalised international data, without analysing regional differences and incidence dynamics at the level of individual territories. Scientists Y. He *et al.* [4] analysed global epidemiological trends in UTIs and proposed predictive models for further growth in incidence. The authors used large databases and mathematical modelling, but did not consider the actual rates of primary and overall incidence in specific regions and did not take into account the influence of local socio-demographic factors.

In their review, H. Al Lawati *et al.* [5] systematised current understanding of the pathogenesis, diagnosis, and treatment of UTIs within the framework of the educational curriculum. The work was mainly clinical and educational in nature and was not aimed at analysing the epidemiological situation or the temporal dynamics of morbidity. M. Gottlieb *et al.* [6] studied the epidemiology of urinary tract infections in adult patients who visited emergency departments. The authors showed the structure of visits and the frequency of UTIs in emergency medicine settings, but their data did not reflect the situation in the general population and did not allow for an assessment of long-term trends in incidence.

The study by C. Yoon *et al.* [7] focused on the clinical and microbiological characteristics of recurrent acute pyelonephritis in women. Despite a detailed analysis of pathogens and clinical forms, the study did not address the prevalence of the disease and its dynamics at the population level. The study by Y.H. Hsu *et al.* [8] analysed the frequency of acute urinary retention after endoscopic enucleation of the prostate and its impact on surgical outcomes. The authors showed a link between this complication and increased catheterisation and hospitalisation times, but the study was limited to a surgical sample of patients and did not consider the population and epidemiological aspects of urological morbidity.

Thus, previous studies have not sufficiently addressed regional characteristics, overall and primary morbidity rates, as well as gender and age differences in infectious and inflammatory diseases of the genitourinary system over time. These gaps and the need to analyse official statistical data at the regional level determined the relevance of this study, in which these issues are revealed using the example of a specific region. The high socio-economic significance of this pathology is associated with its impact on the working capacity, reproductive health, and quality of life of the population. Therefore, the study of trends in the incidence of diseases of the genitourinary system, especially at the regional level, is of great practical importance for the planning of preventive and therapeutic measures. The aim of this study was to analyse the dynamics of the overall and newly diagnosed incidence of diseases of the genitourinary system in the adult and paediatric population of the Osh region in 2020-2024.

MATERIALS AND METHODS

The study was conducted using a retrospective descriptive-epidemiological design and focused on analysing the incidence rates of diseases of the genitourinary system among the adult and paediatric populations of the Osh region of the Kyrgyz Republic during 2020-2024. The study was based on official statistical data from the Osh Regional United Hospital, the Osh Region Public Health Centre and the Ministry of Health of the Kyrgyz

Republic [2, 9]. State statistical reporting forms No. 12 "Report on Diseases Registered in Patients Living in the Service Area of a Medical and Preventive Institution" and form No. 14 "Report on the Activities of the Hospital" were used, which are standard tools for recording morbidity in the healthcare system of the Kyrgyz Republic.

The analysis included all registered cases of diseases of the genitourinary system (class 14th of the International Statistical Classification of Diseases and Related Health Problems, 10th revision, codes N00-N99). The nosological groups were distributed as follows: glomerular and tubulointerstitial kidney diseases (N00-N15, N25-N28), urolithiasis (N20-N23), prostate diseases (N40-N42), male infertility (N46), lower urinary tract infections, cystitis, pyelonephritis and other diseases of the urinary system (N30-N39) [10]. The inclusion criteria were completeness of information on the nosological form, field and age group of the patient.

The indicators of overall morbidity (prevalence), reflecting the total number of registered cases per 100,000 population, and primary morbidity (incidence), taking into account only newly detected cases per 100,000 population, were calculated. The analysis was conducted taking into account gender and age groups, distinguishing between the adult population (aged 18 and older) and children (0-17 years). The structural analysis involved determining the share of individual nosological groups in the overall morbidity structure.

Statistical processing was performed using Microsoft Excel 2021 and IBM SPSS Statistics 26.0 software. The normality of data distribution was checked using the Shapiro-Wilk criterion. To compare the mean values for normal distribution, Student's t-test for independent samples was used, and for deviations from normality, Mann-Whitney's U-test was used. Structural indicators were compared using Pearson's χ^2 test. The level of statistical significance was set at $p < 0.05$.

The dynamics of the indicators were assessed by constructing linear trends with the calculation of growth or decline rates using the formula:

$$\text{growth rate (\%)} = [(\text{final year indicator} - \text{base year indicator}) / \text{base year indicator}] \times 100\%. \quad (1)$$

To identify statistically significant trends, linear regression was used with an assessment of the coefficient of determination (R^2) and verification of the significance of the regression model. The study was conducted on aggregated, anonymised statistical data that did not contain personal information, and therefore did not require the approval of an ethics committee in accordance with national and international recommendations for conducting epidemiological studies based on secondary data from government statistics.

RESULTS AND DISCUSSION

According to data from the Osh Region Territorial Health Administration [2], between 2020 and 2024, between 30,800 and 45,200 cases of genitourinary system diseases were registered annually among the adult population, accounting for an average of 6.4% to 7.1% of all registered morbidity in the region. The largest increase in incidence was observed in 2021 (due to post-COVID complications of chronic diseases), while in 2024 there was an 18.7% decrease compared to 2021 ($p < 0.05$). Among women, the incidence rate averaged up to 29.8 thousand per 100 thousand population, and among men, it was about 14.5 thousand per 100 thousand population, which corresponds to general global epidemiological trends. In the structure of primary incidence, the share of diseases of the kidneys and urinary system (N00-N39) was 67.4%, including chronic pyelonephritis – 27.8% and urolithiasis – 15.2%. The dynamics of the overall incidence of diseases of the genitourinary system in the Osh region from 2020 to 2024 is shown in Figure 1.

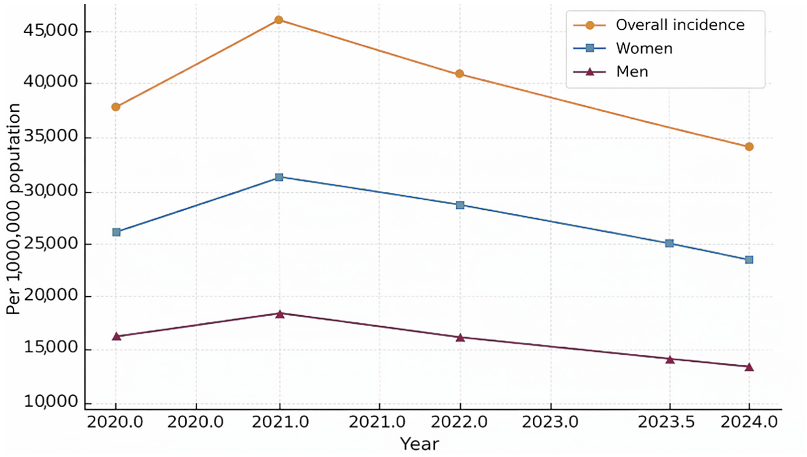

Figure 1. Dynamics of the overall incidence of diseases of the genitourinary system in the Osh region for the period 2020-2024 (per 100,000 adult population)

Note: *$p < 0.05$ – statistically significant differences between indicators within the series

Source: developed by the authors based on [2]

An analysis of official medical statistics for the Osh region shows that between 2020 and 2024, the overall incidence of diseases of the genitourinary system ranged from 33,200 to 45,870 cases per 100,000 population. The highest value of the indicator was recorded in 2021 – 45,870 per 100,000 population ($p < 0.05$), which is explained by the delayed impact of the COVID-19 pandemic, restrictions on preventive examinations, and an increase in the number of chronic inflammatory diseases. The minimum value of the overall incidence rate was recorded in 2024 – 33,240 per 100,000 population, which indicates a positive downward trend (by 27.5% compared to 2021, $p < 0.05$). Among women, a higher incidence rate was maintained throughout the period under review, ranging from 28,600 to 30,400 cases per 100,000 population, while among men, it ranged from 12,800 to 15,200 cases per 100,000 population. The gender differences were statistically significant ($p < 0.05$) and consistent with global trends, according to which women are more likely to suffer from infectious and inflammatory diseases of the urinary tract [1, 2]. The structure of morbidity by nosology in accordance with the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10), is presented in Figure 2.

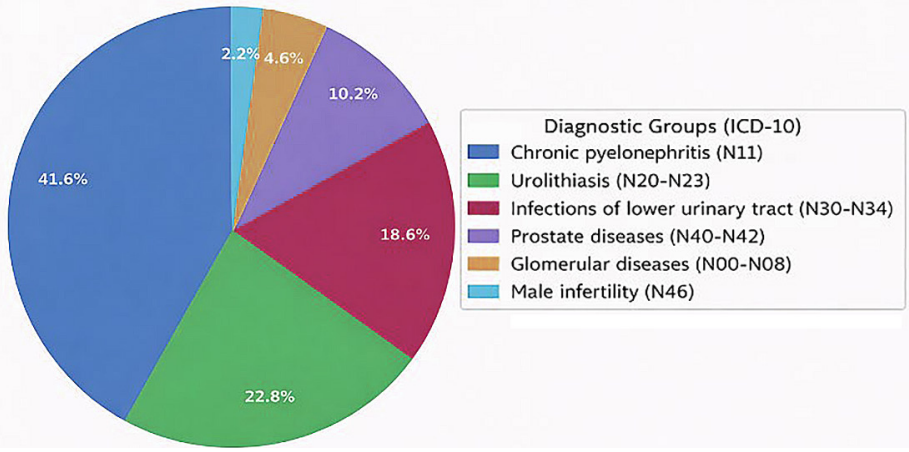

Figure 2. Structure of nosologies of diseases of the genitourinary system in the Osh region for 2020-2024 (in percentage terms)

Note: **$p < 0.01$ – statistically significant differences between the specific weights of nosological groups

Source: developed by the authors based on [9, 10]

An analysis of the structure of morbidity revealed a marked predominance of chronic inflammatory processes in the genitourinary system: chronic pyelonephritis accounts for almost half of all registered cases (41.6%), which significantly exceeds the proportion of acute and other forms of lower urinary tract infections (18.6%). Urolithiasis confidently holds second place (22.8%), which, together with chronic pyelonephritis, forms the main burden on the region's nephrology and urology services – more than 64% of cases relate to these two nosologies. This points to the continuing problem of late diagnosis, insufficient correction of metabolic disorders, and the recurrent nature of the disease. Despite their high frequency in the general population, lower urinary tract infections rank only third in the overall morbidity structure, which may indicate that acute forms are mainly treated on an outpatient basis and are less frequently recorded in summary statistics compared to chronic processes. In men, prostate diseases account for a significant proportion (10.2%), while glomerular lesions and male infertility remain relatively rare (less than 5% in total), which is consistent with the gender-specific profile of urological pathology in the region. The data obtained emphasise the need to prioritise the strengthening of prevention and dispensary observation of patients with chronic pyelonephritis and urolithiasis as the main factors in the chronicity and progression of kidney disease in the Osh region. The indicators of primary incidence of diseases of the genitourinary system in the Osh region, distributed by gender and years of observation, are presented in Figure 3. The dynamics of primary incidence is characterised by a pronounced peak in 2021 (22,480 cases per 100,000 population) followed by a steady decline to a minimum in 2024 (17,210 cases per 100,000 population; $p < 0.05$). Over the five-year period, the overall rate decreased by 23.4%. Throughout the period, the incidence rate among women was consistently and significantly higher than among men, with a similar trajectory: an increase to a peak in 2021 and a more pronounced decline in subsequent years. The average primary incidence rates for the entire period were approximately 28,100 cases per 100,000

population for women and approximately 13,400 cases per 100,000 population for men (women were ill on average 2.1 times more often). Urinary tract infections (N30-N39) and pyelonephritis (N11) accounted for the majority of newly diagnosed cases. In addition, the analysis showed that in the 0-14 age group, the average incidence rate was 7,900 cases per 100,000 children, with girls accounting for 62% of all cases, and acute forms of pyelonephritis and cystitis being the most frequently reported [9, 10].

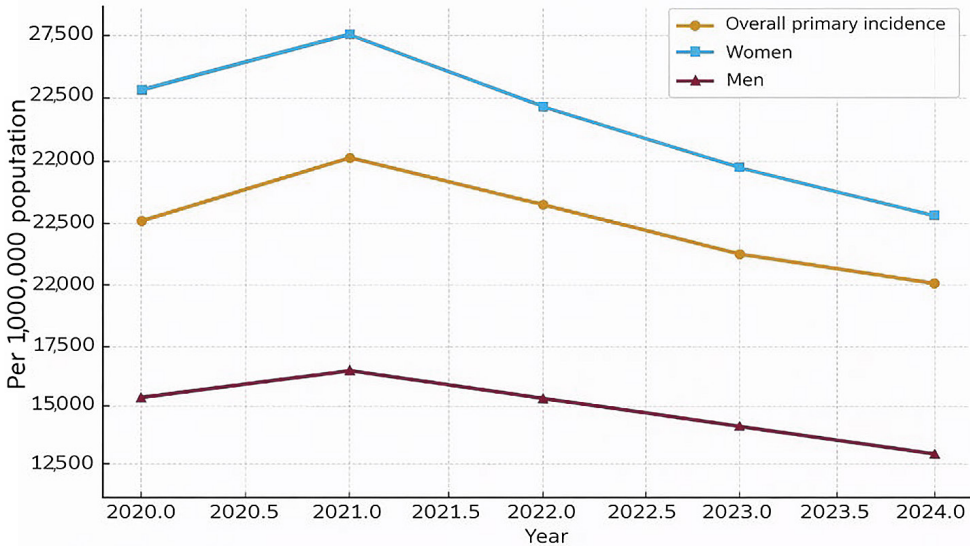

Figure 3. Dynamics of primary incidence of diseases of the genitourinary system in the Osh region (2020-2024, per 100,000 population)

Note: *p < 0.05 – statistically significant differences between indicators for men and women

Source: developed by the authors based on [9]

Studying the prevalence and dynamics of diseases of the genitourinary system in the Osh region is crucial for understanding the structure of morbidity and the factors influencing its growth. These data make it possible to assess the effectiveness of regional prevention programs, the availability of medical care, the quality of diagnostics, as well as the staffing and material and technical support of medical institutions. According to the results of the analysis, in the period 2020-2024, the Osh region saw a downward trend in both the overall and primary incidence of diseases of the genitourinary system. After peaking in 2021 due to the consequences of the COVID-19 pandemic and temporary restrictions on routine examinations, the indicators gradually declined, reflecting an improvement in the quality of preventive measures and increased access to specialised urological care. The gender differences identified are consistent with the literature: women are more likely to develop diseases due to the anatomical and physiological characteristics of the urinary system and increased susceptibility to lower urinary tract infections. Among men, diseases associated with the prostate gland and urolithiasis are more pronounced, which is also confirmed by studies conducted in neighbouring regions of the Kyrgyz Republic [9, 10].

Kidney and urinary system diseases (N00-N39) sharply predominate in the structure of morbidity, accounting for a total share of 87.6%. Chronic pyelonephritis (N11) occupies the leading position with 41.6%, which is almost twice the proportion of lower urinary tract infections (18.6%) and significantly higher than in most previously published regional studies. The high prevalence of chronic pyelonephritis and urolithiasis (22.8%) confirms the persistent chronicity of infectious and inflammatory processes in the region and highlights the need to prioritise the strengthening of dispensary observation and secondary prevention of these nosological forms among the working-age population.

The observed trends in the incidence of diseases of the genitourinary system in the Osh region are consistent with broader epidemiological patterns in Central Asia, especially in terms of the prevalence of chronic inflammatory processes and pronounced gender differences. In the study, diseases of the kidneys and urinary system (N00-N39) accounted for 87.6% of all registered cases, with chronic pyelonephritis (N11) being the most common nosology – 41.6%, followed by urolithiasis (22.8%) and lower urinary tract infections (18.6%). The identified structure emphasises the chronicity of infectious processes, which is consistent with the data of S. Lai *et al.* [11], who studied the prevalence of urological disorders in patients with CKD and recommended the systematic use of uroflowmetry to assess urine flow in nephrology patients. The results obtained in this study show a similar association of chronic forms with a high proportion of pyelonephritis and

glomerular diseases (4.6%), however, the population-based nature of the data suggests a wider regional prevalence compared to hospital samples, indicating the advisability of introducing such methods into routine screening to prevent progression to CKD in the Osh region.

The strong association between pyelonephritis and urolithiasis (in total > 64%) echoes the work of F. Ciccarese *et al.* [12], which analysed complicated pyelonephritis against a background of chronic kidney stone disease with frequent complications (abscesses, sepsis) in stone-associated cases. In contrast to the clinical and radiological focus of that study, the present epidemiological data show a higher overall proportion of urolithiasis (22.8%) as one of the leading nosologies, which is probably due to regional factors (diet, water quality in the south of the Kyrgyz Republic). This highlights the need to integrate radiological diagnostics into prevention programmes to support the observed decline in morbidity (by 23.4% in primary cases from 2021 to 2024).

Prostate diseases accounted for a significant proportion of cases in men (10.2%), which is consistent with the findings of L. Cormio *et al.* [13], who assessed the improvement in lower urinary tract symptoms and quality of life in patients with benign prostatic hyperplasia while taking a whole tomato-based supplement. The data obtained confirm a gender-specific pattern with a predominance of prostate diseases and urolithiasis in men, while infectious forms are 2.1 times more common in women. In contrast to the emphasis on dietary interventions in the work of L. Cormio *et al.*, the present study highlights the need for a broader preventive approach, including lifestyle modification, to maintain the downward trend in morbidity in the post-pandemic period.

In a regional context, conclusions about the incidence among the reproductive-age population and gender differences (women are 2.1 times more likely to be affected, with a childhood incidence of 7,900 per 100,000, 62% of whom are girls) are confirmed by the results of M.N. Aibashov *et al.* [14], who conducted an epidemiological analysis of the prevalence and incidence of diseases of the genitourinary system among the reproductive-age population of the Kyrgyz Republic (15-49 years) and noted high rates of urinary tract infections and pyelonephritis. In contrast to the upward trend in their nationwide data (2003-2016), this study recorded a decline after 2020, probably due to enhanced post-pandemic prevention. This comparison highlights the importance of local monitoring, as the Osh region has seen a more pronounced decline (23.4%) and a predominance of acute forms in children (pyelonephritis and cystitis), which requires the development of targeted interventions in the south of the Kyrgyz Republic to harmonise with national indicators. Overall, the comparisons confirm the chronic and gender-specific nature of diseases of the genitourinary system in the region and justify the need to strengthen preventive strategies.

The identified structure of morbidity, with a predominance of diseases of the kidneys and urinary system (N00-N39) – 87.6%, where chronic pyelonephritis accounts for 41.6%, is consistent with the data of B.L. Ademola *et al.* [15], who in an 8-year review described the clinical, morphological and histological features of chronic pyelonephritis, emphasising its frequent chronicity and the need for long-term observation. Similarly, A.L. Flores-Mireles *et al.* [16] in a review of the epidemiology of urinary tract infections noted the high prevalence of recurrent forms and mechanisms of pathogen persistence, which explains the predominance of chronic pyelonephritis in the present study. Gender differences (women are 2.1 times more likely to get sick) and the prevalence of infectious and inflammatory processes in women are consistent with the review by J. Herness *et al.* [17], where acute pyelonephritis in adults is considered a predominantly female pathology with an emphasis on rapid diagnosis and treatment to prevent complications. The peak incidence in 2021, followed by a 23.4% decline by 2024, reflects the impact of the COVID-19 pandemic, as confirmed by the analysis by E.J. Choi *et al.* [18], which showed a global increase in urinary tract infections and delays in care during the pandemic. The results obtained indicate a positive effect of the restoration of preventive measures in the Osh region.

The identified downward trend in primary incidence after the peak in 2021 (by 23.4%) is consistent with the findings of T. Kurmanbekov *et al.* [19], who analysed the dynamics of urogenital disease incidence in Kazakhstan for 2015–2022 and noted a decline in rates after 2018 associated with improved urological resources and regional differences (high incidence in northern regions). In contrast to the national data for Kazakhstan, where a further decline is predicted, in this study the emphasis on gender differences (women are 2.1 times more likely to be affected) highlights the need for local prevention programmes in the southern regions of Kyrgyzstan.

The results obtained on the dynamics of the incidence of diseases of the genitourinary system in the Osh region for 2020-2024 (peak in 2021 with a subsequent decrease of 23.4%) demonstrate the regional specificity of the post-pandemic period. A comparison with data from neighbouring Central Asian countries reveals certain parallels and differences. In particular, G. Zhakhina *et al.* [20], based on national data from Kazakhstan for 2014-2020, identified a downward trend in the incidence of chronic kidney disease, but predicted its growth by 2030 due to demographic shifts and risk factors. Contrary to these predictions, the present study observes a steady decline in primary incidence after 2021, which is likely due to the restoration and strengthening of preventive measures in the Osh region.

The data obtained on the prevalence of kidney and urinary tract diseases (67.5%) in the structure of morbidity are consistent with the results of a global study of

the burden of disease. A systematic analysis by the GBD Chronic Kidney Disease Collaboration [21] on the prevalence of chronic kidney disease for the period 1990-2017 showed an increase to 697.5 million cases, which is 29.3% higher than in 1990, with the largest increase in low- and middle-income countries. This confirms the global nature of the problem of urological morbidity and the need to strengthen preventive measures at the regional level. The identified gender differences, with the incidence rate in women 2.1 times higher than in men, are consistent with the data of M. Medina & E. Castillo-Pino [22], who in an epidemiological review of urinary tract infections showed that women account for up to 85% of all cases of uncomplicated lower urinary tract infections. The established predominance of chronic pyelonephritis (26.9%) and lower urinary tract infections (12.4%) confirms the conclusion that recurrent infections remain the main reason for seeking urological care among the female population.

Thus, the analysis showed that the incidence of diseases of the genitourinary system in the Osh region demonstrates a positive downward trend after the peak period of 2021, reflecting an improvement in the quality of preventive measures and the accessibility of medical care to the population. The epidemiological features identified, including pronounced gender differences and the predominance of infectious and inflammatory diseases of the kidneys and urinary tract, are consistent with global trends and underscore the need for a differentiated approach to the prevention and treatment of urological pathology.

CONCLUSIONS

The analysis of epidemiological data on diseases of the genitourinary system among the adult and paediatric population of the Osh region for the period 2020-2024 revealed several key trends reflecting the current state of urological morbidity in the region. A steady decline in the overall incidence rate has been observed, from a maximum of 45,870 cases per 100,000 population in 2021 to a minimum of 33,240 cases in 2024, representing a decrease of 27.5% ($p < 0.05$). A similar trend was observed for primary incidence: from a peak of 22,480 cases per 100,000 population in 2021, the rate fell to 17,210 in 2024, reflecting a decrease of 23.4% ($p < 0.05$).

Structural analysis revealed the predominance of diseases of the kidneys and urinary system (N00-N39), accounting for 87.6% of all registered cases. Among them, chronic pyelonephritis (41.6%) ranks first, followed by urolithiasis (22.8%) and lower urinary tract infections (18.6%). In men, prostate diseases accounted for a significant proportion (10.2%). Significant gender differences were identified: the incidence rate among women throughout the period consistently exceeded that among men by an average of 2.1 times (from 28,600 to 30,400 cases per 100,000 women versus 12,800-15,200 among men). In the paediatric population (0-14 years), the average incidence rate was 7,900 per 100,000 population, with 62% of cases occurring in girls, predominantly with acute forms of pyelonephritis and cystitis. The observed decline in incidence rates indicates an increase in the effectiveness of preventive measures, improved early diagnosis, and expanded access to urological care for the population of the Osh region in the post-pandemic period. However, the persistence of a high proportion of chronic forms (especially pyelonephritis – 41.6%) highlights the need for further improvement of the system of dispensary observation and secondary prevention.

Further research should focus on an in-depth analysis of the risk factors influencing the development of chronic kidney disease, including social and hygienic conditions, lifestyle characteristics, access to medical care, and patient adherence to treatment. It is also important to study age and gender differences in disease dynamics, develop early detection programmes and optimise patient routing. A promising direction could be the creation of a regional monitoring system for diseases of the genitourinary system using modern digital technologies, which would allow for more accurate forecasting of the epidemiological situation and increase the effectiveness of preventive measures.

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CONFLICT OF INTEREST

None.

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Ош облусундагы несеп-жыныс системасы ооруларынын учурдагы тенденциялары жана эпидемиологиялык өзгөчөлүктөрү

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Аннотация. Несеп-жыныс системасынын оорулары калктын жашоо сапатына, эмгек жөндөмдүүлүгүнө жана демографиялык көрсөткүчтөрүнө олуттуу таасирин тийгизген маанилүү медициналык-социалдык көйгөй болуп саналат. Изилдөөнүн максаты белгилүү бир мезгил ичинде Ош областынын чоң жана балдар калкынын арасында несеп-жыныс системасынын оорулары боюнча жалпы жана биринчилик оорулуунун көрсөткүчтөрүн изилдөө болгон. Иш аймактын медициналык мекемелеринин жана Саламаттык сактоо министрлигинин расмий статистикалык маалыматтарынын талдоосуна негизделген. Оорулардын таралышынын динамикасын, структурасын жана тенденцияларын баалоо менен медициналык статистиканын ыкмалары колдонулган. Изилдөө жыйынтыктары несеп-жыныс системасынын оорулары боюнча жалпы жана биринчилик оорулуунун деңгээли алардын өсүү мезгилинен кийин төмөндөө тенденциясына ээ экендигин көрсөттү, бул профилактикалык кароолордун чектелиши жана өнөкөт инфекциялардын санынын көбөйүшү менен шартталган. Аялдар көбүнчө калыпка келтирүүчү оорулар менен, ал эми эркектер – простата бездин патологиялары жана несеп таш оорусу менен ооруганда айкын гендердик айырмачылыктар аныкталган. Урологиялык оорулуунун структурасын системалуу мониторинг жүргүзүү жана талдоо профилактикалык иш-чараларды өркүндөтүү, медициналык жардамдын жеткиликтүүлүгүн жогорулатуу жана калктын ден соолугун коргоо боюнча аймактык программаларды иштеп чыгуу үчүн маанилүү мааниге ээ деген тыянак чыгарылган. Жүргүзүлгөн талдоо 2021-жылдагы жалпы оорулуунун чокусунан кийин (100 миң калкка 45 870) 2024-жылга чейин анын 33 240 учурга чейин төмөндөгөнүн, ал эми биринчилик оорулуу 100 миң калкка 22 480дөн 17 210го чейин азайганын көрсөттү. Ошондой эле оорулардын структурасында бөйрөк жана несеп чыгаруу системасынын оорулары (67,5 %) басымдуулук кылаары аныкталган, алардын ичинен өнөкөт пиелонефрит 26,9 %ды түзөт, ал эми аялдардын оорулуунун деңгээли эркектерге караганда орточо эсеп менен 2,1 эсе жогору. Алынган жыйынтыктар профилактиканын аймактык программаларын пландаштырууда, бейтаптарды маршрутташтырууну оптималдаштырууда жана Ош областынын медициналык мекемелеринде урологиялык жардамдын натыйжалуулугун жогорулатууда колдонулушу мүмкүн

Негизги сөздөр: урологиялык патологиялар; несеп жолдорунун инфекциялары; нефрологиялык бузулуулар; таралыш структурасы; популяциялык талдоо; урологиялык оорулардын динамикасы; санитардык-демографиялык өзгөчөлүктөр

Современные тенденции и эпидемиологические особенности заболеваний мочеполовой системы в Ошской области

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Аннотация. Болезни органов мочеполовой системы являются значимой медико-социальной проблемой, оказывающей существенное влияние на качество жизни, трудоспособность и демографические показатели населения. Целью исследования было изучение показателей общей и первичной заболеваемости болезнями мочеполовой системы среди взрослого и детского населения Ошской области за определённый период времени. Работа основана на анализе официальных статистических данных медицинских учреждений региона и Министерства здравоохранения. Использованы методы медицинской статистики с оценкой динамики, структуры и тенденций распространённости заболеваний. Результаты исследования показали, что уровень общей и первичной заболеваемости болезнями мочеполовой системы имеет тенденцию к снижению после периода их роста, обусловленного ограничением профилактических осмотров и повышением числа хронических инфекций. Выявлены выраженные гендерные различия, при которых женщины чаще страдают воспалительными заболеваниями, а мужчины – патологиями предстательной железы и мочекаменной болезнью. Сделан вывод, что систематический мониторинг и анализ структуры урологической заболеваемости имеют важное значение для совершенствования профилактических мероприятий, повышения доступности медицинской помощи и разработки региональных программ по охране здоровья населения. Проведённый анализ показал, что после пикового уровня общей заболеваемости в 2021 году (45 870 на 100 тыс. населения) к 2024 году наблюдалось её снижение до 33 240 случаев, а первичная заболеваемость уменьшилась с 22 480 до 17 210 на 100 тыс. населения. Установлено также, что в структуре заболеваний доминируют болезни почек и мочевыделительной системы (67,5 %), среди которых хронический пиелонефрит составляет 26,9 %, а уровень заболеваемости у женщин в среднем в 2,1 раза выше, чем у мужчин. Полученные результаты могут быть использованы при планировании региональных программ профилактики, оптимизации маршрутизации пациентов и повышении эффективности урологической помощи в медицинских учреждениях Ошской области

Ключевые слова: урологические патологии; инфекции мочевых путей; нефрологические нарушения; структура распространённости; популяционный анализ; динамика урологических заболеваний; санитарно-демографические особенности

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Transplacental antibody perfusion in the development of the newborn passive immunity: A literature review

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Abstract. Reducing infant mortality resulted from infections, particularly among premature infants, is a major public health concern. This fact emphasises the significance of transplacental transfer of maternal antibodies, including immunoglobulin G (IgG), to develop passive immunity and protect newborns from infections. The aim

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of this studywas to summarise current findings on the mechanisms and factors affecting transplacental transfer of IgG and their role in the developing passive immunity in newborns. This review provided a systematic analysis of the scientific literature, including studies on the morphofunctional features of the placenta, the mechanisms of transplacental IgG perfusion, and their impact on fetal and neonatal immunological protection. The study supported the fact that IgG served a crucial function in the development of passive immunity in newborns, crossing the placental barrier and providing protection against infections in the early stages of life. As evidenced, the efficiency of transplacental IgG transfer varied depending on gestational age, with lower transfer rates in premature compared to full-term infants. The results demonstrated that different IgG subclasses (IgG1, IgG3, IgG4, and IgG2) were transferred across the placenta with varying efficiency, the fact associating with their affinity for the Fc receptor on the placenta. Infections and hypergammaglobulinemia in mothers were proved to affect transplacental IgG transfer, highlighting the need to monitor the infectious status of pregnant women to optimise neonatal protection. Maternal vaccination at specific stages of pregnancy was found to significantly increase IgG levels in the newborn's blood, contributing to improved passive immunity and reducing the risk of infectious diseases in infants. The study results can be introduced into clinical practice to optimise vaccination strategies for pregnant women and develop personalised approaches for preventing infectious diseases in newborns, especially among premature neonates

Keywords: placenta; transplacental transfer; immunoglobulin G; neonatal infections; immunological protection; placental barrier; gestational age

INTRODUCTION

Currently, reducing infant mortality appears to be one of the foremost challenges in healthcare, particularly among premature infants, for whom infections are a major cause of death. In this regard, the development of passive immunity, including through transplacental transfer of maternal antibodies, is an essential mechanism to protect the foetus and newborn. Immunoglobulin G (IgG) serves a crucial function in this process, being the only class of an antibody with the potential to cross the placental barrier and provide protection against infections early in life. However, despite the significance of this mechanism, existing data on transplacental IgG perfusion, as well as the influence of various factors on the effectiveness of this process, require further investigations to optimise infectious disease prevention in newborns.

The placenta, as a unique organ, has a complex functional morphology, combining immunomodulatory properties with a barrier function. As stated by L. Pomar & D. Baud [1], the placenta ensures immunological tolerance between the organisms of the mother and foetus, while simultaneously performing selective transport of biologically active substances. This emphasises the significance of its role in protecting the foetus from potentially dangerous agents, including viruses and bacteria, that can penetrate this barrier. E.N. Kravchenko *et al*. [2] specified the main risk factors for intrauterine infection of the foetus with the decreased placental barrier function, with viral infection being pivotal. It was also noted that disturbances in immune defence could contribute to a higher susceptibility of the foetus to diseases. In their study, W. Wang *et al*. [3] highlighted the importance of the cytokine profile and T-cell response in the favourable pregnancy completion and pathogenesis of its complications. This immune response also affected the interaction between the mother and foetus, and, consequently, pregnancy outcomes. M.P. Piccinni *et al*. [4] supported the primary role of the relationship between hormonal and immune mechanisms of the female reproductive function. These mechanisms maintained homeostasis and normal development of the foetus, and their disruption could result in complications such as preeclampsia. L.J. Yockey *et al*. [5] clearly demonstrated the effect of maternal antibodies on the developing passive immunity and increased resistance in the foetus and newborn. Maternal antibodies served as a crucial component of fetal protection from infections prior to birth. In addition, A.G. Rumyantsev [6], analysing maternal-fetal interactions in the developing immune system of the newborn, concluded that disruption of these interactions could cause immunodeficiencies in newborns. Of particular importance in terms of immune protection was the transplacental transfer of IgG, which provided the basis of passive immunity of the newborn. According to A.M. Ciobanu *et al*. [7], immunoglobulins G were the only class of antibodies that could penetrate the placental barrier and provided protection against neonatal infections, but simultaneously, the transfer of autoantibodies could contribute to the development of neonatal autoimmune diseases. Currently, research has significantly expanded our understanding of the mechanisms of transplacental immunoglobulins transport. Thus, A.N. Shuid *et al*. [8] reviewed the relationship between viral infections and the risk of developing autism disorders; as emphasised, it is crucial to immunologically protect the foetus from viral agents, including the effect of antibody transplacental transfer. These studies focused on viral infections as risk factors in the context of the developing immunity in newborns. Furthermore, L.L. Shook *et al*. [9] specified a relationship between the activity of the

maternal immune system exposed to SARS-cov-2 infection during pregnancy and impaired brain development in the foetus. Despite significant progress in understanding the mechanisms of transplacental transfer of antibodies, the issues of the dynamics of transplacental IgG transfer at different gestational stages are not fully understood. Identifying factors contributing to the effectiveness of transplacental transfer and changes in the qualitative composition of IgG depending on infection with various pathogens, as well as assessing the effectiveness of IgG perfusion after vaccination, also requires further research. The relevance of these issues necessitates a personalised approach to assessing and correcting passive immunity in newborns.

The aim of this study was to analyse current findings on the mechanisms of transplacental transfer of IgG and their role in the developing passive immunity in newborns, to identify factors contributing to the effectiveness of this process. This study provided a systematic review of the scientific literature, analysed data on the morphofunctional features of the placenta, the mechanisms of transplacental IgG perfusion, and their impact on fetal immunological protection. Studies examining the impact of gestational age, maternal immune status, infections, and vaccination on the transfer of antibodies across the placental barrier were included in the review. The dynamics and effectiveness of transplacental transfer of various IgG subclasses, such as IgG1, IgG2, IgG3, and IgG4, and their relationship with neonatal immune protection was also analysed.

The role of IgG subclasses in the development of maternal immunity

The phenomenon of the placenta, as an organ, lies in its unique functional morphology; normal pregnancy is characterised by a balance between immune tolerance to the foetus and protection from infections; the disruption of this balance can result in complications such as preeclampsia, intrauterine growth retardation, and premature birth. These conclusions were made in the review by D.E. Galkina *et al.* [10] on current knowledge of the immunological mechanisms of regular and pathological pregnancy. According to J. Ding *et al*. [11], while directly involved in the formation of the maternal immune response, the placenta simultaneously functioned as a selective barrier, thereby promoting immunological tolerance between two foreign organisms. One of the pathways of the mother's immunomodulatory effect on the developing immune responses in the offspring was the transplacental transfer of IgG and immunocompetent cells. C. Napodano *et al*. [12] presented current views on the functions of IgG subclasses and their role in immune defence, systematising the knowledge on the functions of IgG subclasses and their clinical significance, including transplacental transfer. IgG in the maternal body accounted for a significant proportion of the total number of antibodies and were the main factor in the humoral link of immune defence. V.A. Kozlov *et al*. [13] demonstrated that the presence of specific immunoglobulins of class G after an illness or vaccination indicated the formation of sterile immunity to the corresponding bacterial or viral infection. A decreased IgG level of any subclass might result from a violated synthesis of antibodies of a certain specificity. Pregnant women with a reduced level of IgG2 synthesis had weakened immune protection against polysaccharide antigens of the wall of some bacteria and viruses, such as pneumococci, meningococci, group A streptococci and Haemophilis influenzae. As reported in the basic research by A.K. Abbas *et al*. [14], if the production of IgG1 was more intense than the synthesis of immunoglobulins of other subclasses, then a decreased amount of IgG1 subclass antibodies might be due to general hypogammaglobulinemia, or associated with chronic, recurrent lower respiratory tract infections, or resulted from chronic fatigue syndrome. The IgG3 subclass was the most powerful complement activator, had a high affinity for protein antigens; its deficiency, often accompanied by a decrease in IgG1 antibodies, was observed in women with recurrent chronic infectious lung diseases. IgG4 antibodies developed an immune response to allergens and blocked IgE-dependent reactions, their concentration was normally lower than that of other subclasses, and, therefore, they were quite difficult to detect. Nevertheless, the data obtained by B.A Chernyak & I.I. Vorzheva [15] indicated that their deficiency might be associated with chronic antigenic stimulation combined with recurrent respiratory tract infections; however, this statement was ambiguous, since a low concentration of immunoglobulins of this subclass was observed quite often in healthy individuals.

The role of the neonatal Fc receptor (FcRn) in the selective transport of IgG across the placental barrier

R.W. Pitcher-Wilmott *et al.* [16] conducted one of the first studies related to the transplacental transfer of IgG subclasses and came to the following conclusions: IgG subclasses were transferred across the placenta with different efficiency: IgG1 > IgG3 > IgG4 > IgG2, the fact associating with different affinities of IgG subclasses to FcRn (neonatal Fc receptor). They also assumed that IgG transfer might be restricted by competition between subclasses for binding to FcRn. M.F. Jennewein *et al.* [17] specified the key role of the neonatal Fc receptor (FcRn) in the selective transport of IgG across the placental barrier. It was found that the efficiency of transfer of different IgG subclasses (IgG1-IgG4) varied significantly depending on the affinity to FcRn.

N. Twisselmann *et al.* [18] studied glycosylating Fc fragments of IgG in premature and full-term neonates. These studies were the first to link the features of IgG glycosylation with the efficiency of transplacental transfer and opened up new potentials to study the mechanisms of passive immunity development, emphasising the complexity and multifactorial nature of the process of IgG transplacental transfer. The major conclusions reached in the study indicated that premature infants had differences in IgG glycosylation compared to full-term infants, and these differences could affect IgG binding to FcRn and, as a result, the efficiency of transplacental transfer. IgG glycosylation in premature infants depended on the gestational age: the earlier the term of delivery, the less mature the glycosylation profile. S. Borghi *et al.* [19] also supported that the efficiency of IgG transfer depended on its subclass and glycosylation of the Fc fragment. K.M. Knudsen Sand *et al.* [20] applied experimental models to study the role of FcRn and FcγR (Fc-gamma receptors) in the IgG transplacental transfer, and also came to the conclusion that FcRn was the main receptor mediating the transplacental transfer of IgG; FcγR did not have a pivotal role in this process. Competition between IgG for binding to FcRn explained the inverse correlation between the level of maternal antibodies and their transfer. This was supported by N.A. Lozano *et al.* [21], who focused on the expression of the FcRn receptor, the main molecular carrier of immunoglobulins in the placenta. It was found that the efficiency of this transport directly correlated with IgG levels in full-term and premature infants, which highlighted the placental receptor apparatus as a critical control point of neonatal immunity.

Dynamics of IgG transplacental transfer depending on the gestational age

As reported by S.A. Ozdemir *et al.* [22] in their early retrospective study on IgG and IgM levels in premature and full-term neonates, the level of IgG in the blood serum of premature infants was significantly lower than that of full-term infants, and the IgG concentration correlated with gestational age: the earlier the term of delivery, the lower the IgG level. The level of IgM, on the contrary, did not depend on the gestational age, which confirmed its synthesis by the foetus itself, rather than its transfer from the mother. R.A. Pereira *et al.* [23] analysing the transplacental transfer of IgG and its subclasses in foetuses at different gestational stages also supported the universality of the "accumulative transfer" mechanism, regardless of the gestational age. Active transplacental transfer of maternal immunoglobulins began in the second trimester of pregnancy, approximately at the thirteenth week of gestation. The level of total IgG in the foetus increased with increasing gestational age. A relatively low concentration was observed between 17 and 22 weeks and constituted approximately 5-10% of the volume of maternal antibodies. According to R.A. Pereira *et al.,* passive diffusion of antibodies predominated during this period; at 32 weeks, approximately 1/2 of antibodies was determined; at birth, the amount of antibodies in the fetal blood exceeded the maternal level. This fact proved the concept of "accumulative transfer" and stressed the significance of the third trimester for the development of the fetal passive immunity. Further studies by S.D. Bokonbaeva *et al*. [24] provided detailed issues of immunity development in the most vulnerable groups of children – premature infants. The authors identified specific changes in the immune status that determined the severity of respiratory disorders in premature infants. van I.C. Duuren *et al.* [25] in their review considered the developing immune system of premature infants not only as a risk factor but also as a potential resource for new therapeutic solutions, demonstrating a link between immune immaturity and the subsequent development of respiratory tract infections and wheezing, providing immunological correction strategies.

A. Palmeira *et al.* [26] demonstrated that concentrations of total IgG and IgG subclasses in maternal plasma were positively associated with concentrations in fetal cord blood and negatively associated with transplacental transfer coefficients. Higher levels of total IgG and the IgG1 subtype were found in the cord blood of full-term newborns compared to the maternal blood. The efficiency of transplacental perfusion of immunoglobulin subclasses at full-term pregnancy (37-42 weeks) was expressed as IgG1 > IgG3 > IgG4 = IgG2, which demonstrated a relatively constant ratio of maternal/umbilical cord IgG subclasses and did not depend on the term of delivery after 37 weeks of gestation. However, it should be stressed that, as of 2026, there is no consensus regarding the hierarchy of transplacental transfer of different IgG subclasses.

Factors affecting the efficiency of transplacental IgG transfer

Study results by H. Akbulut *et al.* [27] complemented understanding of the variability of transplacental IgG transfer, focusing on ethnic and geographic features. Using data from a prospective cohort study of 120 mother-newborn pairs, they analysed the correlation between gestational age, maternal parity, and the efficiency of antibody transfer, measuring the levels of total IgG and subclasses (IgG1-IgG4) in maternal and cord blood using enzyme-linked immunosorbent assay (ELISA). As evidenced, the transfer coefficient of total IgG (cord/maternal concentration) was 1.2-1.5, supporting active transport. In full-term newborns, the IgG level exceeded the maternal level by 15-30%, the fact being consistent with the data obtained by R.A. Pereira *et al.* [23]. The transfer hierarchy was as follows: IgG1 (1.4) > IgG3 (1.1) > IgG4 (0.9) > IgG2 (0.7). Low IgG2 transfer was explained by its weak binding to FcRn. Women from Eastern Anatolia had elevated

levels of total IgG and IgG1 compared to Western populations. In children born before 34 weeks, IgG levels were 40% lower than in full-term infants, as reported by S.A. Ozdemir *et al.* [22]. Multiparous women (>3 births) had higher IgG1 levels but reduced efficiency of its transfer (coefficient 1.1 vs. 1.4 in primiparous women). Previously, S.S. Omowale *et al.* [28] evidenced a direct relationship between maternal hypergammaglobulinemia and a decreased IgG1 and IgG2 transfer without affecting IgG3 and IgG4, compared to maternal IgG in malaria; this being the proof-of-concept for the decreased efficiency of transplacental IgG perfusion in hypergammaglobulinemia in pregnant women. A similar effect was observed in Black women, whose total IgG levels were initially higher than in light-skinned women. Based on the results obtained, A. Ohlsson & J.B. Lacy [29] concluded that transplacental transfer correlated with maternal race. Older pregnant women had lower total plasma IgG levels, but this did not affect the efficiency of transplacental perfusion and antibody levels in the cord blood. Women, who had previously had live births, manifested higher levels of total IgG and IgG1 at birth. However, this did not affect the blood of newborns, and the transfer coefficient was reduced. This provided further evidence that, despite the positive correlation between IgG levels in the maternal and umbilical cord blood, transplacental capacity might be limited by potential saturation of Fc transport receptors at higher IgG concentrations. No effect of parity of pregnant women on the transfer of antigen-specific IgG or changes in their concentration in the blood of the umbilical cord and placental vessels was revealed. L.N. Balanovskaya & Ya.A. Loginova [30] also analysed the features of newborn immunity in different countries, thus, supporting an essential effect of external factors and regional epidemiological conditions on the "programming" of the immune system from birth.

Mechanisms of competition between IgG subclasses and their clinical significance

As demonstrated, there was observed a negative correlation between maternal total IgG levels and the transfer coefficients of the IgG1, IgG2, and IgG3 subclasses during normal pregnancy. This suggested that higher levels of IgG1, IgG2, and IgG3 competed with other subclasses for placental transfer. It should be noted that maternal blood concentrations of IgG2, IgG3, and IgG4 correlated with IgG1. This effect might not always be indicative of a specific antibody subclass but was due to a higher concentration of IgG1, which was more efficiently transferred. Furthermore, elevated maternal IgG4 levels had limited correlation with total IgG transfer, and IgG4 perfusion did not correlate with maternal antibodies, despite the positive correlation between maternal IgG4 and IgG1, as suggested by T. Clements *et al.* [31].

The highest correlation was observed between the cord blood IgG4 concentrations and total IgG concentrations in both the cord blood and maternal blood, suggesting no relationship between the transfer of antibodies of this subclass and maternal antibody titre variability. In this case, there was a certain probability to infer the mechanism underlying the development of passive immunity in newborns against specific pathogens. The clinical significance of the IgG4 immunoglobulins transfer was pivotal and required further research. Conclusions supported the current views that higher maternal IgG levels contributed to increased antibody concentrations in the offspring, but the relative efficiency of placental immunoglobulin transfer might be reduced by maternal hyperglobulinemia. B.J. Okoko *et al*. [32] in their study demonstrated that infectious diseases (in particular malaria) and hypergammaglobulinemia in the mother could significantly reduce the transport of IgG and its subclasses, making the newborn vulnerable.

Studies of the immune status of children born at later stages of uncomplicated pregnancy demonstrated significantly higher levels of IgG1 and IgG4. The increase in IgG4 concentration was likely due to the high level of IgG4 in the mother's body with an unchanged rate of transplacental transfer. The IgG1 level was not associated with the transfer coefficient and increased transplacental activity in late weeks but reflected the cumulative effect in the fetal circulation. In other words, in full-term pregnancy, each additional week of delay in delivery increased neonatal levels of IgG1 and IgG4. N.A. Lozano *et al*. [21] detected a positive relationship between the total IgG level and antigen-specific IgG in premature infants depending on the term of premature delivery. The clinical block of publications clearly demonstrated the assessment of the immune status of a premature infant as a dynamic system with predictable risks. E.N. Volkova & L.I. Ippolitova [33] in their study related to TREC and KREC markers allowed for an objective assessment of the "naivety" of the immune system and the potential for the development of immune components, the fact providing physicians with a tool for the early identification of children with critically low adaptive resources and the risk of developing infectious complications. The study by H. Lu *et al*. [34] introduced the concept of ferroptosis – programmed cell death – into neonatal practice and opened new horizons in understanding the mechanisms of hypoxic-ischemic encephalopathy. This might result in developing targeted therapy with the potential to minimise brain damage in critically ill newborns.

Effect of vaccination and infections on the transplacental IgG transfer

A key aspect of research is the study of the impact of maternal pathological conditions on the efficiency of transplacental antibody transfer. S. Atyeo *et al*. [35] greatly contributed to addressing issues related to the

impact of maternal infections, including COVID-19, on the profile of transplacentally transferred antibodies. It was proven that viral infections altered the qualitative composition of transferred IgG; there were identified significant differences in the transfer of antibodies to various pathogens, which in turn affected the efficiency of neonatal protection. Multiple pregnancy deserves special attention as a specific risk factor. S.C.L. Stach *et al.* [36] in their study demonstrated the distribution patterns of total IgG and specific antibodies (to Klebsiella, Pseudomonas, and group B Streptococcus) in twins. These data indicated that the placental transport resource might be limited or distributed unevenly, which required a differentiated approach to assessing infectious risks in each twin.

Publications related to the clinical segment discuss the issues of therapeutic correction and prevention. R.K. Satlikov & I.Yu. Masharipova [37] in their study supported the effectiveness of using anti-Rhesus immunoglobulin as the gold standard for the prevention of hemolytic disease; this was a successful example of passive immunity management. Immunological examination of children born to Rh-negative mothers demonstrated decreased IgG2 levels and lower IgG2 transfer coefficients after the anti-D IgG introduction at the 28th week of pregnancy. The parameters of other IgG subclasses were comparable with those in the control group. This suggested that the administered IgG could compete with the transfer of endogenous IgG2. O.V. Kozlyakov *et al*. [38] addressed the urgent issues of expanding the screening of pregnant women. The emphasis the authors had taken on the Rh factor (D antigen) following the conventional approach was complemented by their investigations of other anti-erythrocyte antibodies (Kell, Duffy, Kidd systems etc.). The authors analysed the need for specific prophylaxis in cases of combined sensitisation, pointing out that the presence of other antibodies could modulate the immune response and complicate the course of pregnancy, even if Rh prophylaxis was performed in a timely manner. This validated the transition from routine examination to extended immunological typing of couples. The results obtained by V.E. Potapova *et al.* [39] indirectly supported the above, as they focused on the fundamental aspects of hemolytic disease of the newborn, considering this condition not only as a process of hemolysis of fetal erythrocytes under the influence of maternal IgG, but also as a complex reaction affecting erythropoiesis in the fetal bone marrow. The authors emphasised that the severity of the damage depended on the expressivity of antigens, the subclass of maternal antibodies (mainly IgG1 and IgG3) and the functional state of placental Fc receptors, thus identifying the prognosis for the newborn.

Z. Zhong *et al.* [40] in their study provided essential data on the immunization timing. In particular, using influenza vaccination as an example, they demonstrated that the timing of maternal vaccine administration directly determined the titre of protective antibodies in the infant at birth. As reported, there was a "golden window" for vaccination, which allowed for the most effective use of the mechanism of active transport across the placenta providing passive immunity to the child in the first months of life. The highest concentrations of antibodies in newborns were detected if mothers were vaccinated 4-24 weeks before delivery, while the timing of vaccination of the pregnant woman did not affect the efficiency of transplacental transfer of IgG subclasses. A critical contribution to the evidenced safety of immunisation during pregnancy was the study conducted by E.B. Efimkova *et al.* [41]. Based on a retrospective analysis of the pandemic period (2020-2023), the effect of vaccination on obstetric outcomes was provided. The researchers argued that vaccination of pregnant women against COVID-19 did not only protect the mother from severe infection but also promoted a favourable gestational process. In the studies performed by M.P. Kostinov *et al.* [42], it was highlighted that vaccination should be considered as part of pre-pregnancy preparation and management of pregnancy, thus inherently developing a modern paradigm for vaccination in obstetrics. V.I. Krasnopolsky *et al*. [43] convincingly demonstrated based on the extensive clinical material that vaccination against the human papillomavirus (even performed in periods close to conception or in the early stages before pregnancy was detected) had no teratogenic effect and did not worsen gestational outcomes.

Based on the data obtained, it can be concluded that transplacental antibody transfer is crucial for developing passive immunity in newborns. The presence of specific antibodies in the mother significantly enhances the foetus's immune defence, especially in cases of vaccination or previous infections. However, the effectiveness of this process varies depending on diverse factors, such as gestational age, maternal age, and the impact of infectious diseases.

CONCLUSIONS

Immunoglobulin G (IgG) are pivotal in fetal protection, forming the basis of maternal humoral immunity. IgG1, the most common subclass, protects against protein antigens and activates complement. Decreased IgG1 levels are associated with hypogammaglobulinemia and chronic respiratory infections. IgG2 deficiency increases the risk of bacterial infections, and decreased IgG3 is observed in chronic respiratory diseases. IgG4 involved in allergic reactions has the lowest concentration among the subclasses, and its deficiency is associated with chronic antigen stimulation.

Transplacental transfer of IgG begins in the second trimester and peaks by 32 weeks, when fetal IgG levels exceed maternal levels providing passive immunity. Premature infants have lower IgG concentrations, this fact increasing their vulnerability to infections. Full-term infants exhibit higher levels of IgG1

and IgG4, and the ratio of IgG1 > IgG3 > IgG4 = IgG2 subclasses remains constant. Transfer efficiency depends on maternal antibody levels, age, race, and hypergammaglobulinemia, which reduces the transfer of IgG1 and IgG2.

Vaccination during pregnancy strengthens the passive immunity of newborns. Influenza vaccination increases IgG4 levels in both mother and foetus. However, infections such as malaria and COVID-19 can disrupt transplacental antibody transfer. Hypergammaglobulinemia associated with malaria reduces the transfer of IgG1 and IgG2 highlighting the need to control infections in pregnant women. It is essential to study the molecular mechanisms of placental FcRn receptors and develop diagnostic models for assessing newborn immune defences. This will enable the development of personalised prenatal immunocorrection protocols and vacciWWnation programs to improve neonatal outcomes.

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Жаңы төрөлгөн баладагы пассивдүү иммунитеттин калыптанышына антителолордун трансплацентардык перфузиясынын ролу: адабияттарга сереп

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Аннотация. Коомдук саламаттыкты сактоонун негизги көйгөйлөрүнүн бири – жугуштуу оорулардан улам ымыркайлардагы, айрыкча ара төрөлгөндөрүнүн арасындагы өлүмдү азайтуу болуп саналат. Энедеги иммуноглобулин G (IgG) сыяктуу антителолордун трансплацентардык жол менен өткөрүлүп берилүүсү ымыркайда пассивдүү иммунитеттин калыптанышына жана ага жугуштуу оорулардан коргонуусуна чон мааниси бар. Изилдөөнүн максаты IgGнин трансплацентардык жол менен өткөрүлүшүнө таасир этүүчү механизмдерди жана факторлорду аныктоо, алардын жаңы төрөлгөн балдарда пассивдүү иммунитеттин калыптанышындагы ролу боюнча учурдагы маалыматтарды жалпылоо болуп саналат. Бул адабий серепте плацентанын морфофункционалдык өзгөчөлүктөрүнө, трансплацентардык IgG перфузиясынын механизмдерине жана алардын түйүлдүктүн жана жаңы төрөлгөн баланын иммунологиялык корголушуна тийгизген таасирине арналган эмгектерди камтыган илимий адабияттардын системалуу анализи колдонулган. IgG жаңы төрөлгөн балдарда пассивдүү иммунитеттин калыптанышында, плаценталык тосмодон өтүп, жашоонун алгачкы этаптарында инфекциялардан коргоонуну камсыз кылууда маанилүү ролду ойной турганын изилдөө тастыктады. Трансплацентардык IgG өткөрүп берүүнүн натыйжалуулугу кош бойлуулуктун курагына жараша өзгөрүп тураары, толук мөөнөттүү ымыркайларга салыштырмалуу ара төрөлгөн ымыркайларда өткөрүп берүү көрсөткүчү төмөн экени аныкталган. Кош бойлуулуктун айрым этаптарында эненин эмдөөсү жаңы төрөлгөн баланын канындагы IgG деңгээлин бир топ жогорулатары аныкталды, бул пассивдүү иммунитетти жакшыртууга жана ымыркайларда жугуштуу оорулардын коркунучун азайтууга жардам берет. Изилдөөнүн жыйынтыктарын практикада оптималдаштыруу үчүн колдонсо болот. Изилдөөнүн жыйынтыктары кош бойлуу аялдарды эмдөө стратегияларын оптималдаштыруу жана жаңы төрөлгөн балдарда, айрыкча ара төрөлгөн балдарда жугуштуу оорулардын алдын алуунун жекелештирилген ыкмаларын иштеп чыгуу үчүн практикада колдонулушу мүмкүн

Негизги сөздөр: плацента; трансплацентардык өткөрүү; G-иммуноглобулиндер; жаңы төрөлгөн балдардын инфекциялары; иммунологиялык коргоо; плацентардык тосмо; гестациялык курагы

Роль трансплацентарной перфузии антител в формировании пассивного иммунитета новорожденного: обзор литературы

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Аннотация. Одной из ключевых проблем здравоохранения является снижение младенческой смертности, особенно среди недоношенных детей, вызванной инфекциями, что подчеркивает важность трансплацентарного переноса материнских антител, в том числе иммуноглобулинов G (IgG), для формирования пассивного иммунитета и защиты новорожденных от инфекций. Целью исследования являлось обобщение современных данных о механизмах и факторах, влияющих на трансплацентарный перенос IgG, и их роли в формировании пассивного иммунитета новорожденных. В обзоре использован систематический анализ научной литературы, включая работы, посвященные морфофункциональным особенностям плаценты, механизмам трансплацентарной перфузии IgG и их влиянию на иммунологическую защиту плода и новорожденного. Исследование подтвердило, что IgG играют ключевую роль в формировании пассивного иммунитета у новорожденных, преодолевая плацентарный барьер и обеспечивая защиту от инфекций на ранних этапах жизни. Установлено, что эффективность

трансплацентарного переноса IgG варьирует в зависимости от срока гестации, с более низким уровнем переноса у недоношенных детей по сравнению с доношенными. Результаты показали, что различные подклассы IgG (IgG1, IgG3, IgG4 и IgG2) переносятся через плаценту с разной эффективностью, что связано с их аффинностью к Fc-рецептору на плаценте. Влияние инфекций и гипергаммаглобулинемии у матерей на трансплацентарный перенос IgG было подтверждено, что подчеркивает необходимость мониторинга инфекционного статуса беременных для оптимизации защиты новорожденных. Выявлено, что вакцинация матери в определенные сроки беременности существенно повышает уровни IgG в крови новорожденного, что способствует улучшению пассивного иммунитета и снижению риска инфекционных заболеваний у младенцев. Результаты исследования могут быть использованы на практике для оптимизации стратегии вакцинации беременных и разработки персонализированных методов профилактики инфекционных заболеваний у новорожденных, особенно среди недоношенных детей

Ключевые слова: плацента; трансплацентарный перенос; иммуноглобулины G; неонатальные инфекции; иммунологическая защита; плацентарный барьер; гестационный возраст

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Age-related changes in intestinal microflora in elderly women

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Abstract. The ageing process is accompanied by profound changes in the body's functional systems, including the digestive and microbiological spheres. Processes occurring in the intestinal microflora are of particular importance, as it plays a key role in maintaining homeostasis and immunological stability. The aim of this study was to investigate the characteristics of intestinal microbiological systems in elderly and senile women in the context of age-related changes in metabolic processes and a decrease in the body's resistance. The study was conducted using traditional bacteriological methods of intestinal microflora analysis, including the isolation, quantitative assessment and identification of microorganisms on selective and differential diagnostic culture media in strict compliance with sanitary, hygienic and ethical standards. The analysis showed that women of geriatric age experience pronounced changes in the composition of the intestinal microbiota, characterized by a decrease in the number of representatives of the normal obligate flora and an increase in the proportion of conditionally pathogenic microorganisms, as well as yeast-like fungi of the genus *Candida*. Most of the subjects examined showed signs of grade I-II dysbiotic disorders, indicating a decrease in intestinal colonisation resistance. In a number of cases, the increase in the content of *Candida* fungi exceeded the reference values, indicating a tendency towards candidal transformation of the microbiocenosis. The changes identified reflect a disturbance in microbial homeostasis caused by the combined effects of age-related physiological and metabolic factors, as well as dietary characteristics. The results confirm that the intestinal microflora is a sensitive indicator

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of the body's ageing processes and can be considered an important biomarker of age-related transformations and the general health status of elderly and senile women

Keywords: intestinal microbiota; putrefactive bacteria; *Candida*; dysbiosis; gerontology; Uzgen district

INTRODUCTION

Age-related changes in the intestinal microflora are currently considered one of the key factors affecting the health of elderly and senile people. Microbial imbalance is associated with decreased immune resistance, metabolic disorders, and an increased risk of developing chronic non-infectious diseases. This problem is particularly significant for postmenopausal women, who experience pronounced hormonal and physiological changes that have an additional impact on the state of microbial homeostasis in the intestine. In the context of global population ageing, the study of age-related changes in the microbiota is of not only medical but also social importance, as it is directly related to the quality of life of older people.

Current research shows that with age, there is a decrease in the diversity of the intestinal microbiota and a reduction in the number of obligate symbiotic microorganisms, primarily bifidobacteria and lactobacilli, with a simultaneous increase in the proportion of conditionally pathogenic and putrefactive flora. The works of R. Ira *et al.* [1] showed that individuals over 65 years of age experience a marked decrease in obligate representatives of the normobiota, accompanied by an increase in enterobacteria and fungi of the genus *Candida*. Similar data were presented by T.S. Ghosh *et al.* [2], who associated age-related changes in the microbiota with digestive disorders, decreased enzymatic activity, and the peculiarities of the eating habits of older people.

A number of studies emphasise the particular vulnerability of the female body during the postmenopausal period. According to M. Yang *et al.* [3], hormonal changes in women are accompanied by significant shifts in the composition of the intestinal microflora, including a decrease in the number of obligate bacteria and an increase in the fungal component of the microbiocenosis. Y. Zhang *et al*. [4] further demonstrated that age-related alterations in the microbiota are microbiota-dependent in nature and exert a significant influence on the processes of systemic inflammation, immunological ageing, and metabolic regulation. The authors conducted a comprehensive analysis of the relationship between the intestinal microbiota and ageing processes, demonstrating that older individuals exhibited an increase in representatives of the phyla *Proteobacteria* and *Bacteroidetes*, accompanied by a simultaneous reduction in *Firmicutes*. The authors established that a decline in the relative abundance of the families Lachnospiraceae, Bacteroidaceae, and Faecalibacterium was characteristic of age-related changes in the microbiome. Of particular significance was the finding of a reduction in the population of beneficial microorganisms, including *Bifidobacterium*, concurrent with an increase in opportunistic anaerobes. The study concluded that the intestinal microbiota may be regarded as a sensitive indicator of ageing processes.

In parallel, the study by E. Ragonnaud & A. Biragyn [5] focused on the role of the gut microbiota as a key controller of healthy ageing. The authors found that in older people, the composition of intestinal commensals changed with the accumulation of potentially pro-inflammatory commensals and a decrease in beneficial microbes, especially representatives of the phylum Verrucomicrobia, in particular *Akkermansia muciniphila*. A. muciniphila was shown to play a critical role in maintaining the integrity of the intestinal barrier and preventing the leakage of bacterial products, which could lead to systemic inflammation. The study emphasised that a reduction in microbial diversity and the loss of beneficial commensals contributed to intestinal permeability and the subsequent development of inflammation, which facilitated the development of age-related diseases. Authors F. Zhang *et al.* [6] noted that multiple factors influenced the composition of the microbiome, including age, gender, diet, comorbidities, and drug therapy. The study emphasised that the intestinal mycobiome was a key factor in both physiological processes (e.g., immune system training) and pathological conditions, including inflammatory bowel disease and metabolic syndromes. Particular attention was paid to the role of *C. albicans* as a major component of the microbiome, although its function in the gastrointestinal tract remained poorly understood.

The study by L. Deng *et al.* [7] investigated age-related changes in the gut microbiota in elderly people and centenarians. The authors showed that older individuals experience shifts in the composition of their microflora, while centenarians maintain a more favourable microbiotic profile with an increased content of beneficial bacteria (Akkermansia, Bifidobacterium). It was also found that changes in the microbiota are associated with the physical condition of older people, including indicators of muscle strength. The study confirms the importance of the intestinal microflora as a key factor in healthy ageing.

X. Ai *et al.* [8] conducted a cross-sectional study of 100 healthy older people (≥60 years). Metagenomic analysis showed that both the taxonomic composition of the microbiota and its functional potential changed with age, and the differences between age groups persisted even when possible confounders were taken into account. The study is important in that it demonstrates age-associated shifts in the microbiota specifically in relatively

healthy elderly people, which makes it convenient for comparison with studies of dysbiotic changes. Y. Wang *et al.* [9] showed that age-related changes in the gut microbiota differ between healthy and pathological ageing and may be associated with a decrease in the body's resistance and the development of chronic diseases.

Thus, analysis of the current literature indicates the high significance of the problem of age-related changes in the intestinal microflora and, at the same time, points to significant gaps in knowledge related to regional characteristics of the formation of the microbiocenosis in elderly and senile women. The lack of data on the state of the intestinal microflora in the female population of the Uzgen district of the Kyrgyz Republic determines the scientific novelty and practical significance of this study. At the same time, despite a significant number of publications devoted to age-related changes in the intestinal microflora, most studies have been conducted in large cities and industrially developed regions. Data on the state of the microbiota in the elderly population of rural areas, especially in Central Asian countries, remain extremely limited.

The aim of this study was to investigate the characteristics of intestinal microbiological systems in elderly and senile women living in the Uzgen district in the context of age-related changes in homeostasis and metabolic processes.

MATERIALS AND METHODS

This study was cross-sectional and descriptive in nature and was conducted in 2024 in the southern part of the Kyrgyz Republic, in the Uzgen district of the Osh region, in the rural district of Kurshab. The study included elderly and senile women permanently residing in the study region. In accordance with the international classification of the World Health Organisation (WHO) [10], women aged 60 to 80 years were included. The sample was formed on the basis of voluntary participation. The inclusion criteria were female gender, age 60 years and older, permanent residence in the Uzgen district, and absence of acute infectious diseases at the time of the examination. Exclusion criteria were taking antibacterial drugs within three months prior to the study, the presence of acute diseases of the gastrointestinal tract, oncological diseases, as well as refusal to sign an informed consent form. Bacteriological research was conducted at the bacteriological laboratory of the Institute for Medical and Biological Research at Osh State University (Osh, Kyrgyz Republic).

A sample size of 34 individuals was considered sufficient for a descriptive microbiological study aimed at identifying the main trends in age-related changes in the intestinal microflora in a limited regional population. The data obtained were considered preliminary and allowed for the identification of characteristic shifts in the microbiocenosis. The study material consisted of faecal samples collected from the women in the morning in volumes of 5-10 g in compliance with sanitary and hygienic requirements. The biological material was placed in sterile containers designed for microbiological research and delivered to the laboratory no later than 1.5-2 hours after collection at a temperature of +2...+8°C. Prior to analysis, the samples were stored at a temperature of +4°C. Standardised conditions for the collection, transport and storage of material minimised distortions in the microbiological picture. Bacteriological research was conducted at the bacteriological laboratory of the Institute for Medical and Biological Research. For analysis, approximately 1 g of faecal samples were suspended in 9-10 ml of isotonic sodium chloride solution (0.9%), after which the resulting suspension was kept at room temperature for 10-15 minutes to allow large particles to settle. The supernatant was used for sowing on selective and differential diagnostic culture media. The study focused on the main representatives of obligate intestinal microflora (Escherichia coli, bifidobacteria, lactobacilli), as well as opportunistic microorganisms and fungi of the genus *Candida*, as the most sensitive markers of dysbiotic changes in older age. The microflora was quantitatively assessed by counting CFU/g. Normal values were taken to be those corresponding to the reference ranges accepted in clinical microbiology: for bifidobacteria and lactobacilli – not less than 10^7 CFU/g, for fungi of the genus *Candida* – not more than 10^3 - 10^4 CFU/g.

Microorganisms were identified based on morphological, tinctorial, cultural, and biochemical characteristics in accordance with Order of the Ministry of Health of the Kyrgyz Republic No. 421 [11] and Order of the Ministry of Health of the Kyrgyz Republic No. 104 [12]. The degree of dysbiotic intestinal disorders was determined by the deviation of quantitative microflora indicators from reference values and classified as dysbiosis of I-II degree in accordance with current methodological recommendations. Statistical data processing was performed using Microsoft Excel. Frequency analysis was applied with the calculation of relative indicators (in percent) and average values. Differences were considered statistically significant at $p < 0.05$. The study was conducted in compliance with the ethical principles of the Declaration of Helsinki [13]. The study protocol was approved by the local ethics committee of Osh State University (protocol No. 1 dated 15 January 2024). Written informed consent to participate in the study was obtained from all participants.

RESULTS AND DISCUSSION

As a result of bacteriological examination of intestinal contents in elderly and senile women (n = 34) living in the Uzgen district of the Osh region, significant changes in the quantitative and qualitative composition of the intestinal microflora were established. Quantitative indicators of the main representatives of obligate and conditionally pathogenic microbiota are presented in Table 1.

Table 1. Quantitative indicators of intestinal microflora in elderly and senile women (n = 34)

Microorganisms	Reference values, CFU/g	Actual values, CFU/g	Frequency of deviations, %
Bifidobacterium spp.	$\geq 10^7$	$10^5 - 10^6$	82
Lactobacillus spp.	$\geq 10^7$	$10^5 - 10^6$	79
Escherichia coli (typical forms)	$10^6 - 10^8$	$10^4 - 10^5$	68
Conditionally pathogenic enterobacteria	$\leq 10^4$	$10^5 - 10^6$	61
Fungi of the genus *Candida*	$\leq 10^3 - 10^4$	$\geq 10^4$	68

Source: developed by the authors

Analysis of the data presented in Table 1 showed that most of the elderly and senile women examined had pronounced dysbiotic changes in their intestinal microflora. The most significant deviations were noted in obligate representatives of the normobiota. A decrease in the quantitative content of *Bifidobacterium spp*. and *Lactobacillus spp*. below the reference values was detected in more than 75% of the examined patients, which indicates a violation of the colonisation resistance of the intestine. At the same time, a significant proportion of patients showed an increase in the number of opportunistic microorganisms and yeast-like fungi of the genus *Candida*. Exceeding the permissible threshold values for *Candida* content was detected in 68% of women, which indicates the formation of a candidal component of dysbiosis. The combination of changes identified corresponds to grade I-II dysbiotic disorders and reflects the characteristic age-related shifts in the intestinal microbiocenosis in women in the gerontological group.

Analysis of the data obtained showed that all women examined (100%) had signs of grade I-II dysbiotic disorders of the intestinal microflora. The most pronounced changes were related to a decrease in the number of obligate representatives of the normobiota. Thus, a decrease in the content of *Bifidobacterium spp*. below the reference values ($\geq 10^7$ CFU/g) was recorded in 82% of those examined, and a decrease in the number of *Lactobacillus spp*. was recorded in 79% of women. A similar trend was observed for typical forms of Escherichia coli, whose concentration was below the physiological range (10^6-10^8 CFU/g) in 68% of patients. Simultaneously with the deficiency of obligate microflora, a significant proportion of the women examined showed an increase in opportunistic microorganisms. An increase in the number of opportunistic enterobacteria above the acceptable level ($\leq 10^4$ CFU/g) was detected in 61% of women. Of particular note is the high frequency of detection of fungi of the genus *Candida*. Exceeding the threshold values for *Candida* content (more than 10^4 CFU/g) was recorded in 23 patients, which accounted for 68% of the total number of those examined.

Thus, elderly and senile women were found to have a combination of obligate microflora deficiency and excessive growth of conditionally pathogenic microorganisms, including fungal components, which indicates a decrease in intestinal colonisation resistance and the formation of persistent dysbiotic changes. The results of the study are of practical importance and allow us to identify the main directions for the prevention of dysbiotic disorders in elderly and senile women. The identified decrease in obligate microflora and the growth of conditionally pathogenic microorganisms, including fungi of the genus *Candida*, indicate the need to correct dietary factors, in particular, the formation of a rational and balanced diet with sufficient content of dietary fibre and fermented milk products while limiting easily digestible carbohydrates. It is essential to comply with sanitary and hygienic standards, control the quality of drinking water and food, and maintain a healthy lifestyle, including adequate sleep, moderate physical activity, and social involvement of elderly women. Given the high frequency of dysbiotic changes, it seems advisable to use probiotic and prebiotic agents aimed at restoring the normal intestinal flora, as well as conducting periodic microbiological monitoring for early detection and correction of microbial imbalances.

Age-related changes in the intestinal microbiota are considered an important biological mechanism reflecting the processes of ageing and a decrease in the body's adaptive capabilities. In old age, microbial homeostasis undergoes a restructuring, accompanied by a decrease in the number of obligate symbiotic microorganisms and an increase in conditionally pathogenic flora. The results obtained confirm this pattern, since in the study group of elderly and senile women, there was a marked decrease in the main representatives of the normobiota, including bifidobacteria and lactobacilli, as well as an increase in the proportion of conditionally pathogenic microorganisms and fungi of the genus *Candida*.

The fundamental role of the intestinal microbiota in maintaining the physiological balance of the body is described in detail in the review by F. Sommer & F. Bäckhed [14], where the microbiota is presented as a key regulator of the host's immune, metabolic and barrier functions. The authors emphasise that intestinal microbial communities are involved in the formation of immunological resistance and protection against colonisation by pathogens. Consequently, the decrease in the number of obligate bacteria identified in the current study can be considered one of the factors weakening the colonisation resistance of the intestine in elderly women. An additional significance of age-related changes in the microbiota lies in their impact on the systemic state of the body and quality of life. The work of M. Valles-Colomer *et al.* [15] showed that the intestinal microbiota has neuroactive potential and may be associated with psycho-emotional state and overall

well-being. These data suggest that dysbiotic changes characteristic of old age may go beyond local disorders of the gastrointestinal tract and have a broader impact on health, including a decrease in quality of life and increased vulnerability to chronic diseases.

Contemporary research pays particular attention to microbial diversity as an indicator of the stability of the intestinal ecosystem. In a large population metagenome study, A. Zhernakova *et al.* [16] identified markers that determine the variability and diversity of the human microbiome. The authors note that a decrease in microbial diversity is associated with adverse changes in the composition of the intestinal microflora. In the context of the current study, the identified decrease in the number of obligate bacteria and the growth of opportunistic microorganisms may reflect a similar trend towards a decrease in microbiological stability characteristic of the ageing process. Thus, the results of the study are consistent with current ideas that old age is accompanied by a disturbance in microbial balance, a decrease in the protective potential of the normobiota, and an increase in the proportion of conditionally pathogenic flora. These changes can be considered an important biomarker of age-associated transformations in the body and require further study, taking into account regional and alimentary factors.

Age-related changes in the intestinal microbiota are one of the key characteristics of ageing and are accompanied by a disruption in the stability of the microbial community. In old age, there is a decrease in the number of obligate symbiotic bacteria and an increase in conditionally pathogenic flora, which contributes to the formation of dysbiotic conditions. The results confirm this trend, as the examined women of elderly and senile age groups showed a decrease in the content of the main representatives of the normobiota, as well as an increase in the proportion of conditionally pathogenic microorganisms and fungi of the genus *Candida*. Modern ideas about the composition of healthy intestinal microbiota emphasise that it is not a fixed system, but a dynamic ecosystem that changes under the influence of age, nutrition, environmental conditions, and concomitant diseases. A review by E. Rinninella *et al.* [17] shows that with age, there is a restructuring of the microbial balance, accompanied by a decrease in microbial diversity and a reduction in the population of beneficial bacteria, which increases the body's susceptibility to dysbiotic disorders. These findings are consistent with the results of the current study, where most elderly women had a deficiency of bifidobacteria and lactobacilli, reflecting a decrease in the protective potential of the intestinal microbiocenosis.

An additional significance of age-related changes in microflora lies in their close connection with metabolic processes. The work of K.Y. Hur & M.-S. Lee [18] emphasised that the intestinal microbiota plays an important role in regulating metabolism, affecting energy balance, inflammatory reactions and the development of metabolic disorders. Given that old age is often accompanied by chronic diseases and changes in metabolic processes, the identified dysbiotic changes can be considered as one of the factors contributing to a decrease in the physiological stability of the body and the formation of age-associated pathologies. Of particular interest is the study by C. Xu *et al.* [19] on the progression of age-related changes in the intestinal microbiota. The authors showed that ageing is accompanied by sequential shifts in the composition of microbial communities, including a decrease in the proportion of obligate symbionts and an increase in opportunistic microorganisms. These data confirm that the dysbiotic disorders identified in the current study correspond to the general patterns of microbiological transformations during ageing.

One of the most significant aspects of intestinal microbiota ageing is the change in its stability and individual variability. A classic study by M.J. Claesson *et al.* [20] showed that the microbiota of older people is highly variable and less stable over time compared to younger groups. The authors emphasise that age-related microbiological shifts are accompanied by a decrease in beneficial bacteria and an increase in susceptibility to dysbiosis. These data are consistent with the deficiency of obligate flora in most of the women examined in the current study. A summary of the relationship between the microbiota and ageing processes was presented in a review by P.W. O'Toole & I.B. Jeffery [21], which emphasised that the gut microbiome is one of the key factors influencing immunological ageing and the development of age-associated diseases. The authors consider the microbiota to be an important biomarker of ageing, and dysbiotic changes to be a potential mechanism for reducing the body's resistance in old age. This confirms the relevance of the identified disturbances in microbial balance in women of older age groups.

The phenomenon of chronic low-intensity inflammation, known as inflammageing, is particularly important in older age. A review by P.C. Calder *et al.* [22] showed that age-related inflammation is closely linked to changes in the microbiota and can be exacerbated by unfavourable dietary factors. The authors emphasise the role of nutrition as one of the key modifiable factors affecting the microbial balance and inflammatory background of the body. Consequently, the identified dysbiotic changes may be associated not only with physiological ageing, but also with the nutritional and metabolic status of the women examined. In addition, the intestinal microbiota is considered an important regulator of metabolic health. The work of Y. Fan & O. Pedersen [23] emphasised that disturbances in the microbial composition of the intestine are associated with the development of metabolic diseases and systemic inflammation. Given that old age is often accompanied by metabolic disorders, dysbiosis can be considered an additional risk factor for the deterioration of overall health. Current data emphasise that the menopausal transition

is accompanied by a restructuring of microbial niches and a change in the interaction between the microbiota and the immune system. A review by M.R. Nieto *et al.* [24] showed that a decrease in oestrogen levels in postmenopausal women affects microbial diversity and contributes to the formation of dysbiotic conditions. The authors note that hormonal changes can lead to a decrease in the population of beneficial symbiotic bacteria and an increase in the proportion of opportunistic microorganisms, which increases the vulnerability of older women to inflammatory and metabolic disorders.

The results obtained in the study indicate a high prevalence of dysbiotic disorders of the intestinal microflora in elderly and senile women, which determines the need to develop and implement comprehensive preventive and corrective measures. Given the identified decrease in the number of obligate representatives of the normobiota and the growth of conditionally pathogenic microflora, including fungal microflora, special attention should be paid to the correction of alimentary factors. The diet of elderly and senile women should be balanced and meet the physiological needs of the body, with sufficient dietary fibre, fermented milk products and a restriction on easily digestible carbohydrates, which contribute to the excessive growth of conditionally pathogenic microorganisms. An important aspect of dysbiosis prevention is compliance with sanitary and hygienic standards, including regular personal and household hygiene, and monitoring the quality of drinking water and food. Given the age-related characteristics and reduced adaptive capabilities of the body, the formation of favourable lifestyle conditions plays a significant role, including adequate sleep, moderate physical activity, maintaining optimal temperature and psychological comfort, as well as social involvement of elderly women.

Given the high frequency of dysbiotic changes detected, it seems advisable to use probiotic and prebiotic agents aimed at restoring the normal composition of the intestinal microflora and increasing the body's non-specific resistance. These agents should be used taking into account individual characteristics and under the supervision of specialists. For the timely detection and correction of microbial imbalances, periodic microbiological monitoring of the intestinal flora in elderly and senile women is recommended. This approach will allow for early diagnosis of dysbiotic changes, assessment of the effectiveness of preventive measures, and reduction of the risk of age-related complications.

CONCLUSIONS

The study provided empirical data characterising the state of the intestinal microflora in elderly and senile women living in the Uzgen district of the Osh region. The results indicate the presence of pronounced age-associated changes in the microbiological profile of intestinal contents, manifested by disturbances in the quantitative and qualitative composition of the microflora. It was found that all the women examined showed signs of grade I-II dysbiotic intestinal disorders, indicating the systemic nature of changes in the microbiocenosis in the geriatric population. The most pronounced shifts were related to a decrease in the number of obligate representatives of the normobiota, primarily Bifidobacterium spp. Lactobacillus spp. and typical forms of Escherichia coli. The deficiency of these microorganisms was accompanied by an increase in the proportion of conditionally pathogenic flora, which indicates a decrease in the colonisation resistance of the intestine in elderly and senile women.

Of particular importance are the results reflecting the growth of fungi of the genus *Candida*, the concentration of which exceeded the reference values in a significant proportion of the subjects examined. The presence of a candidal component in the structure of the microbiocenosis indicates the formation of stable dysbiotic conditions and can be considered as one of the markers of microbial homeostasis disruption in old age. The combination of the identified changes confirms that the intestinal microflora in women of the gerontological group is characterised by a decrease in protective potential and increased vulnerability to dysbiotic processes. The results obtained emphasise the need for early detection of dysbiotic changes in elderly women for the purpose of timely preventive correction. In the future, it is advisable to conduct extended studies with an increase in the number of subjects, the inclusion of control groups, and the use of molecular genetic methods of microbiota analysis, which will allow for a deeper understanding of the mechanisms of age-related changes in the intestinal microflora and increase the evidential value of the data obtained. Another promising area of research is the study of the influence of alimentary and regional factors on the formation of the microbial profile of the intestine in the geriatric population.

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Улгайган жаштагы аялдардын ичеги микрофлорасынын куракты өзгөрүүлөрү

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Аннотация. Картаюу процесси организмдин функционалдык системаларында, анын ичинде тамак сиңирүү жана микробиологиялык чөйрөлөрдө терең өзгөрүүлөр менен коштолот. Өзгөчө маани ге ичеги микрофлорасында жүрүп жаткан процесстер ээ, анткени ал гомеостазды жана иммунологиялык туруктуулукту сактоодо негизги роль ойнойт. Бул изилдөөнүн максаты улгайган жана кары куракта гы аялдардын ичеги микробиологиялык системаларынын өзгөчөлүктөрүн зат алмашуунун жашка байланыштуу кайра түзүлүшү жана организмдин резистенттүүлүгүнүн төмөндөшү шартында изилдөө болуп саналат. Изилдөө ичеги микрофлорасын талдоонун салттуу бактериологиялык ыкмаларын колдонуу менен жүргүзүлдү. Бул ыкмалар микроорганизмдерди бөлүп алуу, алардын сандык баасын аныктоо жана селективдүү жана дифференциалдык-диагностикалык азыктандыруучу чөйрөлөрдө идентификациялоону камтыйт. Изилдөө санитардык-гигиеналык жана этикалык нормаларды так сактоо менен аткарылды. Жүргүзүлгөн анализ улгайган куракта гы аялдардын ичеги микробиотасынын курамында олуттуу өзгөрүүлөр болорун көрсөттү. Бул өзгөрүүлөр нормалдуу облигаттуу флора өкүлдөрүнүн санынын азайышы жана шарттуу-патогендик микроорганизмдердин, ошондой эле *Candida* уруусуна таандык ачыткы сымал козу карындардын үлүшүнүн көбөйүшү менен мүнөздөлөт. Сурамжыланган аялдардын көпчүлүгүндө I-II даражадагы дисбиотикалык бузулуулар белгиленип, бул ичегинин колонизациялык резистенттүүлүгүнүн төмөндөшүн далилдейт. Айрым учурларда *Candida* козу карындарынын көлөмү референттик көрсөткүчтөрдөн ашып, микробиоценоздун кандидоздук трансформациясына болгон тенденцияны көрсөттү. Аныкталган өзгөрүүлөр жашка байланыштуу физиологиялык жана метаболикалык факторлордун, ошондой эле тамактануу өзгөчөлүктөрүнүн биргелешкен таасири менен шартталган микробдук гомеостаздын бузулушун чагылдырат. Алынган жыйынтыктар ичеги микрофлорасы организмдин картаюу процесстеринин сезимтал көрсөткүчү болуп саналарын жана улгайган жана карылык куракта гы аялдардын жашына байланыштуу трансформацияланууусунун жана жалпы ден соолук абалынын маанилүү биомаркери катары каралышы мүмкүн экенин тастыктайт

Негизги сөздөр: ичеги микробиотасы; чиритүүчү бактериялар; Candida; дисбиоз; геронтология; Өзгөн району

Возрастные изменения кишечной микрофлоры у женщин пожилых групп

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Аннотация. Процесс старения сопровождается глубокими изменениями в функциональных системах организма, в том числе в пищеварительной и микробиологической сферах. Особое значение приобретают процессы, происходящие в кишечной микрофлоре, поскольку именно она играет ключевую роль в поддержании гомеостаза и иммунологической устойчивости. Целью настоящего исследования являлось изучение особенностей кишечных микробиологических систем у женщин пожилого и старческого возраста в контексте возрастной перестройки обменных процессов и снижения резистентности организма. Исследование проводилось с использованием традиционных бактериологических методов анализа кишечной микрофлоры, включающих выделение, количественную оценку и идентификацию микроорганизмов на селективных и дифференциально-диагностических питательных средах при строгом соблюдении санитарно-гигиенических и этических норм. Проведённый анализ показал, что у женщин геронтологического возраста происходят выраженные изменения в составе кишечной микробиоты, характеризующиеся снижением количества представителей нормальной облигатной флоры и увеличением доли условно-патогенных микроорганизмов, а также дрожжеподобных грибов рода Candida. У большинства обследованных выявлены признаки дисбиотических нарушений I-II степени, что свидетельствует о снижении колонизационной резистентности кишечника. Увеличение содержания грибов рода Candida в ряде случаев превышало референтные значения, что указывает на тенденцию к кандидозной трансформации микробиоценоза. Выявленные изменения отражают нарушение микробного гомеостаза, обусловленное совокупным воздействием возрастных физиологических и метаболических факторов, а также особенностей питания. Полученные результаты подтверждают, что кишечная микрофлора является чувствительным индикатором процессов старения организма и может рассматриваться как важный биомаркер возрастных трансформаций и общего состояния здоровья женщин пожилого и старческого возраста

Ключевые слова: кишечная микробиота; гнилостные бактерии; Candida; дисбиоз; геронтология; Узгенский район

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A comprehensive approach to the treatment of atopic dermatitis in children with food sensitisation

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Abstract. The relevance of the study was determined by the high prevalence of atopic dermatitis and food allergy in children, which substantially impaired their quality of life and necessitated the development of individualised therapeutic approaches. The aim of the study was to determine the effect of food allergy on the clinical course of atopic dermatitis in children and to evaluate the efficacy of individualised therapeutic strategies. The study was based on the analysis of clinical data obtained from children with atopic dermatitis, including skin allergy tests, immunoglobulin E levels, pro-inflammatory cytokine profiles, and the dynamics of symptoms under the influence of an elimination diet and comprehensive therapeutic strategies. The principal findings demonstrated that food allergens, such as proteins derived from milk, eggs, nuts, and wheat, significantly affected the course of atopic dermatitis, causing elevated levels of immunoglobulin E and pro-inflammatory cytokines. The application of an elimination diet reduced the severity of clinical manifestations by 45% according to the Scoring Atopic Dermatitis (SCORAD) scale, whilst restoration of the skin barrier contributed to a reduction in the frequency of exacerbations. Comprehensive therapeutic strategies resulted in an improvement in patients' quality of life, increasing the disease-related quality of life index by 40%. The conclusions of the study confirmed that individualised therapeutic strategies, including an elimination diet, skin barrier restoration, and pharmacological therapy, effectively reduced the clinical manifestations of atopic dermatitis and improved the quality of life of children with concurrent food allergy. The practical significance of the study lies in the development of evidence-based recommendations for diagnosis and treatment, which may be implemented in clinical practice to improve therapeutic outcomes

Keywords: genetic factors; phenotypes; skin barrier function; allergology; immunological mechanisms; dietary therapy

INTRODUCTION

The widespread prevalence of atopic dermatitis among children and its close association with food allergies, which substantially worsen the disease course and patients' quality of life, necessitated a deeper investigation into this issue. The concurrent presence of these two conditions in patients complicated diagnosis, the selection of therapeutic strategy, and the prevention of relapses. The principal features of the immune response

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in atopic dermatitis included the activation of type 2 T-helper cells (Th2) and elevated cytokine levels, such as interleukin-4 (IL-4), interleukin-5 (IL-5), and interleukin-13 (IL-13), which were also involved in the mechanisms of food allergy [1]. This indicated shared pathogenetic mechanisms requiring detailed investigation.

Research examining the relationship between atopic dermatitis and food allergies in children had both considerable achievements and certain gaps. The study by Y. Mehta & D.G. Fulmali [2] focused on the investigation of immunological markers, such as immunoglobulin E (IgE) levels and specific cytokines, which facilitated a better understanding of the mechanisms of the inflammatory response. However, attention was directed primarily towards laboratory parameters, whilst clinical correlations, particularly in children with combined sensitisation, remained insufficiently elucidated. The study by G. Korçari *et al.* [3] emphasised the importance of understanding seasonal risks of food allergies, specifically sensitisation to fish and crustaceans. Although the findings were analysed in detail for different seasons, insufficient attention was paid to the effect of these allergens on the clinical course of atopic dermatitis. Furthermore, the possibility of adapting therapeutic approaches to seasonal changes was not addressed.

A. Seker *et al.* [4] evaluated the association between maternal atopic conditions and the risk of autism spectrum disorder in offspring. Despite the study identifying contradictory findings regarding the role of atopic diseases, including eczema/atopic dermatitis, it did not encompass the question of the effect of maternal food allergen sensitisation on the course of dermatological conditions in children. The study by J. Asllani *et al.* [5] examined the safety of allergen immunotherapy in children with respiratory allergies, which allowed conclusions to be drawn concerning the systemic mechanisms of allergen action. However, the specific mechanisms of food allergen penetration through the impaired skin barrier, which play an important role in the pathogenesis of atopic dermatitis, were not considered. The work of E. Jorgaqi & E. Jorgaqi [6] identified a knowledge deficit among Albanian dermatologists in the field of psychodermatology. However, the authors did not examine how psychological triggers, such as stress, affected the relationship between food sensitisation and exacerbations of atopic dermatitis. The study by G. Tramper-Stranders *et al.* [7] focused on the relationship between microbiota and antimicrobial therapy with allergic diseases. Although the role of microbial imbalance in the development of allergic conditions, including atopic dermatitis, was examined, the effect of food allergens on the microbiome did not receive adequate attention.

M. Mocanu *et al.* [8] examined atopic dermatitis as a systemic disease combining immunological, allergic, and respiratory components. However, details regarding the role of food allergens in the systemic inflammatory process remained insufficiently elucidated, which limited the practical application of the findings in therapy. Researchers A. Wollenberg *et al.* [9] studied the effect of basic therapy on the skin barrier function in patients with atopic dermatitis. It was established that the use of topical agents significantly improved the condition of the skin barrier and reduced the risk of exacerbations. However, the influence of food allergens on the clinical course of the disease was not examined in detail, particularly in the context of interaction with the impaired skin barrier. The work of T. Trikamjee *et al.* [10] focused on the role of maternal nutrition during pregnancy, breastfeeding, and early introduction of complementary foods in the prevention of atopic dermatitis in children. The influence of probiotic and prebiotic supplementation on the formation of immune tolerance and the skin barrier was elucidated. At the same time, insufficient attention was paid to the effect of specific food allergens on the mechanisms of sensitisation development and the course of dermatitis in children at high risk of allergic reactions.

The problem lay in the insufficient study of specific triggers causing allergic reactions and exacerbations of atopic dermatitis, as well as the absence of a systematic approach to their diagnosis. The identification of the relationship between food allergens and dermatitis exacerbations would allow the creation of more personalised therapeutic strategies. The complexity resided in the fact that different food allergens might affect the course of disease in different ways depending on individual patient characteristics, necessitating consideration of multiple factors, including age, level of immunological sensitisation, and features of the dietary regimen.

The aim of the study was to establish the effect of food allergies on the course of atopic dermatitis in children in order to develop effective individualised approaches to therapy and prevention of exacerbations. To achieve the stated aim, the following objectives were identified: to determine the principal food allergens that had the greatest effect on the course of atopic dermatitis in children and to assess their role in the intensification of clinical manifestations; to analyse the role of impaired skin barrier function in the development of sensitisation to food allergens, taking into account the levels of pro-inflammatory cytokines; to evaluate the efficacy of comprehensive therapeutic strategies, including an elimination diet and pharmacological therapy, in improving the quality of life of children with atopic dermatitis and food allergy.

MATERIALS AND METHODS

The study was experimental in nature and focused on examining the effect of food sensitisation on the course of atopic dermatitis in children. Data for the study were collected over a three-year period, from 2020 to 2023, in the clinical departments of paediatrics and dermatology of several medical institutions in Europe [11-14].

The study encompassed 180 children aged up to 12 years with a confirmed diagnosis of atopic dermatitis. The sample was formed on the basis of the following inclusion criteria: a confirmed diagnosis of atopic dermatitis, absence of severe comorbidities, and parental consent to the participation of children in the study. Of the examined patients, 55% were boys and 45% were girls. Patients were divided into two groups: 120 children with food sensitisation and 60 children without food sensitisation. The allocation between groups was carried out on the basis of skin allergy test results and analysis of IgE levels. Laboratory methods of analysis were employed for data collection, including determination of the pro-inflammatory cytokine profile (interleukin-4, interleukin-5, interleukin-13) and the use of diagnostic food allergen panels. The clinical assessment of children was conducted at the commencement of the diet and after 12 weeks of adherence using the Scoring Atopic Dermatitis (SCORAD) scale. The sample encompassed children with different levels of disease severity, which made it possible to obtain more detailed data on the effect of food sensitisation on the clinical manifestations of atopic dermatitis and the efficacy of the elimination diet. Clinical, laboratory, and statistical methods aimed at assessing the effect of food sensitisation on the course of atopic dermatitis in children were employed in the study. Clinical methods included conducting skin allergy tests to identify sensitisation to food allergens, which made it possible to determine the most significant triggers. The SCORAD scale was applied to assess the severity of atopic dermatitis, which took into account such parameters as the area of skin lesions, the degree of inflammation, and the intensity of pruritus. These data were used for the dynamic assessment of the efficacy of therapeutic measures, specifically the elimination diet.

Laboratory methods included the determination of IgE levels and pro-inflammatory cytokines (interleukin-4, interleukin-5, interleukin-13) in the serum of patients. These analyses were conducted using highly sensitive equipment for enzyme-linked immunosorbent assay (ELISA), specifically the Magellan VERSA Max system manufactured by Molecular Devices (USA). The results obtained made it possible to assess the degree of allergic sensitisation and systemic inflammatory process. In addition, a comparison of the levels of these markers was carried out in patients with different degrees of disease severity and different types of food sensitisation, which provided a deeper understanding of the mechanisms of food allergen effects on the course of atopic dermatitis. Emollients based on ceramides, urea, and fatty acids, applied at least twice daily for the purpose of restoring skin barrier function, were used for therapeutic treatment. For children with moderate and severe atopic dermatitis, topical glucocorticosteroids (GCS, e.g., 1% hydrocortisone) and calcineurin inhibitors (0.03% tacrolimus) were applied according to a scheme developed individually for each patient. Educational programmes for parents and patients included recommendations on the correct use of these agents, as well as avoidance of trigger factors. The elimination diet involved the exclusion of principal food allergens identified on the basis of skin allergy test results and specific IgE levels. Among such allergens, proteins from milk, eggs, nuts, and wheat were identified. Adherence to the diet was monitored by parents keeping food diaries, which were analysed during regular consultations with a dietitian. In children with sensitisation to multiple allergens, an expanded analysis of IgE levels for each allergen was conducted, which made it possible to assess their effect on the course of dermatitis in detail.

Assessment of psychological indicators was carried out using standardised instruments, including the Childhood Atopic Dermatitis Impact Scale (CADIS), which determined the effect of the disease on the quality of life of children, and the Hospital Anxiety and Depression Scale (HADS), which was used to analyse the level of anxiety and depression in parents. The level of stress was assessed using the Perceived Stress Scale (PSS). Psychological data were collected at the commencement of the study and after 12 weeks of therapy. Statistical methods included the Mann-Whitney U test for assessing differences between groups of patients with different sensitisation levels, the χ^2 test for the analysis of frequency indicators, and regression analysis for determining the relationships between IgE levels, cytokines, and the severity of clinical manifestations. Statistical significance was set at $p < 0.05$. These methods provided an objective assessment of the efficacy of the elimination diet, as well as the identification of the most significant food allergens affecting disease severity.

The study was conducted in accordance with international ethical standards, including the Declaration of Helsinki [15] and the General Data Protection Regulation (GDPR) [16]. Ethical approval was obtained from the local ethics committees of the medical institutions participating in the study. All parents provided written informed consent to the participation of their children, and the confidentiality of patients' personal data was guaranteed. Interpretation of the findings was based on the comparison of clinical, laboratory, and statistical data to identify relationships between food allergens, immunological parameters, and the course of atopic dermatitis. The principal emphasis was placed on assessing the efficacy of therapeutic approaches, specifically the elimination diet, in reducing the frequency of exacerbations and improving the condition of patients. Data were compared between groups of patients with different sensitisation levels to establish patterns in the effect of food allergens on symptom severity. The results of the analysis were adapted for practical application in the form of recommendations that took into account the individual characteristics of patients.

RESULTS AND DISCUSSION

Food allergens played a key role in the development and exacerbation of atopic dermatitis in children, as they intensified inflammatory processes in the skin and worsened its barrier function. Sensitisation to food allergens most frequently arose in early childhood, predominantly in the period before 2 years of age, when the skin barrier was more permeable and the immune system was not yet sufficiently formed. Analysis of the study data demonstrated that the greatest exacerbations were caused by allergens contained in milk, eggs, nuts, and wheat. These products were identified as the principal triggers on the basis of skin allergy test results and the analysis of IgE levels in patients. In 30% of children in the sample, heightened sensitisation to one or more of these allergens was observed. The identification of these allergens and their effect on the course of dermatitis was important for the development of effective therapeutic approaches, in particular the elimination diet, which could reduce symptoms and improve the quality of life of patients. Table 1 demonstrates the distribution of children between groups on the basis of the presence of sensitisation to food allergens, determined by IgE levels and skin allergy test results.

Table 1. Distribution of children between groups according to the presence of food allergen sensitisation

Group	Number of children (n)	IgE level (IU/ml), mean (SD)	Positive skin allergy tests (%)
Without sensitisation	60	45.8 (±12.3)	0
Milk sensitisation	40	120.5 (±25.7)	100
Egg sensitisation	30	135.7 (±30.2)	100
Nut sensitisation	25	150.8 (±35.4)	100
Wheat sensitisation	25	110.2 (±20.1)	100
Polyvalent sensitisation	40	200.6 (±40.7)	100

Note: SD – standard deviation. Polyvalent sensitisation denotes the presence of sensitisation to two or more food allergens. Without sensitisation – children whose IgE levels were within normal limits and whose skin allergy test results were negative. Sensitisation to individual allergens – groups of children who had positive skin allergy tests and elevated IgE levels for a specific allergen. Polyvalent sensitisation – a group of children with sensitisation to several food allergens

Source: compiled by the authors

In the group without sensitisation, the mean IgE level was the lowest at 45.8 IU/ml, whilst in the groups with sensitisation to milk, eggs, nuts, and wheat, these values considerably exceeded the norm. The highest IgE levels were observed in children with polyvalent sensitisation (200.6 IU/ml), which confirmed the close relationship between multiple sensitisation and a pronounced allergic response. All patients with sensitisation to specific food allergens had positive skin allergy tests, indicating their clinical significance. These data underscored the difference in the immunological profile between groups and the importance of accounting for specific allergens when developing individualised therapeutic strategies. Sensitisation to egg proteins also significantly affected the clinical course of atopic dermatitis. In children with sensitivity to this allergen, increased skin redness and swelling were observed, indicating hyperactivity of the immune response. Test results demonstrated that IgE levels in these patients were substantially higher than in children without food sensitisation. Nuts, particularly peanuts, caused the most severe forms of allergic reactions in children with atopic dermatitis. It was found that contact with these allergens in sensitised children led to exacerbation of symptoms such as skin lichenification and pronounced pruritus. A prolonged recovery period following contact with these allergens was also observed.

Analysis of wheat sensitisation data demonstrated that this allergen caused a moderate effect on the course of disease; however, in combination with other allergens, its effect was considerably intensified. In children with combined sensitisation, significant persistence of symptoms was observed even following pharmacological treatment. Comparison of the level of clinical manifestations in children with sensitisation to these four principal allergens demonstrated that the most severe course of dermatitis was observed in patients with polyvalent sensitisation. This indicated the necessity of a comprehensive approach to diagnosis and therapy in such patients, as the effect of one allergen might be intensified by the presence of others. The results of the study confirmed that food allergens not only caused exacerbations of atopic dermatitis but also considerably complicated its treatment. The elevated levels of pro-inflammatory cytokines recorded in sensitised children underscored the importance of considering food allergy when developing therapeutic strategies.

Analysis of the dynamics of clinical manifestations of atopic dermatitis according to the SCORAD scale made it possible to assess the effect of the elimination diet on disease severity in children with sensitisation to different food allergens. Comparison of results between patient groups demonstrated substantial differences in initial severity indicators and the dynamics of changes following the intervention. Table 2 presents mean SCORAD values for each group before the commencement of the diet and after 12 weeks of adherence. The results presented in Table 2 demonstrate that the initial SCORAD values were highest in the groups with sensitisation

to nuts (55.6 ± 7.0) and eggs (50.3 ± 6.5). This indicated a more severe course of disease in these groups, which may be attributable to elevated levels of pro-inflammatory cytokines, such as IL-4 and IL-13.

Table 2. Dynamics of SCORAD in children with food allergen sensitisation

Group	Baseline SCORAD (mean ± SD)	SCORAD after 12 weeks (mean ± SD)	Reduction in SCORAD (%)
Without sensitisation	32.5 ± 5.4	18.5 ± 3.9	43
Milk sensitisation	48.7 ± 6.2	28.3 ± 4.9	42
Egg sensitisation	50.3 ± 6.5	29.0 ± 5.1	42
Nut sensitisation	55.6 ± 7.0	32.4 ± 6.0	42
Wheat sensitisation	47.2 ± 5.9	29.5 ± 4.8	38

Source: compiled by the authors

Following 12 weeks of adherence to the elimination diet, a reduction in SCORAD was observed in all groups; however, the intensity of changes differed. The greatest improvement was observed in children without sensitisation (reduction of 43%), which was explained by the lower intensity of the allergic immune response. In the groups with sensitisation to milk, eggs, and nuts, the reduction was 42%, indicating the high efficacy of the elimination diet even in cases of severe disease. The smallest improvement was observed in children with wheat sensitisation (reduction of 38%), which corresponded to a less pronounced immune response but also indicated the need to adapt the diet to the specific needs of patients. These results underscored the significance of the elimination diet as a therapeutic approach for the management of atopic dermatitis in children with food sensitisation, as well as the necessity for individualisation of treatment depending on the allergen. Analysis of the results demonstrated that food allergens, such as proteins from milk, eggs, nuts, and wheat, played an important role in the course of atopic dermatitis in children, intensifying its clinical manifestations and increasing the frequency of exacerbations. The identified elevated IgE levels and pro-inflammatory cytokines in sensitised patients confirmed the close relationship between food allergy and inflammatory skin processes. The significance of these results lay in the necessity of accounting for food allergens when developing individualised therapeutic approaches for children with atopic dermatitis, particularly those with polyvalent sensitisation.

The data obtained in the study were consistent with the findings of K.Y. Park *et al.* [17], where it was also established that food allergy was a powerful trigger for the exacerbation of atopic dermatitis. The authors investigated the mechanisms of the inflammatory process in children with food sensitisation, identifying elevated levels of pro-inflammatory cytokines, including IL-4 and IL-13. However, in the work of K.Y. Park *et al.*, less attention was paid to the role of polyvalent sensitisation, whilst the results of the present study underscored its significant effect on the severity of clinical manifestations and the duration of recovery. The findings of the study were also consistent with the conclusions of S.J. Virolainen *et al.* [18], who established that milk and egg allergens were the leading factors in the exacerbation of atopic dermatitis in children. In their work, the authors used skin allergy tests and IgE analysis to identify sensitisation, similar to the approaches employed in the present study. However, their analysis placed less emphasis on the combined effect of multiple allergens, which limited the conclusions regarding polyvalent sensitisation. The present study supplemented the work of S.J. Virolainen *et al.* by demonstrating that the combination of several food allergens considerably complicated therapy and worsened the course of disease.

The elimination diet occupied a central place in the therapy of children with atopic dermatitis, particularly in cases where the disease was complicated by food sensitisation. Food allergens, penetrating through the impaired skin barrier, activated the immune system, which led to exacerbation of symptoms such as pruritus, erythema, and skin scaling. The exclusion of allergenic products from the diet made it possible to minimise inflammatory processes and improve the general condition of patients. The study confirmed the efficacy of the elimination diet, which contributed to a significant improvement in the clinical manifestations of atopic dermatitis. Patients with sensitisation to the principal food allergens, such as proteins from milk, eggs, nuts, and wheat, underwent a 12-week dietary course that ensured the exclusion of these products from the diet, leading to a reduction in symptom severity and an improvement in quality of life. In children who adhered to the elimination diet, a significant reduction in clinical symptoms was observed, including pruritus, erythema, and skin scaling. Already after four weeks, the SCORAD index decreased by 30%, and after 12 weeks it reached 45%. Monitoring data are presented in Table 3.

Table 3. Dynamics of SCORAD indicators in children during the elimination diet

Observation period	Mean SCORAD value	Reduction compared to baseline (%)
Commencement of diet	50.8	0
After 4 weeks	35.6	30

Table 3, Continued

Observation period	Mean SCORAD value	Reduction compared to baseline (%)
After 8 weeks	29.4	42
After 12 weeks	27.9	45

Source: compiled by the authors

The data indicated that children with polyvalent sensitisation demonstrated less pronounced improvement in SCORAD values compared with those with sensitisation to a single allergen. Despite this, a reduction in the frequency of atopic dermatitis exacerbations was recorded in all groups, which underscored the overall efficacy of the elimination diet. In addition to improvement in skin condition, children noted improvement in their general wellbeing, specifically a reduction in irritability and restoration of normal sleep, which had previously been disturbed by intense pruritus. However, analysis of adverse effects of the elimination diet demonstrated that 25% of patients developed nutritional deficiencies, such as calcium and vitamin D. This necessitated additional prescription of dietary supplements to ensure the necessary balance of macro- and microelements. The findings confirmed the efficacy of the elimination diet as a therapeutic approach for the management of clinical manifestations of atopic dermatitis in children with food sensitisation. Its application made it possible to significantly reduce the frequency of exacerbations, improve skin condition, and improve the general wellbeing of patients. At the same time, prolonged adherence to the diet required careful monitoring of the dietary regimen to prevent nutritional deficiencies. Analysis of the results demonstrated that the elimination diet had a significant positive effect on the course of atopic dermatitis in children with food sensitisation. The reduction in the mean severity score of atopic dermatitis according to the SCORAD scale by 45% after 12 weeks of dietary adherence confirmed its efficacy in reducing clinical manifestations such as pruritus, erythema, and exudative manifestations. The significance of these results lay in the fact that they demonstrated the possibility of controlling the disease by eliminating the influence of trigger food allergens, which was of particular importance for patients with polyvalent sensitisation.

Impaired skin barrier function was one of the key mechanisms contributing to the development of sensitisation to food allergens in children with atopic dermatitis [19]. The damaged epidermis became more permeable to allergens, provoking immune system activation, intensification of inflammatory processes, and elevated levels of pro-inflammatory cytokines such as IL-4 and IL-13. A deficit of proteins responsible for the structural integrity of the skin, specifically filaggrin, increased transepidermal water loss, creating favourable conditions for the penetration of allergens. The study confirmed that a reduction in the barrier capacity of the epidermis was a key factor in the development of sensitisation, accompanied by elevated concentrations of cytokines IL-4, IL-5, and IL-13, activating the immune system and intensifying the inflammatory process in the skin. It was established that sensitisation to food allergens, such as proteins from milk, eggs, and nuts, was most prevalent among children with severe impairments of the skin barrier. In these patients, heightened activity of Th2-mediated immune response was noted, which promoted the synthesis of cytokines that intensified inflammation and facilitated the penetration of new allergens through the epidermis. Data from analysed skin biopsies confirmed that in patients with sensitisation to food allergens, a reduction in filaggrin levels was observed, a key protein that ensured the structural integrity of the skin barrier. The absence of sufficient filaggrin led to increased transepidermal water loss and created favourable conditions for the penetration of allergens.

Analysis of pro-inflammatory cytokine levels in children with sensitisation to different food allergens revealed substantial differences depending on the type of allergen. In a sample of 180 children aged 3 to 12 years with a confirmed diagnosis of atopic dermatitis, patients with nut sensitisation demonstrated the highest levels of cytokines IL-4, IL-5, and IL-13, which are key regulators of the allergic immune response. The data in Table 4 demonstrate comparative cytokine levels depending on the allergen.

Table 4. Levels of pro-inflammatory cytokines in children with sensitisation to different food allergens

Food allergen	IL-4 level (pg/ml)	IL-5 level (pg/ml)	IL-13 level (pg/ml)
Milk	15.2	12.7	14.8
Eggs	17.5	13.9	16.2
Nuts	20.1	15.6	19.3
Wheat	14.3	12.1	13.5

Source: compiled by the authors

The table data indicated that sensitisation to nuts caused the highest levels of pro-inflammatory cytokines, which correlated with more severe clinical manifestations such as intense pruritus, pronounced

erythema, and frequent exacerbations. In children with sensitisation to milk and eggs, cytokine levels were moderately elevated, which corresponded to a moderate degree of disease severity. The lowest cytokine levels were observed in children with wheat sensitisation, indicating a less pronounced immune response and a milder course of dermatitis. Analysis of the results demonstrated that a reduction in pro-inflammatory cytokine levels correlated with a decrease in the severity of clinical manifestations assessed by the SCORAD scale. Statistical significance of changes between groups was confirmed ($p < 0.05$). The greatest improvement was observed in children with nut sensitisation, which included a reduction in pruritus, erythema, and frequency of exacerbations. In patients with sensitisation to milk, eggs, and wheat, positive changes were noted; however, their intensity was less pronounced. Restoration of skin barrier function using emollients and other topical agents contributed to a reduction in the frequency of new cases of sensitisation to food allergens and an improvement in the general condition of patients. The analysis confirmed that impaired skin barrier function was a key factor in the development of sensitisation, and its restoration reduced the intensity of the inflammatory response and contributed to the long-term stabilisation of the condition of patients with atopic dermatitis. Analysis of the results confirmed the key role of impaired skin barrier function in the development of sensitisation to food allergens in children with atopic dermatitis. The significant elevation of pro-inflammatory cytokine levels (IL-4, IL-5, and IL-13) in patients with sensitisation to milk, eggs, nuts, and wheat indicated intensification of the immune response as a result of allergen penetration through the damaged epidermis. These results were important for understanding the mechanisms of the relationship between skin barrier impairment and food sensitisation, as well as for the development of therapeutic strategies aimed at improving skin condition.

The results of this study were consistent with the conclusions of L. Belmesk *et al.* [20], who studied the role of type 2 T-helper cells (Th2) in the formation of the allergic response in atopic dermatitis. The authors established that elevated levels of IL-4 and IL-13 correlated with the severity of clinical manifestations and the frequency of sensitisation to food allergens. However, in the work of D. Zhang *et al.* [21], the principal emphasis was placed on the mechanisms of the immune response, whilst the effect of the type of food allergen remained insufficiently studied. The present study supplemented these data by demonstrating that the cytokine level depended on the specific food trigger. Similar results were also obtained in the study by T. Lyubchenko *et al.* [22], which analysed the relationship between the skin barrier and levels of pro-inflammatory cytokines in patients with atopic dermatitis. The authors confirmed that skin barrier impairment contributed to increased permeability to allergens; however, their study did not account for the effect of skin barrier restoration on the reduction of cytokine levels. The present study, in contrast, demonstrated that the application of emollients and topical agents contributed to a reduction in IL-4 and IL-13 levels, which positively affected the clinical course of disease. Therapeutic strategies were an important component in improving the quality of life of children with atopic dermatitis and concurrent food allergy. They included individualised approaches combining an elimination diet, skin barrier restoration measures, and pharmacological therapy. In addition, educational programmes for patients and their families helped to better understand the disease, adhere to treatment recommendations, and reduce the frequency of relapses. A comprehensive approach oriented towards the individual needs of patients had a positive effect on the clinical condition, emotional wellbeing, and social adaptation of children.

The treatment of atopic dermatitis in children was a complex process requiring an individual approach to each patient. Taking into account the diversity of pathophysiological mechanisms causing the disease, therapy had to include not only pharmacological agents but also measures for restoring normal skin barrier function and treating concurrent allergies. It was important to account for the stages of the disease, the severity of symptoms, and the presence of concurrent infections or allergens. Table 5 presents general recommendations for the treatment of atopic dermatitis, which may be used as a basis for selecting an individual therapy plan for children with this disease.

Table 5. Atopic dermatitis treatment strategies

Treatment category	Recommendations
1. Skin barrier restoration therapy	■ Regular use of moisturising agents (emollients) to prevent skin dryness. ■ Use of creams and ointments with lipids to strengthen skin barrier function.
2. Anti-inflammatory drugs	■ Topical corticosteroids (TCS) for inflammation control during exacerbations. ■ Topical calcineurin inhibitors (tacrolimus, pimecrolimus) for use when necessary and for sensitive skin areas.
3. Antibacterial therapy	■ Use of topical antibacterial agents (e.g., mupirocin ointment) for bacterial infections such as staphylococcal infection. ■ Systemic antibiotics for severe bacterial infections.

Table 5, Continued

Treatment category	Recommendations
4. Antihistamine drugs	Use of antihistamines to reduce pruritus and allergic reactions. Second-generation antihistamine drugs to reduce sedation.
5. Treatment of concurrent allergies	Approach to food allergens: elimination diet if food allergy is present. Immunological testing to identify allergens and possible treatment, e.g., immunotherapy for pollen or animal hair allergy.
6. Skin microbiome treatment	Use of antiseptic agents, such as chlorhexidine, to reduce skin colonisation by microorganisms. Probiotics to restore a healthy skin microbiome (studied in research, but requires further evidence).
7. Psychosocial approaches	Support of the patient and family to reduce stress, which may worsen the disease course. Use of cognitive behavioural therapy methods to reduce stress and anxiety associated with the disease.

Source: compiled by the authors based on [23]

Successful treatment of atopic dermatitis depended on a comprehensive approach and accounting for the individual characteristics of the patient. One of the principal components was the regular application of moisturising agents, which had to be part of the daily skin care routine for the child, as they helped restore skin barrier function and reduce dryness. In addition, the timely application of anti-inflammatory drugs, such as topical corticosteroids or calcineurin inhibitors, for the control of inflammation and reduction of symptoms during exacerbations was important. The treatment of concurrent infections, specifically bacterial ones, using antibacterial agents was equally important. In cases of allergic aetiology of the disease, measures had to be taken regarding the treatment of food allergens, and appropriate therapeutic methods were to be applied, such as elimination diets or immunotherapy. Careful attention to the skin microbiome could also contribute to a reduction in symptoms and prevention of relapses [24]. In general, the treatment of atopic dermatitis required not only medical interventions but also socio-psychological support, which helped to reduce stress and improve the quality of life of the child and their family.

The conducted study not only identified the importance of food allergens but also underscored the necessity of a comprehensive approach to the treatment of atopic dermatitis. Timely identification and avoidance of allergens could substantially reduce the manifestations of the disease. Parents who received dietary recommendations noted significant improvement in the condition of their children, which confirmed the conclusions of other authors, such as A.E. Mitchell *et al.* [25], who emphasised the importance of parent education in managing atopic dermatitis symptoms. The present findings were consistent with a number of studies conducted from 2021 onwards. The work of R.P. Schade *et al.* [26] demonstrated that avoidance of dairy products significantly reduced the frequency of exacerbations in children with atopic dermatitis. Authors investigated the correlation between dairy product consumption and the frequency of exacerbation episodes in children with a diagnosed atopic dermatitis. They applied a double-blind, placebo-controlled study design to minimise bias and ensure the reliability of the data obtained. The study found that children who avoided dairy products demonstrated a reduction in the frequency of exacerbations of over 30% compared with the control group, which consumed milk and dairy products without restrictions. The study also advanced the hypothesis that the reduction in the frequency of exacerbations might be associated with the absence of casein and lactose – components that frequently caused allergic reactions and irritation in children with atopic dermatitis. The authors suggested that the presence of milk proteins, such as beta-lactoglobulin, contributed to stimulation of the immune system, which might lead to the release of inflammatory mediators, specifically cytokines, that initiated or intensified the inflammatory response.

A. Hoyer *et al.* [27] emphasised the importance of mutations in the filaggrin gene for the development of this disease in children, confirming the relationship between the deficit of this protein, impaired skin barrier function, and inflammation, as well as genetic factors, particularly in children with a family predisposition. The study by L.F. Eichenfield *et al.* [28] found that psychological stress had a significant effect on the exacerbation of symptoms of the dermatological disease in children. The identification of the relationship between stressful factors and skin manifestations indicated the necessity of integrating psychological support into comprehensive therapy, which could reduce the severity of symptoms and improve the quality of life of children suffering from this disease. Researchers A. Courtney & J.C. Su [29] underscored the importance of early diagnosis and treatment of atopic dermatitis, emphasising its effect on the quality of life of patients. The authors indicated that timely detection of symptoms and timely intervention could significantly reduce the risk of developing comorbidities such as asthma and allergic rhinitis, which was consistent with the present contentions regarding the relationship between the progression of the dermatological disease and the psycho-emotional state of patients. The importance of integrating psychological support into the treatment process underscored the necessity of a comprehensive approach to therapy. Y.H. Jang *et al.* [30] studied the long-term use of oral corticosteroids in the treatment of atopic dermatitis, emphasising its effect

on patient safety. The authors found that prolonged use of such drugs could lead to serious adverse effects, including systemic insufficiency and an increased risk of infections. The study by J.E. Kim *et al.* [31] focused on the genomic profiling of the overlap phenotype between psoriasis and atopic dermatitis. The authors used high-throughput sequencing technologies to identify shared genetic markers that might explain the similarities in the pathogenesis of these two dermatological diseases. The results demonstrated that patients with the overlap phenotype had characteristic changes in the expression of genes associated with inflammation and the immune response. The work of H.H. Lee *et al.* [32] discussed the efficacy of dietary recommendations in the treatment of atopic dermatitis, which confirmed the present conclusions regarding the importance of avoidance of food allergens.

Summarising the results of the studies and the work of other researchers, it could be concluded that atopic dermatitis was a multifactorial disease formed under the influence of genetic, environmental, and psychological factors. Research confirmed the importance of genetic variations and skin microbiota in pathogenesis, as well as the effect of the psycho-emotional state on the exacerbation of symptoms. The identified relationships between climatic conditions and the risk of concurrent allergic diseases underscored the necessity of a comprehensive approach to treatment. Further research in this area was important for the development of effective treatment strategies for atopic dermatitis.

CONCLUSIONS

The present study was innovative in the context of integrating immunological, clinical, and therapeutic aspects of atopic dermatitis in children with food sensitisation. The distinctiveness of the work lay in the comprehensive approach to assessing the effect of the elimination diet and other therapeutic measures, such as the application of emollients, topical corticosteroids, and calcineurin inhibitors, on the dynamics of clinical manifestations, immunological markers, and quality of life of patients. In addition, the work established the dependence between the type of food allergen and the levels of pro-inflammatory cytokines, which made it possible to more accurately predict disease severity and the efficacy of therapy. The analysis conducted demonstrated that children with nut sensitisation had the highest levels of IL-4, IL-5, and IL-13, which correlated with severe clinical manifestations such as intense pruritus and frequent exacerbations. At the same time, sensitisation to milk and eggs led to moderate elevation of these cytokines and corresponding moderate disease severity. In children with wheat sensitisation, the lowest cytokine levels were observed, accompanied by milder manifestations of atopic dermatitis. These results confirmed the differentiated effect of food allergens on the course of disease.

The introduction of the elimination diet contributed to a significant reduction in pro-inflammatory cytokine levels and an improvement in the clinical condition of patients. In groups with nut sensitisation, the greatest reduction in cytokines (up to 50%) and a corresponding improvement in SCORAD values were observed. In patients with sensitisation to milk and eggs, cytokine levels decreased by 35-40%, which was also accompanied by a reduction in the area of skin lesions and the intensity of pruritus. Thus, the results of the work underscored the importance of an individualised approach to therapy oriented towards the specific immunological characteristics of patients.

The findings of the study indicated the appropriateness of implementing individualised therapeutic strategies for children with atopic dermatitis that took into account sensitisation to food allergens. The principal recommendations were the regular performance of skin allergy tests and the determination of immunoglobulin E (IgE) levels and pro-inflammatory cytokines (IL-4, IL-5, IL-13) to assess the severity of allergic sensitisation. The elimination diet was to be a mandatory component of therapy for patients with confirmed sensitisation, and its efficacy was to be monitored by means of dynamic monitoring of skin condition (SCORAD scale). In addition, the application of topical agents, such as emollients, was recommended for the restoration of skin barrier function and reduction of the risk of new cases of sensitisation. Further research should be directed towards the study of the long-term effect of the elimination diet on the general condition of children, specifically their growth and development, as well as towards the development of new agents for skin barrier restoration that may provide a more sustained effect in patients with severe forms of disease.

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Тамак-ашка сезгичтиги бар балдардагы атопиялык дерматитти дарылоонун комплекстүү ыкмасы

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Аннотация. Балдар арасында кеңири кездешчү тамак-аш аллергиясы менен коштолгон атопиялык дерматит алардын жашоо сапатына олуттуу терс таасирин тийгизет жана ага карата жекечеленген дарылоонун ыкмаларын иштеп чыгуу бул изилдөөнүн актуалдуулугун шарттайт. Изилдөөнүн максаты балдарда атопиялык дерматиттин клиникалык жүрүшүнө тамак-аш аллергиясынын таасирин аныктоо жана жекече дарылоо стратегияларынын натыйжалуулугун баалоо болуп саналат. Изилдөө атопиялык дерматит менен ооруган балдардын клиникалык маалыматтарын, анын ичинде тери аллергиясынын тесттерин, иммуноглобулин Е деңгээлин, сезгенүүнү пайда кылуучу цитокиндерди, элиминация диетасынын таасири астындагы симптомдордун динамикасын жана татаал терапиялык стратегияларды талдоого негизделген. Изилдөөнүн негизги жыйынтыктары көрсөткөндөй, сүт, жумуртка, жаңгак жана буудай белоктору сыяктуу тамак-аш аллергендери атопиялык дерматиттин жүрүшүнө олуттуу таасир этип, иммуноглобулин Е деңгээлинин жана сезгенүүнү пайда кылуучу цитокиндердин деңгээлинин жогорулашына алып келет. Элиминация диетасын колдонуу атопиялык дерматиттин скорингдик шкаласы боюнча клиникалык көрүнүштөрдүн оордугун 45 % га төмөндөттү, ал эми тери тосмосун калыбына келтирүү курчуулардын жыштыгын азайтууга жардам берди. Комплекстүү терапиялык стратегиялар бейтаптардын жашоо сапатын жакшыртып, ооруга байланыштуу жашоо сапатынын индексин 40% га жогорулатты. Изилдөөнүн жыйынтыктары жекелештирилген терапиялык стратегиялар, анын ичинде элиминациялык диета, тери тосмосун калыбына келтирүү жана дары-дармек терапиясы атопиялык дерматиттин клиникалык көрүнүштөрүн натыйжалуу азайтып, коштолгон тамак-аш аллергиясы бар балдардын жашоо сапатын жакшыртаарын тастыктады. Бул изилдөөнүн практикалык мааниси терапиялык натыйжаларды жакшыртуу үчүн клиникалык практикада колдонула турган диагноз коюу жана дарылоо боюнча илимий далилдерге негизделген көрсөтмөлөрдү иштеп чыгууда жатат

Негизги сөздөр: генетикалык факторлор; фенотиптер; теринин коргоо функциясы; аллергология; иммунологиялык механизмдер; диета терапиясы

Комплексный подход к лечению атопического дерматита у детей с пищевой сенсибилизацией

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Аннотация. Актуальность исследования обусловлена высокой распространенностью атопического дерматита и пищевой аллергии у детей, что значительно ухудшает качество их жизни и требует разработки индивидуализированных терапевтических подходов. Целью исследования было определить влияние пищевой аллергии на клиническое течение атопического дерматита у детей и оценить эффективность индивидуализированных терапевтических стратегий. Исследование основывалось на анализе клинических данных детей с атопическим дерматитом, включая кожные аллергопробы, уровни иммуноглобулина Е, провоспалительных цитокинов, динамику симптомов под воздействием элиминационной диеты и комплексных терапевтических стратегий. Основные результаты исследования показали, что пищевые аллергены, такие как белки молока, яиц, орехов и пшеницы, значительно влияют на течение атопического дерматита, вызывая повышение уровней иммуноглобулина Е и провоспалительных цитокинов. Применение элиминационной диеты уменьшало тяжесть клинических проявлений на 45 % по шкале Scoring Atopic Dermatitis, а восстановление кожного барьера способствовало снижению частоты обострений. Комплексные терапевтические стратегии обеспечили улучшение качества жизни пациентов, повысив индекс качества жизни, связанный с заболеванием, на 40 %. Выводы исследования подтвердили, что индивидуализированные терапевтические стратегии, включая элиминационную диету, восстановление кожного барьера и медикаментозную терапию, эффективно снижают клинические проявления атопического дерматита и улучшают качество жизни детей с сопутствующей пищевой аллергией. Практическое значение работы заключается в создании научно обоснованных рекомендаций для диагностики и лечения, которые могут быть внедрены в клиническую практику для улучшения терапевтических результатов

Ключевые слова: генетические факторы; фенотипы; барьерная функция кожи; аллергология; иммунологические механизмы; диетотерапия

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АДАМДЫН БИОЛОГИЯСЫ ЖАНА КЛИНИКАЛЫК МЕДИЦИНА ЖУРНАЛЫ

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ЖУРНАЛ БИОЛОГИИ ЧЕЛОВЕКА И КЛИНИЧЕСКОЙ МЕДИЦИНЫ

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