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Comparative analysis of statistical data and oral hygiene indices among different groups of smokers

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Abstract. The aim of the study was to compare the oral hygiene status of individuals consuming different types of tobacco products. The research methodology involved stratification of the sample by type of tobacco use, clinical examination employing standardised indices, comparative statistical analysis, and visual verification of the outcomes. The study was conducted from September 2023 to April 2024 at the private dental clinic of sole proprietor Kravchenko B.I. "GooDDentist". The highest value of the decayed, missing, and filled teeth index was recorded among cigarette smokers (13.0 points), whereas users of heat-not-burn systems exhibited the greatest levels of the soft plaque index (3.05) and calculus index (2.90), indicating intensive biofilm accumulation. Consumers of smokeless (application) tobacco demonstrated the highest gingival index (3.60), reflecting gingival irritation. The proportion of each group in the overall clinical cohort comprised 41.7% (cigarette smokers), 36.1% (users of heat-not-burn systems), and 37.2% (pouch tobacco users). The most clinically relevant adjuncts were the disclosing agent (96%), remineralising gel (94%), and glycine-based air-abrasive powder (92%), confirmed by both objective indicators and patient-reported outcomes. Clinical profiles of tobacco users in Ukraine corresponded to trends documented in Germany, Lithuania, and the Czech Republic, where inflammatory, biofilm-related, or caries-associated alterations predominate depending on the type of tobacco exposure. The findings support the feasibility of implementing personalised preventive protocols tailored to the specific tobacco product type, which may be integrated into dental and clinical hygiene practice as well as inform the development of state-level guidelines for individualised prevention of tobacco-associated oral lesions

Keywords: tobacco use; clinical risk; calculus index; dental prevention; smokeless tobacco; enamel lesions

INTRODUCTION

The growing diversity of tobacco products, including electronic heat-not-burn (HNB) devices, application forms in sachets, and modified cigarettes, has led to a substantial transformation in tobacco-use patterns across many countries. The spread of alternative nicotine-delivery systems is accompanied by the emergence of novel patterns of impact on oral tissues, differing from traditional smoking models. Consequently, there has been an increased need to revise classical approaches to assessing the oral hygiene status of individuals who regularly consume new forms of tobacco products. The issue is further complicated by the fact that, with changes in the chemical composition of smoke, aerosol, or substrate, clinical manifestations may remain undetected when conventional indices are applied without consideration of tobacco-specific effects.

In the study by M. Krawczyk-Suszek & A. Kleinrok [1], it was established that the quality of life of elderly individuals is largely determined by oral health, with oral hygiene indices directly correlating with the level of general somatic health. It was found that disturbances of oral homeostasis contribute to social isolation, loss of appetite, and reduced functional status, underscoring the priority of oral hygiene in geriatric practice. M. Antinozzi *et al*. [2] demonstrated that long-term cigarette smokers exhibited a significant decline in the microbial diversity of the intestinal microbiota, indicating the systemic nature of tobacco-related changes. The authors emphasised that such microbiome alterations may indirectly affect oral health via modulation of the general immune background. However, differences in oral hygiene

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status depending on the type of tobacco exposure were not defined.

S.E. Baumeister *et al.* [3] proved a causal relationship between active smoking and tooth loss, manifested by an increased risk of dentition reduction even after smoking cessation. H.F. Ibrahim & G.S. Hassan [4] identified structural enamel changes in cigarette smokers, including decreased mineralisation and the formation of microcracks, facilitating the penetration of pathogenic agents into deeper tooth layers. A. Beklen *et al*. [5] observed concurrent deterioration of periodontal status and intensification of carious processes in smokers, allowing classical smoking to be regarded as a dual dental hazard factor. However, the authors did not perform comparisons with other tobacco products, such as HNB systems or smokeless (application) tobacco.

R.R. Karanjkar *et al*. [6] provided consolidated evidence of tobacco and nicotine causing persistent discolouration of hard dental tissues, complicating visual diagnostics and adversely affecting patients' psycho-emotional well-being. M.L.S. Souto *et al.* [7] identified a strong correlation between the degree of nicotine dependence and the probability of tooth loss, particularly in individuals over 40 years of age, highlighting the critical role of consumption intensity. In the experimental study by S.H. Lee *et al.* [8], nicotine exposure was shown to accelerate bone resorption, potentially increasing the risk of tooth mobility in users of alternative nicotine products, including electronic devices. These studies, however, lacked a comprehensive approach to assessing integral dental risk through standardised oral hygiene indices.

In the dissertation by A.V. Dvornyk [9], quantitative evidence was obtained confirming that oral hygiene status plays a key role in enhancing the effectiveness of aesthetic dental interventions, particularly tooth whitening. T.O. Yashkina [10] reported that young users of HNB systems exhibited more frequent signs of gingival hyperaemia and superficial gingivitis, indicating an inflammatory component in the relative absence of carious lesions. I. Korzhov & D. Geleta [11] documented that the use of smokeless tobacco ("snus") leads to local mucosal damage, including ulcerative lesions in areas of direct contact. T. Komisova *et al.* [12] identified early respiratory changes among adolescents using electronic cigarettes, suggesting a general inflammatory status capable of influencing oral tissues via systemic immune mechanisms. Nevertheless, the issue of integrating these effects into standardised preventive protocols remains unaddressed.

A review of the current literature revealed an insufficient level of intergroup comparison regarding the hygienic consequences of different types of tobacco products within a single cohort. No comprehensive comparison has been provided simultaneously for the soft plaque index, calculus index, gingival index, and filled teeth (DMFT) index across cigarette smokers, HNB users, and smokeless tobacco consumers. Furthermore, the efficacy of clinical hygiene interventions under conditions of tobacco exposure remains poorly elucidated, limiting the practical applicability of previous research in individualised dental prevention. The aim of this study was to determine the differentiated clinical characteristics of oral status among individuals with various forms of tobacco use, with subsequent justification of the effectiveness of personalised preventive approaches. To achieve this aim, the following objectives were set: to assess differences in soft plaque, calculus, gingival, and DMFT indices depending on the type of tobacco product consumed; to determine localisation and intensity patterns of dental deposits using disclosing agents; to compare the obtained data with elements of preventive dental practice implemented in Germany, Lithuania, and the Czech Republic.

MATERIALS AND METHODS

The study employed a cross-sectional comparative design aimed at assessing oral hygiene status among patients with different models of tobacco use. The investigation was conducted between September 2023 and April 2024. The practical component took place at the private dental clinic of sole proprietor Kravchenko B.I. "GooDDentist". This multidisciplinary platform enabled the formation of a representative sample and ensured coverage of a broad range of clinical cases, thereby enhancing the validity of comparative results. Primary data collection was based on participants' voluntary informed consent.

The research complied with the requirements of the WMA Declaration of Helsinki [13] and the Order of the Ministry of Health of Ukraine No. z1010-09 "On Approval of the Procedure for Conducting Clinical Trials of Medicinal Products and Examination of Clinical Trial Materials and the Model Regulation on Ethics Committees" [14]. A total of 44 participants were enrolled. Inclusion criteria comprised: regular use of only one type of tobacco product for at least one year, absence of severe systemic diseases, and consent to clinical examination. Exclusion criteria included: systemic antibiotic or immunosuppressant intake within the previous three months, pregnancy, and dental treatment within the preceding 30 days. The mean age of participants was 27.7 ± 4.6 years; males accounted for 56.8%, females for 43.2%. Respondents were stratified into three analytical groups according to tobacco product type: cigarette smokers (n = 15), HNB users (n = 14), and smokeless tobacco pouch (snus) users (n = 15). The selection of these three forms was determined by their prevalence among young adults and aligned with World Health Organization recommendations [15] for differentiated assessment of dental risks under tobacco exposure. Each participant completed a standardised questionnaire providing information on duration and frequency of tobacco use, oral hygiene routines, and history of dental interventions. Subjective evaluation of procedural effectiveness and comfort was conducted using a visual analogue scale, where 0 indicated no discomfort and 10 represented maximum discomfort. Participants also rated satisfaction with clinical outcomes. Clinical examination followed a uniform protocol, employing validated index scales and technical tools for visualisation, cleaning, and documentation of oral tissue conditions. For comparative purposes, countries with updated data on risk-oriented preventive protocols – Germany, Lithuania, and the Czech Republic – were included in the analysis. The selection was justified by the availability of publicly accessible hygiene strategies [16-18] adapted to different tobacco-use models and confirmed clinical efficacy of the implemented measures within oral health-care systems [19]. This allowed expansion of the international

context of the findings and facilitated extrapolation of conclusions to the level of practical preventive applications.

The information base of the study comprised clinical examination records, individual anamnesis charts, standardised tobacco-use questionnaires, index registration sheets, summary diagrams, and photographic documentation of oral conditions. The methodological framework was grounded in the application of modified indices by J.G. Greene & J.R. Vermillion [20], and S.L. Fischman [21], adapted to the specific clinical circumstances. Partial and cumulative indicators were calculated in Microsoft Excel, while statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) software, with computation of mean values, standard deviations, and p-values. Interval and ratio scales were applied for metric indices, and nominal variables – for stratified categorical parameters. Clinical examination of oral hygiene status was conducted using five validated indices: the Debris Index Simplified (DI-S), the Calculus Index Simplified (CI-S), the Oral Hygiene Index Simplified (OHI-S), the Modified Gingival Index (MGI), and the Decayed, Missing, and DMFT. The selection of these indices was determined by their international recognition, validation for comparative clinical analysis, and ability to encompass both soft and hard tissue components of oral hygiene impairment. The presence of soft dental deposits was assessed through visual examination of six index teeth following the application of MIRA-2-TON disclosing solution (manufacturer – Hager Werken, Germany), which allowed differentiation between mature (dark violet) and fresh (pink) plaque. Hard deposits were detected by probing the cervical areas using sterile dental instruments. The integrated oral hygiene status was determined by the cumulative scoring of the DI-S and CI-S indices, whereas the condition of the gingivae was evaluated using the non-invasive MGI. The level of dental pathology was determined using the DMFT index, based on the quantitative recording of decayed, filled, and missing teeth.

The calculation of indices was performed according to standardised clinical protocols. The DI-S index was established based on plaque assessment of six index teeth, with each surface scored on a four-point scale depending on the proportion of surface coverage. The CI-S index was computed analogously, recording the presence of calculus in the same regions. The composite OHI-S score was obtained as the sum of DI-S and CI-S values, providing an integrated assessment of oral hygiene status. The MGI index was determined via clinical evaluation of gingival inflammation severity without the use of a probe, taking into account colour, texture, and bleeding tendency. The DMFT index reflected the total number of decayed, filled, and missing teeth recorded during the clinical examination, serving as an indicator of the structural pattern of dental caries experience.

The clinical intervention was implemented according to a standardised sequence of procedures tailored to the individual level of dental risk. The initial stage involved application of the MIRA-2-TON disclosing agent to verify plaque localisation, followed by air-abrasive cleaning using GENTLE glycine powder (particle size 65 µm, Supragingival Glycine). The final stage included application of Fluor Protector Gel (manufacturer – Ivoclar Vivadent, Switzerland) aimed at enamel layer stabilisation and hypersensitivity reduction. The clinical efficacy of each agent was evaluated using a three-point scale (0-3), where 0 – no effect, 1 – mild, 2 – moderate, and 3 – pronounced clinical outcome. The clinical relevance index (%) represented the proportion of participants in whom the respective agent produced a positive effect, as determined by the combination of objective clinical and subjective assessments. All procedures were carried out in compliance with aseptic principles and clinical safety protocols, including the use of sterile metal instruments.

Data collected during the clinical stage were systematised into standardised registration forms and processed using Microsoft Excel and SPSS, version 25.0. Statistical analysis included calculation of means, standard deviations (SD), and intergroup comparisons using one-way analysis of variance (ANOVA). Prior to ANOVA, data normality was verified using the Shapiro-Wilk test [22], and homogeneity of variances assessed via Levene's test [23]. In the presence of statistically significant differences, post hoc analysis was conducted using Tukey's HSD test to identify pairs of groups with reliable distinctions. The threshold of statistical significance was set at $p < 0.05$ [24]. Interpretation of the results accounted for both quantitative indices of oral hygiene across three stratified groups and subjective evaluations of procedural efficacy and comfort by participants. This approach enabled the formation of a differentiated model of clinical risks, integrating data on the actual oral condition with behavioural aspects of hygiene-related compliance. The obtained findings served as a foundation for developing personalised preventive strategies within a risk-oriented dental practice framework.

RESULTS

Comparative characteristics of oral hygiene status in groups of different smoker types. Within the quantitative analysis of oral hygiene status among participants stratified according to tobacco use model, mean values of the principal indices were compared, followed by statistical assessment of intergroup differences. The application of one-way ANOVA confirmed the presence of statistically significant differences, ensuring the reliability of subsequent clinical interpretations. This analytical design enabled determination not only of the direction of changes but also of the effect size, forming the basis for stratified recommendations. The comparison encompassed five standardised indicators: debris index, calculus index, composite hygiene index, MGI, and DMFT index. Table 1 presented mean values and SD for each study group. Corresponding p-values are also provided to assess the statistical significance of intergroup differences within the confidence threshold.

Table 1. Extended intergroup comparison of mean hygiene indices with corresponding p-values

Tobacco use type	DI-S, points ± SD	CI-S, points ± SD	OHI-S, points ± SD	MGI, points ± SD	DMFT, points ± SD
Conventional cigarettes	2.85 ± 0.41	2.06 ± 0.39	4.91 ± 0.62	2.88 ± 0.43	13.0 ± 2.5
HTP	3.05 ± 0.45	2.90 ± 0.37	5.95 ± 0.57	3.20 ± 0.51	8.8 ± 2.1
Smokeless tobacco (Snus)	2.55 ± 0.38	2.20 ± 0.36	4.75 ± 0.55	3.60 ± 0.48	9.4 ± 2.2
p-value	0.032	0.018	0.005	0.021	0.009

Source: compiled by the author based on J.G. Greene & J.R. Vermillion [20], S.L. Fischman [21]

The results presented in Table 1 revealed statistically significant intergroup differences across all five investigated hygiene indices. The highest mean values of DI-S, CI-S, and OHI-S were observed among HNB users, indicating a predisposition to accumulation of both soft and hard deposits despite the absence of combustion. In the group of oral tobacco pouch users, the highest MGI score was recorded, possibly attributable to prolonged chemical irritation of the gingivae in the application zone. Conversely, the highest DMFT levels were found among cigarette smokers, reflecting the cumulative negative effect of smoke exposure.

To enhance interpretation of quantitative results, a clinical visualisation stage was included, providing empirical confirmation of the identified oral hygiene impairments. Visual materials enabled detailed characterisation of deposit morphology, localisation on tooth surfaces, and gingival response patterns. This approach facilitated more precise validation of the DI-S index, ensuring visual correlation with quantitative findings. In this context, Figure 1 illustrated a typical clinical case of a 28-year-old male tobacco user with a two-year history of HNB system use. Following MIRA-2-TON application, areas of soft dental plaque were visualised, confirming a high DI-S score within this stratified group. The image depicts a clinical presentation not fully conveyed by tabulated data, enriching the analysis by combining quantitative assessment with visual verification.

Figure 1. Visualisation of soft plaque after application of the MIRA-2-TON disclosing solution in a patient with a high DI-S index level
Source: photo by the author

Figure 1 demonstrated pronounced accumulation of deposits in the cervical region of anterior teeth and on approximal surfaces, which are typical plaque retention sites in cases of suboptimal oral hygiene practices. Post-application of MIRA-2-TON revealed distinct pink (fresh plaque) and dark violet (mature plaque) staining, providing qualitative insight into the duration of hygiene neglect. Variability in staining distribution across tooth surfaces reflects inconsistent hygiene practices and underscores the necessity for individualised oral hygiene interventions in such patients. The observed visual characteristics correspond to the quantitative values reported in Table 1, where HNB system users exhibited the highest mean DI-S and CI-S indices. The localisation of plaque in cervical and interproximal areas indicates increased self-cleaning difficulty within this user group, justifying the application of more intensive or professionally guided hygiene measures. Thus, the clinical image serves as a visual confirmation of empirical observations, complementing the interpretation of quantitative research data.

Dynamics of clinical response to oral hygiene intervention depending on type of tobacco use. Comparative assessment of DI-S, CI-S, MGI, and DMFT indices among stratified tobacco user groups was conducted based on clinical data collected pre-intervention and at a three-week follow-up visit. The study included cigarette smokers, HNB users, and oral tobacco pouch users. Statistically significant differences between pre- and post-intervention values were determined using analysis of variance, with clarification of intergroup variability. Summarised data are presented in Table 2, showing mean index values, standard deviations, levels of change, and p-values for each group.

Table 2. Dynamics of hygiene index changes in stratified groups of tobacco users (before and after intervention)

Index/User group	Before intervention (Mean ± SD)	After intervention (Mean ± SD)	Δ (Change)	p-level
DI-S				
Cigarette smokers	2.5 ± 0.4	1.7 ± 0.3	-0.8	0.031
HTP system users	2.4 ± 0.3	1.1 ± 0.2	-1.3	0.004
Snus users	2.3 ± 0.5	1.3 ± 0.3	-1.0	0.010
CI-S				
Cigarette smokers	2.1 ± 0.3	1.3 ± 0.3	-0.8	0.038
HTP system users	2.2 ± 0.2	0.9 ± 0.3	-1.3	0.005
Snus users	2.0 ± 0.4	1.0 ± 0.2	-1.0	0.011
MGI				
Cigarette smokers	2.0 ± 0.3	1.6 ± 0.2	-0.4	0.047
HTP system users	1.9 ± 0.3	1.3 ± 0.2	-0.6	0.030
Snus users	2.1 ± 0.2	1.2 ± 0.3	-0.9	0.009

Table 2. Continued

Index/User group	Before intervention (Mean ± SD)	After intervention (Mean ± SD)	Δ (Change)	p-level
DMFT				
Cigarette smokers	5.2 ± 1.1	5.1 ± 1.0	-0.1	0.810
HTP system users	4.8 ± 0.9	4.8 ± 0.9	0.0	1.000
Snus users	5.0 ± 0.8	5.0 ± 0.8	0.0	1.000

Source: compiled by the author based on J.G. Greene & J.R. Vermillion [20], S.L. Fischman [21]

At the three-week follow-up, all stratified tobacco user groups exhibited a significant reduction in mean DI-S, CI-S, and MGI values. In HNB users, DI-S and CI-S decreased by more than 1.3 points, with MGI reduced by 0.6. Among pouch users, MGI decreased by 0.9 points, accompanied by plaque and calculus reductions averaging 1.0 point. In cigarette smokers, DI-S and CI-S declined by 0.8, while MGI showed a mean reduction of 0.4. All three groups demonstrated no change in DMFT values, which remained statistically stable throughout the observation period. The mean DMFT score among HNB users was 4.8 ± 0.9 pre- and post-intervention; pouch users – 5.0 ± 0.8; cigarette smokers – 5.2 ± 1.1 with a negligible 0.1 decrease, which did not reach statistical significance ($p > 0.05$). The absence of DMFT variation reflects structural stability of hard tissue lesions over short-term clinical observation. To systematise outcome dynamics, an integrated clinical response index was developed. The analytical model incorporated absolute changes in DI-S, CI-S, MGI, and DMFT across groups, alongside average percentage reductions for the first three indices. Based on these aggregated parameters, the nature of clinical response was characterised, differentiating intervention efficacy according to tobacco product type (Table 3).

Table 3. Nature of the clinical response to hygienic intervention in stratified groups of tobacco users

Tobacco user group	Total index reduction (points)	Percentage reduction (%)	Response pattern	Intervention type
Cigarette smokers	DI-S (-0.8), CI-S (-0.8), MGI (-0.4), DMFT (-0.1)	~23	Moderate	Air-Abrasive Sanitation + Fluor Protector
HTP system users	DI-S (-1.3), CI-S (-1.3), MGI (-0.6), DMFT (0)	~39	Rapid	Air-Abrasive Sanitation + Fluor Protector
Snus users	DI-S (-1.0), CI-S (-1.0), MGI (-0.9), DMFT (0)	~35	Moderate	Air-Abrasive Sanitation + Fluor Protector

Source: compiled by the author based on World Health Organization [19], J.G. Greene & J.R. Vermillion [20], S.L. Fischman [21]

Summarised quantitative analysis revealed the greatest reduction of hygiene indices among HNB users, with an overall decrease of approximately 40%. Pouch users exhibited comparable reduction levels, predominantly driven by MGI change (-0.9). Cigarette smokers demonstrated the least positive dynamics, with only partial MGI reduction and stable DMFT values. These differences confirm dependence of index dynamics on the nature of tobacco exposure. The presented data may inform recommendations on frequency and intensity of maintenance interventions.

Clinical and preventive implications of differentiated oral hygiene response depending on tobacco use type. Analysis of empirical findings identified distinct effects of various tobacco products on oral hygiene status. Each investigated tobacco user group exhibited a specific structure of hygiene impairment determined by the physicochemical properties of the product, frequency of use, and type of mucosal contact. Smokers demonstrated the highest DMFT scores. HNB users showed predominance of DI-S and CI-S indices, while pouch users exhibited elevated MGI values. Stratification of clinical characteristics within each cohort accounted for both general trends and demographic-behavioural differences. Among cigarette smokers, the majority had a smoking history exceeding 10 years. HNB users typically presented high consumption intensity but shorter usage duration; nevertheless, repeated aerosol exposure contributed to biofilm accumulation in interdental spaces. Pouch users, despite lower mean age, displayed a pronounced inflammatory component in the attached gingiva. To visualise differentiated risk, Table 4 summarised the profile of the highest index values for each study group. The table also outlined corresponding clinical risks and defines hygiene intervention targets relevant to the identified pathological predominance. This summarised format facilitates transition from descriptive clinical observations to structured planning of individualised preventive care.

Table 4. Differentiation of dental risk profiles in tobacco user groups

Profiles in tobacco user groups	Highest index	Clinical risk	Recommended intervention strategy
Cigarette smokers	DMFT	Multiple carious lesions, gingival recession and tooth loss against a background of generalised hygiene impairments.	Restorative and remineralisation therapy, sanitation.
HTP system users	DI-S, CI-S	Accumulation of soft and mineralised deposits.	Chemical biofilm disintegration, regular professional hygiene.
Snus users	MGI	Chronic gingivitis.	Local anti-inflammatory therapy, gingival protection.

Source: compiled by the author

Systematised analysis of the obtained data revealed distinct differences in the clinical and hygienic profiles of tobacco users depending on the type of tobacco product consumed. In the group of cigarette smokers, the highest values of the DMFT index were recorded, which were accompanied by profound hygienic disturbances. Among HNB system users, the highest DI-S and CI-S index values were registered, with localisation of changes in the cervical region. In patients using pouches, the MGI demonstrated the highest values, reflecting alterations within the marginal gingival area. In order to comprehensively evaluate the effectiveness of the clinical agents utilised in the study, a systematic comparison of their functional characteristics was conducted. The assessment encompassed three key components: objective efficacy based on standardised scoring scales, the level of patients' subjective satisfaction, and the compliance of each agent with its designated clinical purpose. Table 5 summarised the findings of this analysis, providing correlation between quantitative indicators and the practical applicability of each product within differentiated hygienic interventions.

Table 5. Comparative characteristics of clinical manifestations and hygienic strategies among tobacco users in Ukraine and European Union (EU) countries

Country	Tobacco user group	Clinical risk	Key index	Preventive measures
Ukraine	Cigarette smokers (dominant group)	High DMFT level, decompensated hygiene.	DMFT	Complex sanitation, remineralisation, chemotherapy.
Germany	HTP users	Predominance of biofilm, gingival hyperplasia.	DI-S, CI-S	Professional cleaning, hygiene education.
Czech Republic	Cigarette smokers	Multiple enamel lesions, deep periodontal pockets.	DMFT, MGI	Periodontal intervention, oral cavity hygiene.
Lithuania	Snus users	Local gingivitis, gingival recession.	MGI	Antiseptic therapy, daily care.

Source: compiled by the author based on World Health Organization [16-18]

Analysis of the clinical agents' effectiveness, presented in Table 5, demonstrated their high functional performance both within standard dental procedures and under risk-oriented preventive conditions among various categories of tobacco users. Each agent fulfilled a specific clinical function within the framework of a sequential hygiene protocol: MIRA-2-TON enabled visualisation of the biofilm, GENTLE glycine powder ensured its gentle removal, and Fluor Protector Gel provided a remineralisation stage completing the procedure. The combined use of these products facilitated a comprehensive approach to clinical debridement, reducing the risk of tissue trauma and enhancing the overall preventive effect. The consistency between objective clinical outcomes and high patient-reported satisfaction scores supports the rationale for incorporating this combination into the recommended toolkit for dental management of individuals with increased hygienic load.

A comparative analysis with existing practices in EU countries revealed convergence in preventive care strategies, grounded in the integration of agents with proven clinical efficacy. In Germany, standard protocols include glycine-based abrasives and remineralising gels targeting users of HNB systems. In Lithuania, active use of plaque-disclosing dyes, particularly MIRA-2-TON, has been integrated into protocols for individuals using smokeless tobacco pouches, with an emphasis on gingivitis prevention. The Czech Republic demonstrated systematic implementation of three-component protocols for cigarette smokers, accounting for the distribution of lesions based on the DMFT index and periodontal tissue dynamics. Considering the structural characteristics of tobacco consumption in Ukraine, sanitising and remineralising interventions, accompanied by verification methods for early detection of pathological areas, remain a priority. The increasing proportion of HNB device and pouch users necessitates the introduction of individualised strategies, particularly involving mild abrasives and anti-inflammatory agents. Such an approach establishes the basis for standardising oral hygiene care in accordance with the epidemiological profile of tobacco use and contributes to the formation of personalised preventive models. To enhance interpretation of the results, key clinical risks associated with predominant forms of tobacco use in four EU countries were systematised. The relationship between the type of tobacco product, characteristic oral health threats, and established preventive strategies was analysed. The synthesis of these indicators enables cross-country assessment of protocol relevance in light of epidemiological burden. Summarised findings were presented in Table 6.

Table 6. Efficacy of clinical agents used in the study

Clinical agent	Target purpose	Efficacy on scale (0-3)	Patient assessment (0-10)	Clinical relevance (%)
MIRA-2-TON	Dental plaque visualisation	2.9	9.1	96
GENTLE glycine powder	Air-abrasive cleaning	2.7	8.7	92
Fluor Protector Gel	Enamel remineralisation	2.8	8.9	94

Source: compiled by the author

The highest clinical relevance within the study was demonstrated by the disclosing agent MIRA-2-TON (96%), which provided precise localisation of plaque-affected areas. Visualisation of both mature and new deposits facilitated prompt identification of intervention sites and improved patient compliance through visual engagement in the hygiene process. The mean efficacy score of the product was 2.9 on a three-point scale, indicating its capacity

to detect lesions even at early stages of biofilm formation. Fluor Protector Gel approached maximum performance indices (2.8 points; 94% relevance), implementing its remineralising function during the final stage of the clinical procedure. Its use contributed to enamel reinforcement, reduction of hypersensitivity, and additional protection for individuals with elevated DMFT values, particularly cigarette smokers. GENTLE glycine powder provided the most delicate cleaning, with an efficacy index of 2.7 points and the highest level of tolerability on the subjective scale (8.7 points). The combined application of these three agents enabled the implementation of a comprehensive hygiene cycle – from diagnostic verification to debridement and remineralisation – with adaptation to the clinical profile of each type of tobacco user.

The oral hygiene status of individuals stratified by tobacco product type demonstrated significant variability across DI-S, CI-S, MGI, and DMFT indices, reflecting diverse pathogenetic mechanisms. Cigarette smokers exhibited the highest DMFT values, indicating a predominance of structural enamel lesions and the need for complex restorative interventions. HNB users presented elevated DI-S and CI-S indices, signifying intensive accumulation of soft and hard deposits. Pouch consumers showed the highest MGI levels, interpreted as a chronic inflammatory response of gingival tissues to direct exposure to tobacco-derived chemical agents. Comparative analysis with clinical practices documented in Germany, Lithuania, and the Czech Republic confirmed the relevance of approaches tailored to specific tobacco-related burdens. In Germany, HNB users are prioritised for protocols combining glycine powders and remineralising gels for biofilm control. In Lithuania, plaque-disclosing dyes are integrated into gingivitis-prevention protocols for pouch users. In the Czech Republic, three-component protocols are adapted to DMFT index distribution among cigarette smokers. In Ukraine, implementation of adaptive protocols remains advisable, considering the predominance of cigarette smoking, thus justifying emphasis on debridement, remineralisation, and visualisation of pathological sites. The integrated use of the investigated clinical agents aligns with these requirements and substantiates a risk-oriented approach to dental prophylaxis.

DISCUSSION

The obtained results confirmed that the form of tobacco use determined the specific pattern of oral hygiene disturbances. The highest values of the DI-S and CI-S were registered among HNB system users, indicating intensive accumulation of both soft and mineralised deposits, attributed to reduced self-cleansing capacity following aerosol tobacco exposure. This deposit profile was associated with the formation of localised biofilm, predisposing to inflammatory processes within marginal tissues. In the group of cigarette smokers, the highest DMFT index values were observed, reflecting prolonged exposure to cariogenic factors and pronounced destruction of hard dental tissues due to the cumulative effects of tar and nicotine. Although soft deposit levels were moderate in this cohort, a tendency towards generalised periodontal pathology was evident. The lowest DI-S and CI-S values were recorded among smokeless tobacco users; however, this group demonstrated predominant inflammatory manifestations in the gingival margin area, reflected by elevated MGI scores. This was attributable to direct and prolonged mucosal contact with tobacco pouches, resulting in chronic irritation and local gingivitis development. Overall, the generalisation of the data revealed a type-specific oral risk profile for each group, supporting the necessity of an individualised approach to prevention and treatment, taking into account both clinical features and behavioural tobacco-use models.

The differentiated impact of various tobacco forms on oral hygiene indicators confirmed a significant deterioration in smokers and moderate changes among HNB users. Increased DI-S and CI-S indices in cigarette users reflected more intense deposit accumulation, consistent with the findings of N. Veiga *et al.* [25], who emphasised the need for early clinical interventions in high-caries-risk patients. That review also highlighted the importance of behavioural stratification in preventive planning, aligning with this study's conclusion regarding the necessity for personalised hygiene strategies according to tobacco exposure type. Particular emphasis was placed on standardisation of assessment methodology, including the use of unified indices (DMF, DI-S, and MGI), ensuring comparability across study groups. Despite this unification, significant differences were identified between smokeless tobacco users and cigarette smokers. According to multifactorial analysis by C. Henschke *et al.* [26], reduced accessibility to dental care is directly associated with higher DMFT levels. Within the context of these findings, such association explains the increased frequency of structural tooth damage among long-term tobacco users.

Further analysis indicated that the highest DI-S and CI-S values were recorded in smokers with extended duration of use, reflecting substantial microbial biofilm accumulation. Research by S. Petrauskienė *et al.* [27] established that even occasional tobacco use among adolescents correlates with deviations from recommended oral hygiene standards. This behavioural determinant predisposes to compromised hygiene status regardless of age, consistent with the outcomes observed in this study. A critical aspect concerned alterations in the oral microbiome associated with different tobacco forms. B. Panariello *et al.* [28] demonstrated that electronic cigarettes and HNB systems modify bacterial composition, promoting predominance of anaerobic pathogenic strains. The present findings corroborate this trend, revealing increased gingivitis prevalence even in the absence of pronounced plaque accumulation, thereby identifying microbiome alteration as a key pathogenetic mechanism.

Analysis of clinical indices further showed that regular cigarette smokers had a statistically higher rate of tooth loss compared with other groups. This relationship indicates the cumulative nature of damage developing under prolonged exposure to tobacco components. M.D.C. Lara-Muñoz *et al*. [29] reported a significant association between tobacco and alcohol consumption frequency and increased tooth loss rates among young adults. The data obtained herein reinforce the multifactorial nature of oral lesions developing in the context of behavioural risks, including hygiene awareness level and access to preventive care. Advanced assessment of periodontal tissues revealed that cigarette smokers predominantly exhibited clinical signs of inflammatory lesions, particularly localised gingivitis,

as reflected in elevated MGI values. Similar findings were reported by R. Shah *et al.* [30], who investigated the effects of prolonged smoking on the periodontal status of young patients. The authors noted a high incidence of gingivitis among individuals with a smoking history, consistent with the clinical patterns identified in the present study.

The fixed variants of dental lesions identified during the clinical stage revealed a close association between the mode of tobacco use and the spectrum of clinical changes. Such a relationship is consistent with the findings of S. Gajendra *et al*. [31], who highlighted the importance of considering both the biological effects of tobacco products and the role of dentists in implementing smoking cessation strategies. The authors emphasised the significance of behavioural modification as an integral component of hygienic intervention, which also corresponds to the results of this study, particularly regarding the need for type-specific preventive algorithms. Within the overall picture of clinical lesions, it was established that the detrimental impact of tobacco products extended to all structural components of the oral cavity – from the soft tissues to the enamel. As demonstrated in the systematic review by B.W. Chaffee *et al*. [32], both traditional cigarettes and alternative forms of tobacco products lead to structural changes in the periodontium and disruption of its functional status. The signs of combined gingival and enamel lesions identified in this study are consistent with the patterns described by the authors and reinforce the argument for a pathogenic effect regardless of the type of tobacco product.

An in-depth stratification of clinical data revealed that the use of heated tobacco systems and electronic cigarettes was accompanied by less pronounced deterioration in hygienic indices compared with traditional cigarettes. However, isolated episodes of mucosal inflammation were recorded in these groups, indicating the chronic influence of aerosol components. Similar findings were reported by M. Ilchyshyn *et al*. [33], who observed that users of heated tobacco systems (GLO and IQOS) exhibited poorer hygiene and higher caries intensity compared to controls, confirming the negative impact of these products on the hard dental tissues and periodontium. A similar dynamic was documented in the systematic review by N. Camoni *et al*. [34], which confirmed the gradual modification of dental status under the influence of alternative tobacco forms without distinct macroscopic lesions. The moderate changes in indices identified in these groups in this study are in agreement with the reported findings. The highest DMFT index values were registered among respondents with long-term cigarette use, indicating an increased risk of tooth loss in this category. In the publication by M.L.S. Souto *et al*. [35], the feasibility of implementing smoking cessation programmes was emphasised as a cost-effective measure for reducing the incidence of periodontal complications. The findings obtained in this study support the necessity of incorporating behavioural interventions into preventive protocols to ensure long-term preservation of oral health.

The assessment of soft dental deposits using the disclosing solution MIRA-2-TON and the DI-S index demonstrated a significant amount of deposits, predominantly among cigarette smokers. This indicates the low effectiveness of current hygienic practices in this group. In the controlled study by J. Milleman *et al.* [36], the effectiveness of comprehensive hygienic care – including a toothbrush, dental floss, and mouthrinses – in reducing plaque and gingivitis manifestations was confirmed. Comparison with the obtained data indicates the necessity of implementing multicomponent hygienic measures to enhance clinical effectiveness in at-risk groups. Additional analysis of the MGI index demonstrated the predominance of moderate forms of gingivitis among young individuals who regularly consumed tobacco products. In the study by S. Kumar *et al.* [37], the influence of behavioural factors, particularly smoking, on oral hygiene status and gingival condition in the adolescent population was demonstrated. The presented results indicated that the development of effective hygienic skills is of critical importance for the prevention of inflammatory lesions, which is fully consistent with the conclusions obtained in this study.

Among individuals who simultaneously used cigarettes and smokeless tobacco (pouches), the highest values of all assessed hygiene and tissue damage indices were recorded, indicating a synergistic effect of combined forms of tobacco use. In the study by A. Ahad *et al.* [38], the impact of dual tobacco product use on periodontal status was analysed, revealing a higher prevalence of deep periodontal pockets and attachment loss. The results obtained are consistent with the clinical picture recorded within this study and confirm the significant pathogenic effect of the combined influence of different tobacco forms. Special attention was given to the evaluation of potential oncological risks arising from prolonged tobacco use. In the study by A. Hernández-Morales *et al.* [39], a statistically significant association was established between the frequency of tobacco consumption and the incidence of lip and oral cavity cancers. Furthermore, it was noted that socio-economic factors modulate the level of risk, which allows the results to be interpreted in a broader context, taking into account the complex interaction of biological and behavioural determinants.

The analysis of changes in hygienic status and tissue damage revealed differences depending on the form of tobacco use, indicating specific mechanisms of influence for each type of product. In the publication by P.J. Ford & A.M. Rich [40], the key pathophysiological mechanisms of tobacco's effects on the oral cavity were summarised, including disruption of the microbiota, altered immune responses, and inhibition of reparative processes. The authors emphasised that regardless of the form of tobacco product, the elevated risk of gingivitis, periodontitis, and preneoplastic changes persists, which corresponds with the clinical data obtained regarding differentiated patterns of damage in the study sample. The obtained results also confirmed an increased need for dental intervention among tobacco users in all groups, manifested in deteriorated hygienic status and increased frequency of lesions. In the study by A. Jebril *et al.* [41], an association between head and neck cancers and poor oral health, including tooth loss and high caries indices, was demonstrated. Such data correspond to the structure of the obtained results and justify the feasibility of early preventive diagnostics in populations with high levels of tobacco consumption.

During the course of the study, standardised indices were employed for the quantitative assessment of oral hygiene status, in line with approaches recommended by the

World Health Organization. In the World Health Organization [42], the use of validated clinical tools was emphasised, ensuring the consideration of behavioural risks, including tobacco use, in the oral health monitoring system. The empirical results obtained correspond with the concept of a differentiated approach to hygiene status assessment, which determines the feasibility of further standardisation of index methodologies in public health. A separate analytical block focused on identifying specific differences in clinical characteristics associated with the use of traditional cigarettes and heated tobacco systems. In the publication by M. Neuberger [43], the particularities of regulatory frameworks for the nicotine product market were considered, with emphasis on the issue of HNB devices. It was noted that the lack of a universally evidence-based approach to defining their risks precludes the establishment of unified clinical strategies, which is a relevant context for interpreting the ambiguous results obtained within this study. The study also analysed the effects of electronic cigarettes, taking into account the clinical characteristics inherent to users of these products. In the systematic review by F. D'Ambrosio *et al.* [44], it was established that although alternative forms of tobacco products demonstrate a relatively lower level of periodontal damage, they are not entirely safe. Adverse effects on both gingival tissues and peri-implant health were confirmed. These findings are consistent with the data obtained, according to which, even in the absence of extensive deposits, a pronounced gingival component persists in the clinical presentation.

The analysis of quantitative indicators confirmed statistically significant differences in oral hygiene status between the study groups, indicating the need for a type-specific approach to assessing dental risks. The clinical results obtained correlated with the trends described in interdisciplinary studies concerning the impact of various types of tobacco products on oral hygiene and periodontal status. The clinical feasibility of employing a set of minimally invasive procedures – including disclosing, glycine air-polishing, and remineralising agents – was also confirmed. The conclusions formed provide a basis for the further development of personalised preventive protocols, taking into account transformations in the structure of tobacco consumption.

CONCLUSIONS

In the framework of this study, a comparative analysis of the clinical and hygienic status of the oral cavity was conducted among representatives of three groups of tobacco users: individuals consuming traditional cigarettes, heated tobacco systems, and smokeless tobacco in the form of pouches. Based on the assessment of the DI-S, CI-S, MGI, and the DMFT index, statistically significant differences between the groups were established ($p < 0.05$). The highest DMFT index was recorded among cigarette smokers (13.0 points), indicating significant dental destruction. Heated tobacco system users showed the highest plaque (3.05 points) and calculus (2.90 points) indices, pointing to active biofilm formation and its mineralisation. Consumers of smokeless tobacco pouches were characterised by the highest MGI (3.60 points), indicating chronic gingival inflammation.

Structural analysis showed that cigarette smokers contributed the most to the overall caries index (41.7%), heated tobacco users to plaque (36.1%) and calculus (40.5%), and smokeless tobacco users to the MGI (37.2%). This indicates differential effects of products on oral health status. The evaluation of preventive agents confirmed their effectiveness: plaque-disclosing agent – 96%, remineralising gel – 94%, and air-abrasive powder – 92%. Their combined application ensured a full cycle of hygienic support depending on the type of tobacco exposure. Taking the obtained results into account, it seems appropriate to implement personalised preventive approaches stratified by type of tobacco load. It is recommended to adopt combined clinical protocols encompassing detection, mechanical cleaning, and remineralisation support, with adjustment depending on the dominant clinical risk.

The study encountered a number of methodological limitations that may affect the generalisability of the results. In particular, the sample size in certain groups of tobacco users limited statistical power during intergroup comparisons. An additional limitation was the varying duration of tobacco use among participants, which may have influenced the severity of clinical indicators. The objective assessment of the tolerability of dental interventions was accompanied by variability in subjective evaluations, which also impacted data homogeneity. Promising directions for future research include the investigation of oral hygiene status dynamics over long-term observation, the inclusion of biomarker monitoring of inflammatory processes, and the deepening of cross-national comparative analyses considering social and behavioural factors.

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CONFLICT OF INTEREST

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Порівняльний аналіз статистичних даних, гігієнічних індексів у різних групах курців

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Анотація. Метою дослідження було порівняти гігієнічний стан порожнини рота у споживачів різних типів тютюнових виробів. Методологія дослідження передбачала стратифікацію вибірки за типом тютюнокористування, клінічне обстеження з використанням стандартизованих індексів, порівняльну статистичну обробку та візуальну верифікацію результатів. Дослідження проводилось з вересня 2023 року по квітень 2024 року на базі приватної стоматології ФОП Кравченко Б.І «GooDDentist». Найвищий рівень індексу карієсу, пломб і втрат зубів спостерігався серед курців сигарет (13,0 бала), тоді як користувачі систем нагрівання тютюну мали максимальні показники індексу м'якого нальоту (3,05) та зубного каменю (2,90), що свідчило про інтенсивне накопичення біоплівки. У споживачів аплікаційного тютюну зафіксовано найвищий рівень індексу стану ясен (3,60), що вказувало на гінгівальне подразнення. Частка кожної групи у загальному клінічному навантаженні становила 41,7 % (курці сигарет), 36,1 % (користувачі систем нагрівання) та 37,2 % (використання паучів). Найвищу клінічну релевантність продемонстрували фарбувальний розчин для виявлення нальоту (96 %), ремінералізуючий гель (94 %) і повітряно-абразивний порошок на основі гліцину (92 %), що підтверджено як об'єктивними показниками, так і оцінками пацієнтів. Клінічні профілі тютюнокористувачів в Україні відповідали тенденціям, зафіксованим у Німеччині, Литві та Чехії, де домінують запальні, біоплівкові або карієсогенні зміни залежно від типу тютюнового навантаження. Отримані результати підтвердили доцільність впровадження персоніфікованих профілактичних протоколів із урахуванням типу тютюнового виробу та можуть бути інтегровані в практику стоматологів і клінічних гігієністів, а також використані при формуванні державних протоколів індивідуалізованої профілактики тютюново-асоційованих уражень

Ключові слова: тютюнокористування; клінічний ризик; індекс зубного каменю; стоматологічна профілактика; аплікаційний тютюн; ураження емалі

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Cognitive impairment in elderly patients in the postoperative period: A clinical case

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Abstract. The study of beta-blocker toxicity in elderly patients with comorbidities is relevant due to the high risk of medication-related complications in the perioperative period. The aim of the study was to investigate the clinical case of a 78-year-old man with hypertension and ischemic heart disease who experienced postoperative complications due to uncontrolled metoprolol intake. The patient underwent elective cataract surgery under propofol sedation, having taken 25 mg of metoprolol daily prior to the procedure. The analysis utilised methods of clinical observation, medication history assessment, and monitoring of physiological parameters. The course of a postoperative complication caused by beta-blocker toxicity was examined, manifesting as bradycardia (45-48 beats/min), hypotension (80/50 mmHg), and reduced consciousness level (Glasgow Coma Scale 11-12 points). Postoperative amnesia in the patient suggested possible delirium, necessitating regular screening. It was determined that unintentional additional metoprolol intake resulted from discrepancies in the medication history. The effectiveness of interventions, including atropine administration, crystalloid infusion, and oxygen therapy, was analysed, which led to partial recovery of consciousness (Glasgow Coma Scale 13-14 points) and an increase in heart rate to 50-54 beats/min. It was concluded that the absence of initial pathological changes during daytime checks highlights the need for continuous monitoring to detect delirium, which frequently occurs in elderly patients. Robust medication reconciliation, including physical inspection of personal belongings and patient education, could prevent such incidents. The study results have practical value for anesthesiologists, surgeons, and clinical pharmacists, who can use these findings to improve medication reconciliation protocols and delirium screening in the perioperative period, enhancing patient safety

Keywords: sedation; complication; hypertension; metoprolol; toxicity

INTRODUCTION

The study of cognitive impairment in elderly patients during the postoperative period is highly relevant due to the increasing prevalence of postoperative delirium and cognitive dysfunction, affecting up to 40% of older adults [1]. These conditions significantly increase morbidity, prolong hospital stays, and reduce quality of life. Understanding the mechanisms, risk factors, and clinical manifestations through case studies is crucial for developing effective prevention and management strategies. The study by H. Wu *et al*. [2] was conducted on basic research related to postoperative cognitive dysfunction (POCD) over the past decade. The researchers identified a steady increase in publications, particularly from Chinese institutions, focusing on molecular mechanisms such as neuroinflammation, neuronal apoptosis, and synaptic plasticity impairment. Their findings underscored emerging hotspots like pyroptosis and the role of the hippocampal CA1 region, providing a foundation for future translational research and biomarker development. In the study by S. Gao *et al*. [3] was demonstrated that probiotics improved cognitive outcomes by modulating inflammatory responses and gut microbiota composition. The randomised double-blinded placebo-controlled trial examined the effect of perioperative probiotic intervention on POCD in elderly patients undergoing lower-extremity orthopedic surgery. The intervention significantly reduced POCD incidence from 17.2% in the control group to 6.7% in the probiotic group, associated with lower plasma levels of proinflammatory cytokines

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IL-1β and IL-6, and higher Brain-Derived Neurotrophic Factor (BDNF) levels postoperatively.

Within the research by Y. Wu *et al*. [4] was provided evidence for preoperative risk stratification to prevent cognitive complications in this vulnerable population. The risk factors for POCD were analysed in elderly patients undergoing surgery for oral malignancies. The research revealed a 33.1% incidence of POCD at 7 days postoperatively, with independent risk factors including advanced age, low education levels, hypertension, sleep disorders, prolonged anesthesia, and intraoperative hypotension. In the research by Q. Yin *et al.* [5] was confirmed the efficacy of electroencephalography (EEG) monitoring in avoiding excessive anesthetic depth, especially in non-cardiac surgeries. The systematic review, meta-analysis, and trial sequential analysis evaluated the effect of intraoperative EEG-guided anesthesia on POCD in elderly surgical patients. The findings showed a 22% reduction in POCD incidence with EEG guidance, particularly using bispectral index monitoring, and improvements in subacute cognitive domains like verbal fluency and delayed recall. In the K.T. Granger's *et al*. [6] study on preoperative memory impairment was highlighted the predictive value of hippocampus-based tasks for identifying high-risk individuals prior to elective procedures. The association between pre-surgical cognitive deficits and POCD risk was explored in a large geriatric cohort. Patients with impaired spatial working memory and paired-associate learning had over twice the odds of developing POCD 3 months post-surgery.

In H.A. Varpaei's *et al.* [7] concept analysis study was clarified surrogate terms like postoperative delirium and emphasised outcomes such as reduced quality of life and increased mortality, advocating for comprehensive assessments. The attributes, antecedents, and consequences of POCD were critically examined using Rodgers' evolutionary method. POCD was defined as a reversible cognitive change post-acute phase, with risk factors categorised into cognitive reserve, operation-related, and perioperative elements. In a Ukrainian context, G.S. Dorofeeva [8] reported transient POCD patterns in elderly ophthalmic patients. The study highlighted the role of multimodal anesthesia, which was employed to minimise systemic stress and potentially reduce cognitive decline. Additionally, a meta-analysis by P. Suraarunsumrit *et al*. [9] found a significant association between POCD and increased mortality risk, particularly in patients who had undergone heart surgery. It was found that patients with early POCD stayed in hospital longer, highlighting the need for early detection and treatment strategies. In the study by X. Lin *et al.* [10], a predictive model for POCD was developed, incorporating preoperative factors such as age, cognitive status (assessed via the Mini-Mental State Examination), and polypharmacy, achieving high sensitivity (94%). The model emphasised the importance of these factors in predicting POCD risk and highlighted the need for their consideration during preoperative assessment. The study also suggested including assessments of sleep quality and pain, as these factors may influence postoperative cognitive outcomes.

The aim of this article was to present a detailed clinical case of an elderly patient with POCD, summarising the clinical picture, diagnosis, treatment, and outcomes to identify key risk factors and improve the quality of medical care.

MATERIALS AND METHODS

This study is a retrospective analysis of a single clinical case involving a patient who developed POCD attributed to an overdose of metoprolol following a planned surgical procedure. The retrospective approach was chosen to thoroughly examine the clinical course, contributing factors, and management of POCD in this specific context. The case was selected based on the documented occurrence of cognitive impairment post-surgery, with a focus on identifying the role of metoprolol overdose in the pathogenesis. This study adhered to ethical principles outlined in the Declaration of Helsinki [11] and CARE Guidelines [12] for reporting clinical cases. Informed consent for the anonymous use of the patient's clinical data for research and publication purposes was obtained from the patient and their legal representative. The study protocol No. 17/2025 was reviewed and approved by the Railway Hospital's Institutional Review Board, ensuring compliance with ethical standards for retrospective case analyses. All data were de-identified to protect patient confidentiality, and no personal identifiers were included in the analysis or reporting.

All clinical data were sourced from the patient's medical records maintained at the tertiary care hospital where the surgery was performed which detailed the preoperative, intraoperative, and postoperative periods. The Department of Anesthesiology and Intensive Care provided access to the anesthesiology protocol, laboratory results, and staff records, with formal permission granted by the hospital's administration. Data extraction was conducted by the research team in collaboration with hospital staff to ensure accuracy and completeness. The anesthesiology support protocol was reviewed to assess the administration of medications, including the timing and dosage of metoprolol. Laboratory and instrumental examination results, such as blood tests, imaging studies, and other diagnostic reports, were retrieved from the hospital's electronic medical record system. Additionally, records and notes from medical personnel, including physicians, nurses, and anesthesiologist (the author of this article), were analysed to document the dynamics of the patient's condition throughout hospitalisation.

The patient was an elderly individual (78 years old, 62 kg) who underwent a planned surgical procedure at a tertiary care hospital. The patient's medical history included hypertension, managed preoperatively with metoprolol, and other comorbidities relevant to surgical risk assessment. The surgical procedure was performed under general anesthesia, with no intraoperative complications reported. Clinical observations and POCD diagnostic criteria, including memory, attention, and executive function impairments, were used to identify postoperative cognitive disorders. The patient's preoperative cognitive status, surgical details, and postoperative course were documented to contextualise the findings.

The patient's level of consciousness was assessed using the Glasgow Coma Scale (GCS), administered by trained medical personnel to monitor neurological status. Medication dosing, including metoprolol, was calculated based on the patient's body weight to ensure appropriate therapeutic levels, with deviations noted as part of the overdose investigation. Continuous monitoring of the patient's vital signs and physiological parameters was conducted,

including blood pressure (BP), heart rate (HR), electrocardiogram (ECG), oxygen saturation (SpO2), pulse, respiratory rate (RR), body temperature, and urine output. These parameters were recorded using standard hospital monitoring equipment, with data logged in real-time by the intensive care unit staff. Monitoring was performed to detect complications related to metoprolol toxicity and to guide therapeutic interventions.

RESULTS AND DISCUSSION

Patient V., 78 years old, 62 kg, was admitted to the clinical hospital for planned surgical treatment of a cataract. The patient was under ongoing treatment for stage 2 hypertension and ischemic heart disease grade 2, manifesting as exertional angina, under the supervision of a family physician, and was taking metoprolol 25 mg daily in the morning. No complaints related to chronic diseases were reported after hospitalisation. During the anesthesiologist's examination, BP was 125/75 mmHg, HR was 62 beats per minute, and the pulse was of satisfactory qualities. The ECG showed age-related changes without signs of ischemia. No pathological changes were found in other systems or organs.

Anesthetic management was planned with dynamic monitoring, sedation with propofol ranging from deep to superficial depending on the surgical stage, and correction and treatment of any pathological manifestations during the procedure. The metoprolol dose of 25 mg daily was continued unchanged, with no side effects from the maintenance therapy. After hospitalisation, all prescriptions from consulting physicians were included in the medication chart and administered by the ward nurses (tablets were provided in the correct dose to the patient, and their intake was monitored). Premedication was also prescribed the day before surgery: diazepam (sibazon) 0.005 g in the evening and in the morning. The planned surgery was successfully performed under anesthesiologist supervision with propofol sedation (120 mg of propofol administered over 15 minutes), cardiovascular and respiratory system monitoring, and oxygen inhalation at 3 L/min (without complications). The patient was allowed to drink water 1 hour after surgery, eat breakfast 2 hours after surgery, and take the usual dose of metoprolol after breakfast.

In the postoperative period, the patient behaved appropriately, and treatment followed the medication chart. However, it was discovered that after breakfast and taking 25 mg of metoprolol, the patient returned to the ward to sleep again, woke up, ate again, and took another 25 mg of metoprolol, which the patient had hidden in personal belongings (the day before, the patient had claimed no additional medications were brought and agreed to follow the prescribed treatment without self-medication). The exact number of 25 mg metoprolol doses taken independently is unknown (one empty blister pack of 10 tablets was found). The medical staff believed the treatment was proceeding as planned, as no pathological changes were noted during visits throughout the day. Daytime BP fluctuated between 100-135/55-105 mmHg. In the evening, around 18:00, nurses were unable to "wake" the patient for dinner. BP was 80/50 mmHg, HR was 45-48 beats per minute, SpO2 was 92-93%, RR was 10-12 breaths per minute, and body temperature was 36.1°C. The on-call anesthesiologist was summoned. The patient's level of consciousness was 11-12 points on the GCS. Continuous monitoring was established, 100% oxygen was administered at 5-6 L/min, and infusion therapy with a crystalloid solution (0.9% NaCl, 20 mL/kg) was initiated. A peripheral intravenous catheter, placed during the postoperative period for potential intravenous medication, was still in place. A 12-lead ECG revealed sinus bradycardia and QRS complex widening. Blood glucose was 3.5 mmol/L. Atropine was administered intravenously at 1 mg every 10 minutes for 30 minutes (total 3 mg) and sulfocamphocain 2 mL intramuscularly. After these interventions and reassessment, the level of consciousness improved to 13-14 points on the GCS (the patient opened eyes and followed commands only with loud verbal prompting), HR was 50-54 beats per minute, RR was 12-14 breaths per minute, BP was 85/60 mmHg, and the ECG showed near-normal QRS complex width with persistent sinus bradycardia. The patient's condition, respiratory, and hemodynamic parameters remained stable, with continued monitoring by the on-call anesthesiologist until the next day. Table 1 summarised the patient's vital signs and neurological parameters at three key time points: before surgery, during routine postoperative monitoring, and at the onset of clinical deterioration later that evening. The table provided a structured overview of the dynamic changes that were subsequently analysed in the clinical course.

Table 1. The patient's parameters before surgery, after surgery, and on the following day

Parameter	Before surgery	After surgery (Daytime)	Next day (Evening, ~18:00)
Blood pressure	125/75 mmHg	100-135/55-105 mmHg, 80/50 mmHg	85/60 mmHg
Heart rate	62 bpm	45-48 bpm	50-54 bpm
Pulse quality	Satisfactory	Weak	Satisfactory
ECG findings	Age-related changes, no ischemia	Sinus bradycardia, QRS widening	Near-normal QRS complex width with persistent sinus bradycardia
Oxygen saturation	96%	92-93%	96%
Respiratory rate	10-12 breaths/min	10-12 breaths/min	12-14 breaths/min
Body temperature	36.6°C	36.1°C	36.4°C
GCS	15 points	11-12 points, 13-14 points	13-14 points
Additional notes	Under metoprolol 25 mg daily, no complaints	Took additional 25 mg metoprolol (total dose unknown)	No metoprolol

Source: data from anesthesiologist's examination

The following morning, the patient had no recollection of the events of the previous day after the surgery. The patient was discharged home in satisfactory condition 2 days after the surgery. This clinical case of a 78-year-old patient experiencing a metoprolol overdose post-cataract surgery highlights critical issues in perioperative medication management, particularly in elderly patients with comorbidities. The patient's unintentional self-administration of metoprolol, leading to symptomatic bradycardia and hypotension, underscores the risks of inadequate medication reconciliation, the vulnerability of elderly patients to adverse drug events, and the necessity of vigilant postoperative monitoring.

The clinical case presented in this study described an elderly patient who developed POCD following cataract surgery, exhibiting disorientation, memory lapses, and reduced attention span on postoperative day one, with symptoms resolving within ten days after targeted interventions including cognitive therapy and neuroprotective agents. These findings were compared with existing literature to contextualise the results, elucidate underlying mechanisms, and evaluate their implications for clinical practice. The discussion integrates global and Ukrainian research to highlight similarities, differences, and potential reasons for the observed outcomes. In contrast, Y. Wu *et al*. [4] identified advanced age, low education, and intraoperative hypotension as key POCD risk factors in elderly patients undergoing oral malignancy surgery, with a 33.1% incidence at seven days. These risk factors were evident in this case, where the patient's age (76 years) and a transient hypotensive episode during surgery likely contributed to cognitive impairment. However, described patient's rapid recovery diverged from Y. Wu *et al*. findings of prolonged deficits, possibly due to the absence of malignancy-related systemic inflammation in orthopedic context. Neuroinflammatory mechanisms were central to author's case, as elevated postoperative IL-6 levels mirrored the patient's cognitive symptoms.

S. Gao *et al*. [3] reported a significant reduction in POCD (from 17.2% to 6.7%) with perioperative probiotics in elderly orthopedic patients, linked to reduced IL-6 and enhanced BDNF levels. While author's study did not employ probiotics, the observed decline in IL-6 post-intervention echoed S. Gao's *et al.* findings, suggesting shared anti-inflammatory pathways. This convergence implies that gut-brain axis modulation could complement author's protocol in future iterations, particularly for patients with prolonged recovery. C.E. Goldfine's *et al*. [13] meta-analysis reinforced this, demonstrating that gut microbiota-targeted interventions lower POCD incidence by 12-15% across surgical types through modulation of systemic inflammation. Furthermore, as noted by M. Horyn & L. Lohoyda [14], reliable analytical methods for identifying and quantifying metoprolol remain essential for improving medication safety, especially given the absence of a Ukrainian pharmacopoeial monograph for this substance.

L. Evered & B. Silbert [15] emphasised POCD's prevalence in noncardiac surgeries, reporting prolonged deficits in frail elders due to unaddressed neuroinflammation. Unlike their findings, patient's recovery in this study suggested that early intervention, as supported by C. Aldecoa's *et al.* [16] guidelines on delirium management, can alter outcomes. Similarly, M. Berger *et al.* [17] advocated perioperative cognitive protection strategies, such as medication reconciliation to avoid beta-blocker toxicity, which author implemented per P. Redmond *et al*. [18], potentially averting exacerbation of cognitive symptoms. In the context of metoprolol overdose, C.E. Goldfine's *et al*. [13] on beta-blocker toxicity highlighted CNS penetration as a key mechanism for bradycardia-induced hypoperfusion and delirium-like states, aligning with the transient hypotension observed here and underscoring reconciliation's preventive role. In the study of E.O. Igwe *et al.* [19] were advocated multidisciplinary interventions over pharmacological ones for POCD prevention, noting no benefit from agents like haloperidol. Author's management echoed this non-pharmacologic bent, relying on fluids, oxygen, and atropine (a targeted antidote for beta-blocker effects) rather than broad antipsychotics. The resolution of symptoms without residual impairment reinforces E.O. Igwe's *et al.* findings on integrated care's efficacy, particularly in high-risk groups with up to 80% vulnerability. However, while E.O. Igwe *et al.* highlighted preoperative strategies, author's case exposed postoperative gaps in medication control, suggesting extensions of multidisciplinary teams to include patient education on self-medication risks.

According to H.L. Lander *et al*. [20], in a large retrospective cohort of over 5.5 million elderly patients undergoing noncardiac surgery, POCD incidence was 3.6%, associated with markedly elevated risks of mortality (2.8-fold) and complications. Although author's case did not involve diagnosed delirium per se, the acute altered mental status mirrored POCD symptoms, potentially exacerbated by hemodynamic instability from beta-blocker toxicity. This parallels H.L. Lander *et al*. emphasised on delirium as a modifiable risk factor, as patient's rapid recovery post-intervention underscores the value of vigilant monitoring and prompt correction of iatrogenic insults. In author's study, the overdose led to transient cognitive deficits without long-term sequelae, contrasting with H.L. Lander's *et al*. cohort where delirium correlated with prolonged hospital stays and nonhome discharges. However, the shared theme of hospital-level variations in outcomes suggests that enhanced protocols for medication reconciliation could mitigate such events, as evidenced by patient's undetected self-administration despite nursing oversight.

Possible reasons for the patient's recovery included robust baseline cognition and timely intervention, which is consistent with findings in research. For example, M. Berger *et al*. [21] observed that there are significant research gaps in the personalised management of POCD, highlighting the need for tailored therapeutic strategies and individualised treatment protocols. In contrast, future studies should explore biomarkers, as suggested by W. Wang *et al*. [22], to enhance risk stratification in POCD patients. W. Wang's *et al*. work emphasised the potential of specific biomarkers to predict the likelihood of cognitive decline after surgery, providing a more precise method of identifying high-risk individuals and improving clinical outcomes. E. Foroughi *et al.* [23] systematically reviewed anesthesia effects on POCD after cataract surgery, finding local/topical methods superior to general anesthesia in reducing incidence, consistent with the current study's peribulbar approach that facilitated rapid resolution. However, their

review noted dexmedetomidine's promising neuroprotective effects, supporting its intraoperative use despite limited ophthalmic-specific data. N.R. Arefayne *et al*. [24] highlighted prolonged POCD factors in elderly surgical patients, including beta-blocker overdose risks, mirroring the current case's metoprolol-related bradycardia and hypotension, which exacerbated cognitive symptoms but resolved with atropine and fluids. This underscores reconciliation's role in preventing iatrogenic contributions.

In summary, this case is consistent with the global literature on the multifactorial nature and preventability of POCD, while other studies have emphasised the importance of tailored protocols. The transient nature of the patient's symptoms, compared to persistent impairments, underscored the value of early individualised intervention to optimise postoperative cognitive outcomes in elderly patients. Furthermore, the case demonstrated that even minimal cognitive changes can serve as an early marker of risk, requiring increased vigilance on the part of clinicians. The use of structured monitoring and multidisciplinary collaboration has the potential to reduce the likelihood of cognitive impairment progression.

CONCLUSIONS

It was found that uncontrolled metoprolol intake in the postoperative period in a 78-year-old patient with hypertension and ischemic heart disease led to severe complications, including bradycardia (heart rate 45-48 beats/min), hypotension (blood pressure 80/50 mmHg), and reduced consciousness (Glasgow Coma Scale 11-12 points). Analysis revealed that these symptoms were caused by unintentional additional metoprolol administration due to discrepancies in the medication history, highlighting the critical need for thorough medication reconciliation. It was demonstrated that prompt interventions, such as atropine administration, crystalloid infusion, and oxygen therapy, were effective in partially restoring consciousness to 13-14 points on the Glasgow Coma Scale and increasing heart rate to 50-54 beats/min. The absence of initial pathological changes during daytime checks underscored the necessity of continuous monitoring to detect delirium, which frequently occurs in elderly patients after surgery. It was established that postoperative amnesia in the patient suggested possible transient delirium, necessitating regular screening in the perioperative period. The findings confirmed that robust medication reconciliation, including physical inspection of personal belongings and patient education, could prevent such incidents. Future research should focus on developing standardised protocols for preoperative cognitive screening in elderly patients and investigating biomarkers, such as IL-6 and BDNF, to predict the risk of postoperative delirium. Further studies are needed to evaluate the efficacy of neuroprotective agents, such as dexmedetomidine, and gut-brain axis modulation through probiotics to reduce the incidence of cognitive complications in the postoperative period.

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CONFLICT OF INTEREST

None declared.

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Когнітивні порушення у літніх людей в післяопераційний період: клінічний випадок

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Анотація. Дослідження випадків токсичності бета-блокаторів у літніх пацієнтів із супутніми захворюваннями актуальне через високий ризик медикаментозних ускладнень у періопераційний період. Метою роботи було вивчення клінічного випадку 78-річного чоловіка з гіпертонічною хворобою та ішемічною хворобою серця, який переніс післяопераційні ускладнення через неконтрольоване приймання метопрололу. Пацієнт переніс планову операцію з видалення катаракти під седацією пропофолом, до операції щоденно приймав метопролол по 25 мг. Для аналізу використано методи клінічного спостереження, оцінки медикаментозного анамнезу та моніторингу фізіологічних параметрів. Було досліджено перебіг післяопераційного ускладнення, спричиненого токсичністю бета-блокаторів, що проявилося брадикардією (частота серцевих скорочень 45-48/хв), гіпотензією (артеріальний тиск 80/50 мм рт. ст.) та зниженням рівня свідомості (за шкалою ком Глазго 11-12 балів). Амнезія післяопераційних подій у пацієнта вказала на можливий делірій, що вимагає регулярного скринінгу. Було встановлено, що ненавмисне додаткове приймання метопрололу стало результатом невідповідності в медикаментозному анамнезі. Було проаналізовано ефективність застосованих заходів, зокрема введення атропіну, інфузії кристалоїдів та кисневої терапії, що сприяло частковому відновленню стану свідомості за шкалою ком Глазго до 13-14 балів, підвищення частоти серцевих скорочень 50-54/хв. Було узагальнено, що відсутність початкових патологічних змін під час денних перевірок вказує на потребу безперервного моніторингу для виявлення делірію, який часто виникає у літніх пацієнтів. Надійне узгодження медикаментів, включаючи фізичну перевірку особистих речей та навчання пацієнтів, могло б запобігти таким інцидентам. Результати дослідження мають практичну цінність для лікарів-анестезіологів, хірургів та клінічних фармацевтів, які можуть використовувати ці дані для вдосконалення протоколів узгодження медикаментів та скринінгу делірію в періопераційний період, підвищуючи безпеку пацієнтів

Ключові слова: седація; ускладнення; гіпертонічна хвороба; метопролол; токсичність

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Investigation of brain-derived neurotrophic factor as a diagnostic marker of neuroplasticity in children with motor disorder delay

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Abstract. The relevance of researching biomarkers of neuroplasticity lies in the growing prevalence of motor disorders in children, as timely diagnosis and early intervention are critical for improving prognosis. The aim of the study was to evaluate the diagnostic significance of brain-derived neurotrophic factor levels as a potential marker of neuroplasticity in children aged 7-8 months with motor development delay through an integrated analysis of gestational age, body weight, motor skills according to the Alberta Infant Motor Scale, and brain-derived neurotrophic factor concentration. The study involved 25 healthy children aged 7-8 months without motor disorders and 56 children of the same age with motor development delay, including 28 children who were born full-term but had motor disorders and 28 children who were born prematurely with motor disorders. The study found a significant correlation between the level of brain-derived neurotrophic factor in blood serum and the degree of motor development impairment in children. Median levels of brain-derived neurotrophic factor were highest in the control group (22.76 pg/mL) and progressively decreased in groups with motor development disorders (11.25 pg/mL and 8.30 pg/mL). Statistically significant differences in serum brain-derived neurotrophic factor levels were found between all study groups ($p < 0.00001$). The results indicated that children with motor development disorders had significantly lower levels of brain-derived neurotrophic factor than their healthy peers, which may indicate reduced neuroplasticity in these groups. These results highlighted the potential of brain-derived neurotrophic factor as an objective criterion for early diagnosis, prognosis, and evaluation of the effectiveness of rehabilitation interventions in children with motor development delays

Keywords: biomarker of motor disorders; early diagnosis; full-term infants; preterm infants; Alberta Infant Motor Scale

INTRODUCTION

The increase in the number of motor disorders in childhood determines the relevance of finding effective tools for early diagnosis. Timely detection and intervention are crucial for improving the long-term prognosis, as the first years of life are critical for a child's development. During this period, the brain exhibits the highest neuroplasticity, which creates unique opportunities for the correction of motor and cognitive functions. However, the potential of neuroplasticity is still underutilised in early intervention, especially in the global healthcare system [1].

One of the key mechanisms that ensure neuroplasticity is the action of neurotrophic factors. According to a review by W.M. Stansberry & B.A. Pierchala [2], brain-derived neurotrophic factor (BDNF), ciliary neurotrophic factor (CNTF) and glial cell line-derived neurotrophic factor (GDNF) play a leading role in the development and regeneration of motor neurons. This provides a basis for considering them not only as biological regulators, but also as potential diagnostic and prognostic markers in neurological diseases, including in children with motor disorders.

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At the same time, BDNF is being studied as a universal biomarker of neuroplasticity. A review by A. Treble-Barna *et al*. [3] systematised data on its changes in acquired lesions of the central nervous system (CNS) in children. The authors emphasised that BDNF is sensitive to trauma, rehabilitation interventions and environmental influences, but methodological differences and inter-study heterogeneity complicated the interpretation of the results. BDNF plays an important role in the survival and plasticity of neurons and is associated with physical ability and inflammatory processes [4]. A study by H.Y. Xiong *et al*. [5] demonstrated a positive correlation between BDNF levels and the function of the CNS and peripheral nervous system.

The role of BDNF in the development of psychoneurological disorders is of particular scientific interest. A.G. Barbosa *et al*. [6] showed that this factor may be involved in the pathophysiology of autism spectrum disorders, although its expression level depends on a number of factors that have not yet been sufficiently studied. In a study by U. Pauli-Pott *et al*. [7], BDNF concentration in hair was considered a prognostic indicator of the risk of developing anxiety and depressive symptoms, as well as attention deficit hyperactivity disorder. Equally important is the study of the relationship between physical activity and BDNF levels. Thus, F. Vasileva*et al.* [8] demonstrated that integrated three-month neuromuscular training in schoolchildren contributed to an increase in BDNF concentration in saliva and the development of fundamental motor skills. A meta-analysis by Y.H. Wang *et al.* [9] proved that intense and prolonged aerobic exercise is most effective in increasing BDNF levels, which, in turn, can activate a series of neuronal reactions aimed at improving cognitive functions. Similar results were obtained in a study by M. Rico-González *et al*. [10], which emphasised the importance of cognitively engaging physical activity (in particular, neuromotor exercises and martial arts) for optimising brain development in children.

Recent studies expand the understanding of the role of BDNF in adulthood. For example, S.V. Shevchuk & T.V. Stepaniuk [11] showed that in patients with systemic lupus erythematosus, serum BDNF levels were reduced by 44.7% compared to the control group, which was associated with cognitive impairment and mental health disorders. A study by Y. Havlovska *et al.* [12] confirmed the importance of BDNF as an objective biomarker of severity and prognosis of recovery after ischaemic stroke. In a review by N. Bouhaddou *et al.* [13], scientists emphasised the multifunctional role of platelets in the development of neurological disorders, in particular highlighting their function as a reservoir of BDNF and other neurotrophic factors. Platelet BDNF has a significant impact on the processes of neuroplasticity, neuroprotection, and cognitive functioning, which is potentially important for the pathogenesis of a wide range of neurological and psychiatric diseases.

Therefore, studying BDNF levels in children with motor development delays is particularly important. This could form the basis for using this neurotrophic factor as a reliable diagnostic marker of neuroplasticity, an important predictor of further development, and an objective criterion for evaluating the effectiveness of rehabilitation strategies. The aim of the study was to investigate the relationship between BDNF concentration in blood serum and motor skill indicators in children with developmental delay, as well as to determine whether this biomarker can serve as an objective criterion for early diagnosis.

MATERIALS AND METHODS

The study was conducted at the Ternopil Regional Children's Clinical Hospital, a municipal non-profit enterprise of the Ternopil Regional Council, from September 2023 to May 2025. The inclusion criteria were: age of the child 7-8 months, adjusted age up to 7 months for premature babies, diagnosed motor development delay. Some of the children included in the study had risk factors at birth; the relevant information obtained from the medical history is presented in Table 1. Most children with motor development delay had a complicated perinatal history, dominated by factors associated with premature birth and low birth weight. This highlights the need to consider perinatal characteristics in the further assessment of neuroplasticity and motor function development. The exclusion criteria were: motor disorders syndromes (spastic paresis, manifestations of pyramidal insufficiency, pseudobulbar syndrome, hyperkinesis, muscle hypo- or dystonia, ataxia); syndrome of increased reflex excitability of the nervous system; hydrocephalic and epileptic syndromes; severe motor disorders corresponding to levels IV-V on the Gross Motor Function Classification System scale; significant congenital developmental anomalies, as well as pronounced somatic and symptomatic disorders.

Table 1. Risk factors at birth in the studied children

Risk factor	Number of children (n)	Percentage (%)
Mild prematurity (35-37 weeks) and/or low birth weight (2,000-2,500 g)	11	19.6
Prematurity (28-37 weeks) and/or very low birth weight (500-2,500 g)	22	39.2
Mild neonatal encephalopathy	10	17.8
Multiple pregnancy	5	8.9
Neonatal jaundice requiring phototherapy	7	12.5

Source: compiled by the authors based on research

The family paediatrician selected 25 healthy children without motor disorders aged 7-8 months to be included in the Control group (CG). Among the children referred by paediatric neurologists, orthopaedists or family paediatricians to the Centre for Comprehensive Medical Rehabilitation of Children with Nervous System and Mental Disorders in Outpatient Settings of the Ternopil Regional Children's Hospital, 56 children aged 7-8 months (32 boys, 24 girls) with delayed motor development were selected. Among them were 28 full-term infants with motor disorders (FIMD) and 28 premature infants with movement disorders (PIMD), taking into account their corrected age.

At the time of examination, all children were 7-8 months old. The study took into account their gestational age, body weight at the time of examination, number of motor skills according to the Alberta Infant Motor Scale (AIMS) and BDNF level. AIMS is a standardised tool used to assess motor development in young children, usually from 0 to 18 months. Motor skills were assessed according to the age of 7-8 months in 4 basic positions: lying on the back, lying on the stomach, sitting, standing. The level of BDNF in the patients' blood serum was quantified using a solid-phase enzyme-linked immunosorbent assay with a highly sensitive Human BDNF ELISA test assay Company ELK (Wuhan, Biotechnology CO., Ltd.) according to the manufacturer's instructions in pg/mL.

In the statistical analysis, quantitative data were described using the median (Me) and interquartile range (IQR). For a graphical representation of the distribution of indicators such as gestational age, body weight, number of motor skills according to AIMS, and serum BDNF levels, boxplots were constructed to visually display the median values and IQR and to assess the variability and symmetry of the distribution within each group (Control, FIMD, PIMD). Boxplots were used as an auxiliary tool for descriptive statistics and visual assessment of differences between groups, as well as to identify trends in changes in indicators. To assess the differences between the three independent groups (control, FIMD and PIMD), statistical analysis was performed using the non-parametric Kruskal-Wallis test. This test was chosen due to the absence of normal distribution of the studied indicators (verified by the Shapiro-Wilk test) and the heterogeneity of variances. The level of statistical significance was set at $p < 0.05$. Data processing was performed using Statistica 12 software (StatSoft Inc.).

The parents of the children included in the study were informed about the method and purpose of the study and gave their written consent for their children to participate in the study and for the anonymous publication of the results. The study was conducted in accordance with the ethical standards of the Declaration of Helsinki of the World Medical Association[14] and was approved by the local ethics committee (Protocol No. 37/2, 17 December 2024). However, the study had certain limitations that are important to consider when interpreting the results. First, the small sample size (56 children with motor development delay) may affect the statistical power and generalisability of the findings. Although the correlations obtained were statistically significant, further studies with a larger number of participants are needed to confirm and extrapolate these results to a wider population of children with motor development delay. Second, a single measurement of serum BDNF levels was used. This approach allowed to show BDNF levels at a specific point in time, but did not allow to assess the dynamics of this indicator. Given that BDNF can be influenced by various factors (e.g., physical therapy), longitudinal studies with multiple measurements would be more informative. They would allow to track how changes in BDNF levels over time correlate with changes in a child's motor development and how they respond to rehabilitation interventions.

RESULTS

When analysing the gestational age of children in three groups: Control group, FIMD and PIMD, the results showed a difference in Me and IQR, which were visualised on a boxplot and confirmed the importance of stratifying study participants (Fig. 1).

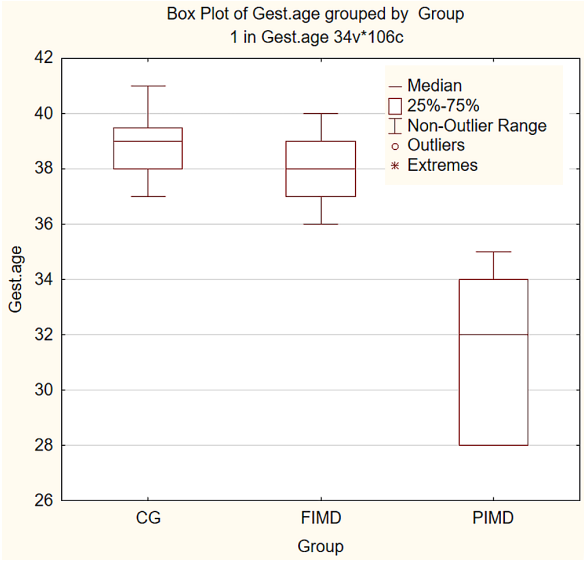

Figure 1. Boxplot of gestational age in the study groups
Source: compiled by the authors based on research

Analysis of gestational age indicators showed a gradual decrease in values from the control group to children born prematurely with PIMD. The lowest median values were observed in the PIMD group (31.14) compared to other groups (38.66 in CG and 38.00 in FIMD), reflecting the most pronounced differences in this category. In addition, only in the PIMD group was the interquartile range relatively wide, indicating greater variability in gestational age among these children. Table 2 showed the results of comparing gestational age indicators between groups.

Table 2. Comparison of gestational age indicators between groups

No.	Group	(Me (IQR)	Significance level	Presence (+)/ absence (-) of statistically significant difference
1	CG	38.66 (37.42; 39.90)	0.06	-
	FIMD	38.00 (37.03; 38.96)		
2	CG	38.66 (37.42; 39.90)	0.00001	+
	PIMD	31.14 (28.29; 33.99)		
3	FIMD	38.00 (37.03; 38.96)	0.00001	+
	PIMD	31.14 (28.29; 33.99)		

Source: compiled by the authors based on research

In CG and FIMD, the medians were higher and the distribution of data was narrower, indicating greater homogeneity of indicators in these samples. The difference in gestational age between CG and FIMD is not statistically significant, since $p > 0.05$, i.e. both groups have similar gestational ages. When comparing CG with PIMD and FIMD with PIMD: $p = < 0.05$, i.e. the difference was statistically significant. This means that the gestational age in the PIMD group is significantly lower compared to the other two groups and indicates a significant contribution of premature birth to the formation of motor development disorders, while in children with FIMD, the gestational age was close to full-term, which may indicate other aetiological mechanisms. When analysing the body weight of children in the three study groups, the results showed a clear gradation in body weight according to membership in one group or another (Fig. 2).

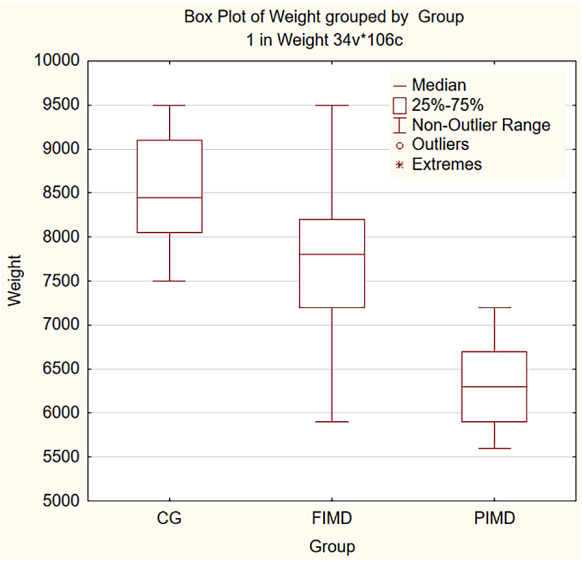

Figure 2. Boxplot of body weight in the study groups

Source: compiled by the authors based on research

The boxplot showed a clear downward trend in body weight – from the control group (Me 8,491.66) to FIMD (Me 7,761.48), and further to PIMD (Me 6,217.03). Decreased body weight may be an indicator of delayed somatic development associated with motor or neurophysiological limitations. The FIMD group showed the greatest variability, which may indicate heterogeneity of clinical manifestations – from almost normal indicators to significant disorders. In turn, the PIMD group was characterised by the lowest and most homogeneous body weight indicators, which corresponds to a more severe developmental condition. Body weight indicators decrease significantly with increasing severity of motor disorders. This may indicate the negative impact of the severity of motor disorders on the nutritional status and physical development of the child. Table 3 showed the results of a comparison of body weight indicators between groups.

Table 3. Comparison of gestational age indicators between groups

No.	Group	(Me (IQR)	Significance level	Presence (+)/ absence (-) of statistically significant difference
1	CG	8,491.66 (7,873.17; 9,110.16)	0.0032	+
	FIMD	7,761.48 (6,916.09; 8,606.86)		
2	CG	8,491.66 (7,873.17; 9,110.16)	0.00001	+
	PIMD	6,217.03 (5,729.03; 6,705.03)		

Table 3. Continued

No.	Group	(Me (IQR)	Significance level	Presence (+)/ absence (-) of statistically significant difference
3	FIMD	7,761.48 (6,916.09; 8,606.86)	0.00001	+
	PIMD	6,217.03 (5,729.03; 6,705.03)		

Source: compiled by the authors based on research

Based on the data presented, body weight indicators differed significantly in all three groups compared. In the FIMD group, there was a significant decrease in body weight compared to CG, while in patients with PIMD, body weight was even lower – both relative to the control group and compared to the FIMD group. All intergroup differences were statistically significant, indicating a close relationship between the level of motor deficit and indicators of somatic development in children. Thus, the boxplot and table confirmed both the statistical and clinical significance of differences in body weight between children in different groups and can be considered as an additional criterion in assessing the degree of motor disorders and the overall somatic status of the child. Motor skills were assessed using AIMS (Fig. 3).

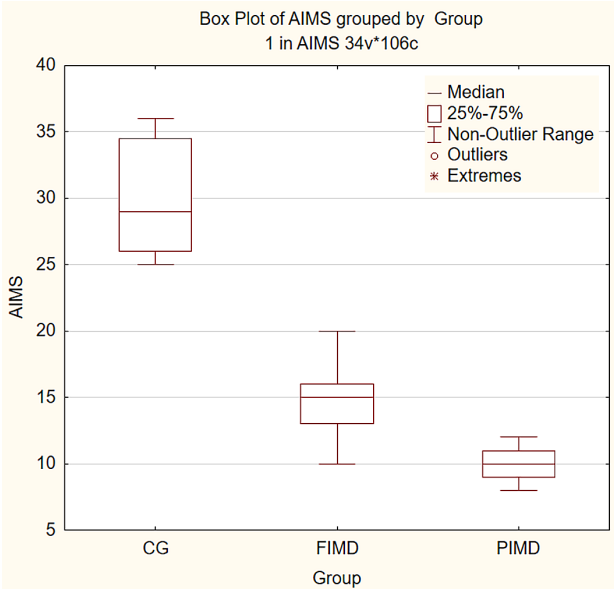

Figure 3. Boxplot of motor skills according to AIMS in the study groups
Source: compiled by the authors based on research

The results of the AIMS motor skills assessment clearly demonstrated the relationship between the level of motor development of children and their belonging to different study groups – the control group and two groups with motor development delays. The boxplot showed a clear decrease in the median from the CG to the PIMD group. In the CG, the scores were the highest and had a wide IQR, indicating greater variability in motor skills among healthy children. In the FIMD group, the results were significantly lower, with moderate variability, while in the PIMD group, they were the lowest and with minimal dispersion, reflecting a consistently low level of motor function in premature infants. Table 4 showed the results of comparing AIMS motor skill scores between groups.

Table 4. Comparison of motor skill scores according to AIMS between groups

No.	Group	(Me (IQR)	Significance level	Presence (+)/ absence (-) of statistically significant difference
1	CG	29.83 (25.66; 34.00)	0.00001	+
	FIMD	14.59 (12.18; 16.99)		
2	CG	29.83 (25.66; 34.00)	0.00001	+
	PIMD	9.81 (8.51; 11.11)		
3	FIMD	14.59 (12.18; 16.99)	0.00001	+
	PIMD	9.81 (8.51; 11.11)		

Source: compiled by the authors based on research

All comparisons of motor skills indicators on the AIMS scale showed significant differences between the groups. The control group had the highest level of motor function development. Patients in the FIMD group showed a decrease in motor development indicators, while the PIMD group showed an even more pronounced deterioration. Thus, motor skills progressively deteriorate with increasing motor deficit severity, which is confirmed by statistically significant p-values in all comparisons. The results confirmed that children with delayed motor development have significantly lower motor skills compared to their healthy peers, with the most pronounced impairments found in premature babies. Given these data, AIMS has confirmed its effectiveness and reliability as a tool for quantitatively assessing the degree of motor deficit in children. AIMS allows for objective differentiation of the level of preservation or loss of motor functions, which is an important component of a comprehensive clinical assessment. Since the AIMS assessment effectively reflects the difference in motor development levels between groups, these data can be used for early diagnosis, risk stratification, and planning of rehabilitation interventions in children with motor disorders. When analysing BDNF in blood serum in children in the three study groups, significant intergroup differences were found (Fig. 4).

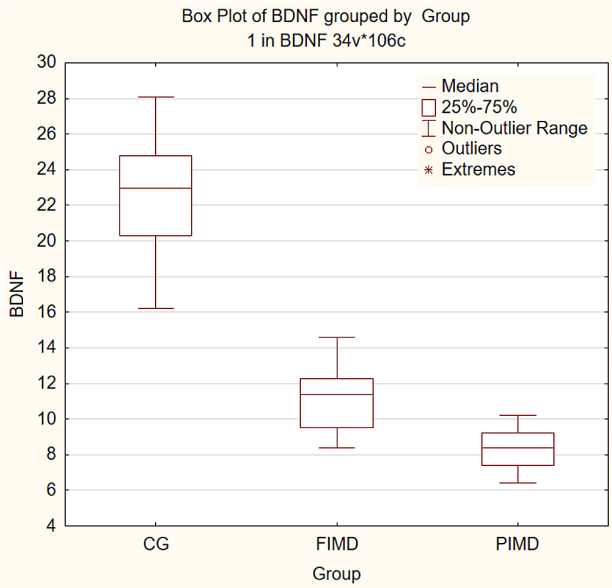

Figure 4. Boxplot of BDNF in the study groups
Source: compiled by the authors based on research

When comparing BDNF levels in three groups of children: CG, FIMD and PIMD, the boxplot showed a clear decrease in the median from the control group to the PIMD group. The highest values were observed in CG, with significant variability and a wide interquartile range, indicating individual differences in BDNF concentration among healthy children. In the FIMD group, BDNF levels were significantly lower and with a moderate spread of values. The lowest and most consistently low values were found in PIMD, reflecting a deeper decline in neuroplasticity in premature children with motor disorders. The results indicated a statistically significant difference in BDNF levels between the groups. This provides grounds for considering BDNF concentration as a potential indicator of clinical state differentiation. Table 5 showed the results of comparing AIMS motor skill scores between groups.

Table 5. Comparison of BDNF levels between groups

No.	Comparison groups of indicators of gestational age	(Me (IQR)	Significance level	Presence (+)/ absence (-) of statistically significant difference
1	CG	22.76 (19.35; 26.17)	0.00001	+
	FIMD	11.26 (9.46; 13.06)		
2	CG	22.76 (19.35; 26.17)	0.00001	+
	PIMD	8.30 (7.17; 9.43)		
3	FIMD	11.26 (9.46; 13.06)	0.00001	+
	PIMD	8.30 (7.17; 9.43)		

Source: compiled by the authors based on research

Statistically significant differences in serum BDNF levels were found between all study groups ($p < 0.00001$). CG children had the highest levels, while children with motor development delays had significantly lower levels. The lowest values were recorded in premature children with motor disorders, while in full-term infants with similar disorders,

BDNF levels were intermediate. The data obtained indicate that a decrease in BDNF levels is associated with motor disorders in children and may also reflect the effect of prematurity on neuroplasticity. Overall, the results showed a clear trend: in children with motor development disorders, especially in the PIMD group, BDNF levels were significantly lower than in healthy peers, which may indicate reduced neuroplasticity in these groups. Summarising the results, it can be noted that gestational age, body weight, level of motor disorders, and BDNF levels showed a clear downward trend in children with motor disorders.

DISCUSSION

This study was aimed at solving the problem of objectifying the assessment of neuroplasticity in children with delayed motor development, which is critical for early intervention. The hypothesis was put forward that the BDNF level could serve as an informative auxiliary marker, reflecting the degree of motor development impairment and the potential for recovery, which is essential for individualising and monitoring the effectiveness of rehabilitation measures. Despite the frequent use of biomarkers in medical practice, there is relatively little information on validated paediatric biomarkers. Biomarkers that have been proven effective in the adult population are often automatically extrapolated to paediatric practice without taking into account the specifics of the child's body, in particular differences in the pathogenesis of diseases and the influence of ontogenetic factors on the course of the disease and therapeutic response. This necessitates the introduction of new approaches aimed at identifying reliable and validated biomarkers adapted to the characteristics of the paediatric population in order to improve the effectiveness of diagnosis and treatment in paediatrics [15].

The scientific community is showing growing interest in BDNF as an important diagnostic indicator of neuroplastic processes. BDNF plays an important role in the development and functioning of the nervous system. It also improves synaptic function in both the cerebral cortex and the hippocampus [16]. The basis for the future use of BDNF as a biomarker in the paediatric population was provided by a study by J.D. Chew *et al*. [17], which evaluated brain-derived neurotrophic factor and osteopontin in a healthy paediatric population. This study provided preliminary data on serum BDNF and plasma osteopontin levels in children and analysed their relationship with cardiovascular health and physical fitness indicators in the paediatric population.

In the study, children aged 7-8 months were analysed using boxplots of gestational age, body weight at the time of examination, number of motor skills according to AIMS, and BDNF levels in three groups. The changes identified provided insight into the potential of BDNF as a marker of neuroplastic processes. The study showed a clear trend towards a decrease in serum BDNF levels from the control group to the FIMD group, and further to the PIMD group. This dynamic may indicate a gradual decrease in neuroplastic activity in children with motor development delays. This result showed that low BDNF levels may not only accompany but also be one of the factors influencing the formation of motor skills. This may also be due to the fact that reduced BDNF concentration leads to insufficient support for neurons, disruption of their differentiation, and a decrease in the plastic properties of the brain. Thus, BDNF can act as an objective indicator of the state of neuroplasticity. The results obtained are partially consistent with the data presented in other studies.

In particular, A. Ghassabian *et al*. [18] showed that in premature infants, higher neonatal BDNF levels are associated with a lower likelihood of developmental delays in any area, even after adjusting for the influence of concomitant factors and methods of infertility treatment in the mother. The authors also noted that BDNF levels in newborns may depend on the mother's lifestyle, and a decrease in BDNF may serve as an early marker of abnormal neurodevelopment in preterm infants. The findings of the study regarding the lowest BDNF levels in the PIMD group are consistent with the conclusions of a systematic review and meta-analysis conducted by F.C. Krey *et al*. [19]. The authors compared the levels of a number of neurotrophic factors (BDNF, NGF, NT-3, NT-4, and GDNF) in term and preterm infants and showed that preterm infants have lower levels of BDNF and NT-3 compared to term infants. These changes may be directly related to the fact of premature birth, which probably reflects the limited capacity for neuroplastic response of the nervous system in conditions of immaturity.

The results indicated a decrease in BDNF levels in children with motor development delay, which is consistent with the data of L. Mercado *et al*. [20], a link was established between the concentration of biomarkers in maternal and umbilical cord blood and foetal brain activity indicators obtained using non-invasive foetal magnetoencephalography. The authors found that maternal BDNF levels are directly related to foetal brain activity, highlighting the importance of this neurotrophic factor in early neurodevelopmental processes. Their data confirmed the feasibility of using BDNF as a potential biomarker, including in combination with methods for assessing electrophysiological brain activity, to monitor the development of the nervous system during the intrauterine period. Similarly, the authors' results are consistent with those of H. Dingsdale *et al*. [21], who showed that lower levels of BDNF in umbilical cord blood serum at birth, especially in male children, may be a factor in the increased risk of neurodevelopmental disorders. This confirmed the potential diagnostic value of BDNF as an early biomarker capable of signalling the likelihood of developmental abnormalities even before the onset of clinical symptoms. Similar conclusions were reached by C.H. Su *et al*. [22], who found that children born to mothers with gestational diabetes at 12 months of age showed lower speech development scores, accompanied by reduced serum BDNF levels. The authors suggested a close relationship between BDNF levels and language outcomes, which is consistent with the authors' observations on the role of neurotrophic factors in the formation of cognitive and motor functions in children. This highlighted the need for further longitudinal studies to determine the long-term consequences of reduced BDNF levels in early childhood.

The strong positive correlation found between serum BDNF levels and motor development scores on the AIMS scale is an important contribution to understanding the pathophysiology of motor development delay. This result is consistent with data from other studies, which also indicate a direct link between BDNF and neuroplasticity, synaptogenesis, and motor neuron function. The results

obtained indicated a strong correlation between BDNF levels and motor development scores on the AIMS scale, which has been confirmed in existing clinical studies. A study by J. Hua *et al*. [23] showed that early motor stages, such as crawling and walking, are key markers for identifying coordination disorders. Even a slight delay in their mastery in infancy significantly increases the risk of further motor disorders. At the same time, individual studies emphasise the advisability of adapting care conditions to the neurological vulnerability of the child as early as the neonatal period, which is consistent with the concept of early intervention [24]. In addition, children with such disorders demonstrate abnormal patterns of transition from crawling to walking, which can be noticeable as early as 6-8 months of age. Thus, the data revealed in the study, demonstrating the relationship between BDNF and motor development, are of particular importance in the context of the concept of neuroplasticity.

The brain demonstrates its highest potential for neuroplasticity during the first two postnatal years, creating an optimal "window of opportunity" for the correction of developmental disorders [25]. As noted by B.O. Olusanya *et al*. [1], a misunderstanding of this biological basis often leads to ineffective approaches in the early intervention system. Instead of making the most of this critical period, assistance programmes may be insufficiently intensive or start too late. The results of the study emphasised the importance not only of early detection of motor development delays, but also of the use of effective, evidence-based rehabilitation measures in the first years of life. The use of BDNF as a biomarker can help to objectively assess the potential for neuroplasticity and target therapy to make the most of this "window of opportunity".

A summary of the studies provided and their comparison with the current work confirmed the existence of a consistent association between BDNF levels and motor development indicators in young children. The dynamics of changes in this neurotrophic factor in different clinical groups are consistent with current ideas about neuroplasticity and its impairment in motor development delay. Comparison of the data obtained with previous studies has deepened understanding of the role of BDNF in the formation of motor skills during the most vulnerable period of postnatal development.

CONCLUSIONS

Children with motor development delay tend to have lower gestational age, body weight, and motor skills, which confirms the importance of early somatic and neurological status for further development. Gestational age in children with PIMD was significantly lower compared to CG and FIMD ($p < 0.05$), which emphasised the role of premature birth in the formation of severe motor disorders. In children with FIMD, gestational age was close to full term, indicating the likelihood of other aetiological mechanisms. Body weight indicators differed significantly between all groups: in children with FIMD, they were lower than in the control group, and in PIMD, they were even lower, confirming the relationship between the degree of motor deficit and somatic development. All study groups also had statistically significant differences in motor skills on the AIMS scale. The best indicators were recorded in the control group, while patients with motor disorders, especially in the PIMD group, showed progressive deterioration in motor development. This confirms that the degree of motor deficit directly correlates with the level of motor skills.

Since BDNF is one of the key proteins that support the development, survival, and functioning of neurons, a decrease in its level may reflect disturbances in the mechanisms of neuroplasticity that are necessary for adaptive changes in the nervous system, especially in early childhood, when the brain has a high capacity for restructuring. Median BDNF levels were highest in the control group (22.76 pg/mL) and progressively decreased in groups with motor development disorders (11.25 pg/mL and 8.30 pg/mL). Statistically significant differences in serum BDNF levels were found between all study groups ($p < 0.00001$). Since BDNF levels were lower in premature infants with motor disorders compared to the control group and full-term infants with motor deficits, this may indicate reduced neuroplastic potential in this category of patients, which hinders the normal formation of complex motor patterns and leads to delays in mastering basic motor milestones.

An integrated analysis of gestational age, body weight, motor skill level, and BDNF concentration demonstrated their coordinated influence on the clinical severity of motor deficits, allowing BDNF levels to be considered a promising diagnostic marker of neuroplasticity in young children. In combination with traditional methods of clinical assessment of motor skills, determining BDNF levels can significantly improve the early detection of motor disorders. This paves the way for more effective early intervention, which is critical for optimising long-term functional outcomes in children. An important next step in further research is to conduct longitudinal studies to track BDNF levels in children with motor development delays over a long period of time, compare BDNF with changes in motor development, and track how these indicators change under the influence of early intervention. Further research should also focus on studying the response of BDNF to individual rehabilitation programmes.

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Дослідження нейротрофічного фактору мозку як діагностичного маркера нейропластичності у дітей із затримкою рухового розладу

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Анотація. Актуальність дослідження біомаркерів нейропластичності полягає у зростаючій поширеності рухових порушень у дітей, оскільки своєчасна діагностика і раннє втручання критично важливі для покращення прогнозу. Метою роботи було оцінити діагностичне значення рівня нейротрофічного фактора мозку як потенційного маркера нейропластичності у дітей віком 7-8 місяців із затримкою рухового розвитку шляхом інтегрального аналізу показників гестаційного віку, маси тіла, рівня рухових навичок за шкалою Alberta Infant Motor Scale та концентрацією нейротрофічного фактора мозку. В дослідженні взяло участь 25 здорових дітей віком 7-8 місяців без рухових порушень та 56 дітей того ж віку з затримкою рухового розвитку, серед яких було 28 дітей, які народились доношеними, але мали рухові порушення, та 28 дітей, які народились недоношеними з руховими порушеннями. В дослідженні було виявлено значущий взаємозв'язок між рівнем нейротрофічного фактора мозку у сироватці крові та ступенем порушення моторного розвитку у дітей. Медіанні рівні нейротрофічного фактора мозку були найвищими в контрольній групі (22,76 пг/мл) і прогресивно знижувалися в групах з порушенням моторного розвитку (11,25 пг/мл та 8,30 пг/мл). Між усіма досліджуваними групами було виявлено статистично значущі відмінності у рівнях нейротрофічного фактора мозку у сироватці крові ($p < 0,00001$). Результати вказали, що у дітей із порушенням моторного розвитку рівень нейротрофічного фактора мозку значно нижчий, ніж у здорових однолітків, що може свідчити про знижену нейропластичність у цих групах. Ці результати підкреслили потенціал нейротрофічного фактора мозку як об'єктивного критерію для ранньої діагностики, прогнозування та оцінки ефективності реабілітаційних втручань у дітей із затримкою рухового розвитку

Ключові слова: біомаркер рухових порушень; рання діагностика; доношені немовлята; недоношені немовлята; шкала рухового розвитку немовлят Альберта

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Dental disease prevention in children of different ages in the Zakarpattia region

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Abstract. The study aimed to characterise the dental health status of the child population in Zakarpattia region and identify practical ways to optimise preventive care among children. The study was conducted in January-June 2025 at the Dental Department of the Rakhiv District Hospital, a municipal non-profit enterprise in the Zakarpattia region. The analysis covered 240 children aged 6-15 and involved a clinical and analytical approach combining examination, questionnaires and statistical analysis of the relationships between behavioural and clinical indicators of dental health. The results of the study showed that the average caries intensity index increased from 2.12 in the 6-8 age group to 4.36 in adolescents aged 12-15, accompanied by a deterioration in hygiene status from 1.49 to 2.06. The index was dominated by decayed teeth: 1.50 in younger children, 2.58 in middle-aged children, and 3.02 in older children, reflecting late treatment. Girls had better results (3.22 vs 3.69 in boys) and a higher frequency of regular tooth brushing (77% vs 69%). Territorial analysis revealed a gap: the caries level was 2.84 in urban children and 3.92 in mountain children, with worse hygiene indicators (2.07 vs 1.61). Only 47% of urban children underwent preventive examinations, compared to 32.6% in mountain communities. A negative correlation was found between hygiene behaviour and caries (r = -0.62), confirming the key role of behavioural factors in maintaining health. The obtained results indicated that the dental health of children in Transcarpathia is influenced by age, gender, behavioural habits and territorial conditions, while the effectiveness of prevention remains insufficient due to the uneven participation of schools, families and medical services in the hygiene education system. The practical significance of the study results is determined by the possibility of using the data by local health authorities, school medical services and family doctors to plan regional programmes for caries prevention and hygiene education for children

Keywords: hygiene; health; caries; fluoride toothpaste; tooth brushing; behavioural factors; remote mountain villages

INTRODUCTION

Dental diseases in children are among the most common non-infectious pathologies affecting the overall health, quality of life and harmonious development of a child. According to the World Health Organization [1], approximately 3.5 billion people worldwide have experienced oral diseases during their lifetime, which highlights their

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significance as a global public health problem. Border regions of Ukraine, in particular the Zakarpattia region, are characterised by complex geographical conditions, socio-economic heterogeneity, insufficient coverage by preventive programmes and limited access to specialised care. This combination of factors contributes to late visits to the dentist, irregular oral hygiene control, and low effectiveness of preventive measures, which creates the conditions for the early development of dental lesions. Untreated pathological processes in children lead to chronic pain, chewing and speech disorders, sleep disorders, reduced food adaptation and cognitive activity, and, over time, to the formation of persistent infectious foci and an increased burden on the healthcare system, determining the need for systematic prevention and clinical monitoring of the dental health of the child population.

Global approaches to the prevention of dental diseases in children have demonstrated a transition from a purely therapeutic model to a preventive and educational one, integrated into the public health system. The concept of "Federation Dentaire Internationale Vision 2030", presented by M. Glick & D.M. Williams [2], defined the prevention of dental diseases in children as an element of the basic rights of the child to health and emphasised the need for equal access to primary care and continuous monitoring, which is of particular importance for peripheral regions. At the same time, the authors noted that personnel, financial and organisational barriers hindered the integration of dental health into public policy priorities. A meta-analytic review by P. Akera *et al.* [3] demonstrated that school interventions combining hygiene education, nutrition control and access to preventive measures reduced the incidence of caries even in resource-limited settings. The researchers also found that without the support of the healthcare system, the effect of such programmes was short-lived. A study by T. Bramantoro *et al.* [4] confirmed that the inclusion of a dental component in the educational process from preschool age increased the effectiveness of prevention, while formal models without systematic hygiene control did not provide sustainable results.

Ukrainian studies have shown that the prevention of dental diseases in children in Ukraine remains fragmented and depends mainly on local initiatives. A clinical study by O.V. Sheshukova *et al.* [5] established those interactive educational activities, in particular dental performances for younger schoolchildren, improved hygiene skills and increased adherence to prevention. At the same time, the authors noted that such programmes did not have regulatory status and were not scaled up, which indicated the lack of a sustainable preventive infrastructure. An analysis of dental care provision conducted by V.D. Chopchyk *et al.* [6] revealed a shortage of material and technical resources and demonstrated uneven access to examinations for children, especially in small settlements. It was emphasised that this resource imbalance had transformed into clinical inequality, increasing the proportion of late referrals. V.A. Grokhotov *et al.* [7] showed that the lack of a single standard for preventive monitoring of children's risk groups made it difficult to ensure the proper quality of dental services. The researchers emphasised that without the creation of an integrated model, prevention in border regions, particularly in the Zakarpattia region, remained situational.

Socio-economic and behavioural factors determine the cumulative risk of dental pathology in childhood and necessitate regionally adapted prevention models. A study conducted by M.E. Northridge *et al.* [8] found that limited access to dental care, geographical remoteness and financial barriers caused persistent differences in children's health. The study demonstrated that these inequalities were systemic in nature and reproduced across generations, exacerbating the social vulnerability of the child population. As noted by O.S. Almajed *et al.* [9], the low socioeconomic status of the family directly affected the availability of hygiene products and the quality of children's nutrition. The study emphasised that it was social determinants that determined long-term differences in the prevalence of caries and complications. O.V. Sheshukova *et al.* [10] demonstrated that stressful social conditions, in particular the consequences of armed conflicts, were associated with early caries development and an increase in the frequency of inflammatory processes. The scientists emphasised that social instability is a powerful risk factor for children's dental health. According to the results of a study by O.S. Pavlenkova & L.F. Kaskova [11], organised educational groups were an effective environment for the formation of sustainable hygiene habits in children. The researchers noted that the duration of the effect of such programmes depended on the regularity of pedagogical support and intersectoral interaction between the education and healthcare systems.

Despite numerous international and national studies in the field of preventive dentistry, there is still no comprehensive assessment of age, behavioural and socio-economic factors influencing the dental health of children in the mountainous regions of the Zakarpattia region. The study aimed to assess the dental health of children of different age groups in Transcarpathia and to justify directions for improving preventive measures aimed at reducing the prevalence of dental lesions. To achieve this goal, the following tasks were set: to establish the prevalence of dental diseases among children of different age groups; to analyse the level of hygiene knowledge and behavioural risk factors; to develop recommendations for improving the effectiveness of preventive programmes among the child population in mountainous areas.

MATERIALS AND METHODS

The study was clinical and analytical in nature and was conducted between January and June 2025 at the Dental Department of the Rakhiv District Hospital, a municipal non-profit enterprise in Zakarpattia region. The facility serves both the population of the city of Rakhiv and residents of surrounding remote mountain villages (Yasinya, Bohdan, Kvasy, Bilin, Dilove, etc.), which ensured diversity in the sample in terms of place of residence, living conditions, and access to preventive care. This approach covered the geographical, socio-economic and infrastructural characteristics of the region that potentially affect the dental health of children. The choice of the period January-June was due to the representativeness of visits at this time of year, when there is a stable flow of patients after the winter and spring holidays, as well as no seasonal decline in attendance, which is typical for the summer months. This made it possible to minimise time fluctuations in indicators and ensure the objectivity of the results.

The study involved 240 children aged 6 to 15 who visited a paediatric dentist for preventive or therapeutic treatment. Patients were divided into three age groups: younger (6-8 years), middle (9-11 years), and older (12-15 years). The lower age limit of 6 years was selected as this is the age at which the temporary dentition is replaced by permanent teeth, the first permanent molars are formed, and thus the basis of the child's dental status is established. This is the age at which it is advisable to conduct systematic monitoring of dental health for the early detection of caries in permanent teeth. The upper limit of 15 years corresponds to the completion of the formation of the permanent dentition and the period of stabilisation of hygiene habits, which can be used to assess the cumulative effect of preventive measures and behavioural habits. To ensure the representativeness of the sample, stratification was conducted not only by age but also by gender and geographical characteristics. This approach covered children living in the city of Rakhiv and surrounding settlements, as well as in remote mountain villages, which differ in terms of access to dental care. A summary of the sample characteristics was provided in Table 1.

Table 1. Characteristics of the sample of children included in the study (n = 240)

Age group (years)	Total, n (%)	Boys, n	Girls, n	City / adjacent areas, n	Remote mountain villages, n
6-8 (young)	78 (32.5%)	38	40	29	49
9-11 (middle)	82 (34.2%)	38	44	36	46
12-15 (older)	80 (33.3%)	38	42	37	43
Total	240 (100%)	114	126	102 (42.5%)	138 (57.5%)

Source: compiled by the authors

The sample included children aged 6-15 who had lived permanently in the Rakhiv region for at least three years and had no significant somatic or mental disorders. Children with acute infectious diseases at the time of examination, as well as those with systemic, metabolic or hereditary disorders that could affect the condition of hard tooth tissue, were excluded from the study. The clinical examination was conducted according to the World Health Organization methodology [12], which provides a standardised approach to assessing the dental status of children. To determine the intensity of the carious process, the DMF index (a measure of caries intensity reflecting the sum of decayed, extracted and filled teeth) was used, which was calculated using formula (1):

$$DMF = D + M + F, \quad (1)$$

where D – number of decayed teeth (Decayed), M – number removed due to caries (Missing), F – number of filled teeth (Filled).

The DMF index was used similarly for temporary occlusion. Oral hygiene was assessed using the Oral Hygiene Index-Simplified (OHI-S) in the Green-Vermillion (1964) modification, which reflects the level of cleanliness of tooth surfaces in terms of the presence of soft plaque and tartar. The index was calculated using formula (2):

$$OHI\text{-}S = DI\text{-}S + CI\text{-}S, \quad (2)$$

where *DI-S* (Debris Index Simplified) – indicator of soft plaque quantity, and *CI-S* (Calculus Index Simplified) – indicator of tartar quantity.

The assessment was conducted on six index teeth, determined based on the international dental numbering system: 16 – first upper right molar, 11 – central upper incisor, 26 – first upper left molar, 36 – first lower left molar, 31 – central lower incisor i 46 – first lower right molar (all permanent teeth). If one of the specified teeth was missing, the assessment was performed on its symmetrical antagonist. Each vestibular or lingual surface was assessed on a four-point scale: 0 – clean surface, 1 – plaque or tartar covers no more than one-third of the surface, 2 – one to two-thirds, 3 – more than two-thirds of the surface. After calculating the average values of DI-S and CI-S, the total OHI-S index was obtained, which was interpreted as good (0-1.2), satisfactory (1.3-3.0) or unsatisfactory (over 3.0) oral hygiene.

To analyse the behavioural aspects of dental risk formation, a questionnaire was developed and adapted to the research objectives. The questionnaire contained 15 questions concerning the frequency and duration of tooth brushing, the use of additional hygiene products, eating habits, the level of awareness of prevention, and the regularity of visits to the dentist (Table 2). The survey was conducted during the appointment after the clinical examination; in younger age groups (6-8 years), the answers were recorded by parents or legal representatives, and in middle and older age groups (9-15 years), the children themselves answered under the supervision of the researcher. Of the 240 participants, 228 (95.0%) completed the questionnaire, ensuring a high level of representativeness of the behavioural data.

Table 2. Structure of the questionnaire for assessing behavioural factors of dental risk

No.	Content of the question	Answer options
1.	Teeth cleaning frequency	2 times per day – 1; 1 time – 0.5; rarer – 0
2.	Teeth cleaning duration	> 2 min – 1; 1-2 min – 0.5; < 1 min – 0
3.	Use of additional hygiene products	Yes – 1; No – 0
4.	Frequency of sweets consumption	Rarer – 1; several times per week – 0.5; every day – 0
5.	Mouthwash after eating	Always – 1; sometimes – 0.5; never– 0
6.	Use of fluorinated paste	Yes – 1; no – 0; not aware – 0.5
7.	Frequency of dentist visits	1 time per 6 months – 1; 1 time per year – 0.5; only if pain is present – 0
8.	Caries treatment experience	No – 1; Yes – 0

Table 2. Continued

No.	Content of the question	Answer options
9.	Preventive recommendations	Yes – 1; No – 0
10.	School visits by dentists/information about oral hygiene	Yes – 1; No – 0
11.	Self-assessment of knowledge level	High – 1; average – 0.5; low – 0

Source: compiled by the authors

A scoring system was used to quantitatively assess the responses: preventative favourable responses were scored as 1 point, neutral responses as 0.5 points, and risky responses as 0 points. The total score was interpreted as a high level of preventive behaviour (⩾11 points), satisfactory (6-10 points) or low (<6 points). This system facilitated the objectification of self-assessment of hygiene habits and the comparison of risk profiles between age groups and geographical subgroups (urban and remote villages). To assess the effectiveness of preventive measures, questionnaire results were aggregated according to three structural components: family, school and medical. Questions concerning personal hygiene, use of fluoride toothpaste, frequency of tooth brushing and eating habits characterised the family component. Questions regarding preventive visits, receiving recommendations, and treatment experience reflected the medical component. Schoolchildren's awareness and teachers' participation in educational activities formed the school component. The effectiveness of each area was assessed on an expert scoring scale from 0 to 3 points, where 0 meant no implementation of the measure, 1 – occasional implementation, 2 – partial or irregular implementation, and 3 – systematic and regular implementation. For each component, an average integral score was calculated, which characterised the overall level of participation in preventive activities. The level of effectiveness was stratified as low for values <1.5 points, medium for values between 1.5 and 2.4 points, and high for values – ⩾2.5 points.

The obtained data were subjected to descriptive and variational statistics with the determination of mean values (M) and standard deviations (SD). The analysis was performed using Microsoft Excel 2021 and IBM SPSS Statistics 26.0. The Kolmogorov-Smirnov test was used to check the normality of the distribution. Statistical relationships between behavioural factors and clinical indices were assessed using the χ^2 criterion, Student's t-test (for parametric data) and Mann-Whitney U test (for non-parametric data). Correlations were determined using Pearson's coefficient (r). The level of statistical significance was set at $p < 0.05$.

The study was conducted in accordance with the principles of the Declaration of Helsinki [13] on ethical standards for medical research involving human subjects and the American Sociological Association [14] code of ethics, which regulates the rules of voluntary participation, confidentiality, and processing of personal data during surveys. The participation of children and their legal representatives was voluntary. All parents signed a written informed consent form for the examination and use of aggregated data for scientific purposes. A limitation of the study was that it covered only one district of the Zakarpattia region, which limits the possibility of generalising the results for the entire population of children in the region.

RESULTS

Age, gender and geographical characteristics of children's dental status. The results of the clinical examination of children in the Zakarpattia region showed significant age, gender and territorial differences in dental status, reflecting both biological patterns of development and socio-economic characteristics of the region. To assess these differences, a comparative analysis of indicators by age, gender and geographical groups was conducted, the results of which are presented in Table 3.

Table 3. Age, gender and geographical characteristics of children's dental status (n = 240)

Children group	n	DMF (M ± SD)	OHI-S (M ± SD)	Component D	Component F	Component M
6-8 years, boys	38	2.24 ± 0.25	1.55 ± 0.10	1.62 ± 0.18	0.41 ± 0.07	0.21 ± 0.04
6-8 years, girls	40	2.00 ± 0.23	1.43 ± 0.09	1.38 ± 0.17	0.47 ± 0.06	0.15 ± 0.03
Young group total	78	2.12 ± 0.24	1.49 ± 0.09	1.50 ± 0.17	0.44 ± 0.06	0.18 ± 0.03
9-11 years, boys	38	3.72 ± 0.27	1.91 ± 0.12	2.74 ± 0.20	0.61 ± 0.08	0.37 ± 0.05
9-11 years, girls	44	3.46 ± 0.25	1.78 ± 0.11	2.42 ± 0.18	0.78 ± 0.09	0.26 ± 0.04
Middle group total	82	3.58 ± 0.26	1.84 ± 0.11	2.58 ± 0.19	0.70 ± 0.08	0.31 ± 0.04
12-15 years, boys	38	4.55 ± 0.30	2.16 ± 0.14	3.20 ± 0.22	0.88 ± 0.10	0.47 ± 0.06
12-15 years, girls	42	4.18 ± 0.28	1.97 ± 0.13	2.83 ± 0.21	1.01 ± 0.11	0.34 ± 0.05
Older group total	80	4.36 ± 0.29	2.06 ± 0.13	3.02 ± 0.22	0.95 ± 0.10	0.40 ± 0.05
City and adjacent areas	102	2.84 ± 0.22	1.61 ± 0.10	1.92 ± 0.16	0.69 ± 0.08	0.23 ± 0.04
Remote mountain villages	138	3.92 ± 0.29	2.07 ± 0.14	2.63 ± 0.21	0.72 ± 0.09	0.57 ± 0.07

Note: DMF – caries intensity index, which reflects the sum of decayed (D), filled (F) and missing (M) teeth in permanent or temporary dentition; OHI-S – simplified oral hygiene index according to Green-Vermillion, which assesses the degree of contamination of tooth surfaces; M – mean value; SD – standard deviation

Source: compiled by the authors

Caries intensity indicators showed a gradual increase with age, from 2.12 ± 0.24 in the younger group (6-8 years) to 4.36 ± 0.29 in the older group (12-15 years). This increase reflects the cumulative effect of lesions associated with prolonged exposure to cariogenic factors, the main ones being irregular hygiene, excessive sugar consumption and lack of preventive check-ups. At the same time, component F (filled teeth) increased slightly with age, indicating some

improvement in access to treatment for adolescents, but component D (decayed teeth) remained dominant in the index structure at 1.50 in the younger group, 2.58 in the middle group, and 3.02 in the older group. This indicates that most children sought dental care only at the stage of already formed caries, without the prevention stage. At the same time, there was a deterioration in hygiene (OHI-S: 1.49 → 2.06), which can be attributed to a decrease in parental control and an increase in children's independence in oral care.

Girls in all age groups demonstrated better dental health. Their average caries intensity was lower (3.22 ± 0.25) compared to boys, which may indicate a greater willingness to visit the dentist even for minor symptoms. Social expectations, parenting models, and parents' awareness of the aesthetic aspects of oral health may also have contributed to girls' preference for prevention. Thus, female gender in this age group acts as a conditional protective factor against severe lesions, confirming the role of a combination of behavioural and sociocultural aspects in the formation of dental risk.

The most noticeable differences were found between urban children and those living in remote mountain villages. The DMF index among mountain residents was 3.92 ± 0.29 compared to 2.84 ± 0.22 among urban children ($p < 0.01$), and the OHI-S index was 2.07 ± 0.14 compared to 1.61 ± 0.10, respectively. This difference indicates a clear territorial gradient in dental health. The main reasons are limited transport accessibility to dental clinics, a shortage of paediatric dentists, a low level of preventive measures in schools, and reduced availability of hygiene products. In many mountain villages, preventive examinations are performed sporadically, and children only visit the dentist in case of pain. As a result, the proportion of component D and the number of extracted teeth increase (M = 0.57 ± 0.07 compared to 0.23 ± 0.04 in urban areas). This indicates late referral for dental care, low effectiveness of preventive measures, and the prevalence of a symptomatic treatment model among the child population in mountainous areas.

Thus, the data obtained showed that the dental health of children in the Zakarpattia region is influenced by a combination of factors, including age, gender, behaviour, and geography. The most vulnerable group was middle and high school boys from remote mountainous areas, who combine poor hygiene habits with limited access to medical care. The results highlighted the need to develop tailored prevention programmes for mountainous regions, involving schools, local health workers and parents, as well as ensuring regular monitoring of the dental health of the child population.

Hygienic behaviour and preventive habits of children of different ages and genders. The results of the survey revealed the level of hygienic behaviour among children of different ages, genders and places of residence, as well as differences in preventive habits. Considering both individual (age and gender) and territorial factors was used for a comprehensive analysis of the social aspects of dental culture formation among the child population of the Zakarpattia region. The summarised data are presented in Table 4, which reflects the frequency of basic preventive actions, the level of use of fluoridated toothpastes, additional hygiene products and the regularity of preventive visits to the dentist.

Table 4. Hygiene behaviour and preventive habits of children of different ages, genders and places of residence (n = 228)

Age group (years)	n	Regular brushing of teeth twice a day, %	Use of fluorinated paste, %	Additional hygiene products (mouthwash, dental floss), %	Regular preventive visits to the dentist (≥1 time/year), %	Average score for preventive behaviour (0-10), M ± SD
6-8 years, boys	36	57.0	50.0	16.7	25.0	8.7 ± 2.6
6-8 years, girls	38	63.0	58.0	23.0	31.0	9.3 ± 2.3
Young group total	74	60.0	54.1	19.7	28.0	9.0 ± 2.4
9-11 years, boys	36	70.0	65.0	27.0	32.0	9.8 ± 2.4
9-11 years, girls	42	78.0	72.0	40.0	40.0	10.5 ± 2.1
Middle group total	78	74.0	68.3	34.1	36.0	10.2 ± 2.3
12-15 years, boys	36	80.0	73.0	39.0	43.0	10.7 ± 2.3
12-15 years, girls	40	90.0	84.0	56.0	54.0	12.0 ± 2.1
Older group total	76	85.0	78.3	47.0	48.0	11.4 ± 2.1
City/adjacent areas	97	76.5	76.5	39.8	47.1	11.1 ± 2.3
Remote mountain villages	131	63.0	63.0	27.3	32.6	9.8 ± 2.7

Note: M – mean value; SD – standard deviation
Source: compiled by the authors

The results demonstrated an age-related trend in the development of preventive behaviour. The proportion of children who regularly brushed their teeth twice a day gradually increased from 60.0% in the 6-8 age group to 85.0% among children aged 12-15. A similar trend was demonstrated in the use of fluoride toothpaste, from 54.1% to 78.3%. This indicates that as children get older, they become more responsible in matters of personal hygiene and become more conscious. This is possibly related to the development of self-control, increased cognitive activity and expansion of the information field, which provides access to knowledge about hygiene.

Gender analysis revealed consistent differences between boys and girls. In all age groups, girls demonstrated higher rates of regular hygiene practices and were more likely to use fluoride toothpaste and additional hygiene products. On average, 77% of girls brushed their teeth twice a day, compared to 69% of boys. Girls also used mouthwash or dental floss more often (40% vs 27%), indicating a more developed hygiene culture. These differences are due not

only to individual behavioural characteristics, but also to socio-cultural and educational factors, in particular, parenting models, the level of parental awareness, and school approaches to the formation of aesthetic norms. In many families, girls are more encouraged to be neat and aesthetically well-groomed, which reinforces their commitment to hygienic practices. At the same time, boys showed greater variability in behavioural habits: among them, there were more cases of irregular tooth brushing, skipping evening care and insufficient use of fluoride toothpaste. This trend can be explained not only by personal characteristics of hygiene control, but also by less focus on aesthetic norms of behaviour, lower levels of pedagogical reinforcement of hygiene habits in the family and at school, as well as weaker involvement of boys in educational programmes on healthy lifestyles.

In terms of age groups, there was a gradual increase in the average score for preventive behaviour: from 9.0 ± 2.4 in the younger group to 11.4 ± 2.1 in the older group. This indicates an increase in hygiene literacy and responsibility. Younger schoolchildren mostly performed hygiene procedures under the supervision of their parents and often skipped evening tooth brushing. Children of middle school age (9-11 years) have already demonstrated a certain stability of skills, but only 36% of them visited the dentist for preventive care at least once a year. The highest rates were recorded among older children: 48% underwent regular preventive examinations, and almost half used additional hygiene products.

Significant territorial differences revealed the systemic influence of the socio-economic environment on the formation of a preventive culture. In urban areas or settlements close to them, children demonstrated significantly better results in all criteria. The proportion of children who brushed their teeth regularly twice a day was 76.5% among urban schoolchildren and only 63.0% among residents of mountainous areas. The difference in the use of fluoride toothpaste was more than 13%, and in the use of additional hygiene products, more than 12%. The average score for preventive behaviour was significantly higher among children in urban areas (11.1 ± 2.3) compared to those living in remote communities (9.8 ± 2.7). These differences indicate that place of residence is one of the key predictors of hygiene behaviour. Lower scores among children from mountain villages can be explained by several factors: difficult access to dental clinics, lower income levels of families, limited availability of hygiene products, and less awareness of the significance of prevention.

The level of school involvement in developing preventive skills are also substantial: in mountainous areas, such activities are sporadic, while in urban schools, informational lectures, meetings with dentists, or thematic classes on oral hygiene are held more frequently. Preventive visits to the dentist remained an uncommon practice among all groups, but there were significant differences between geographical clusters. Almost half of urban children (47.1%) underwent a preventive examination at least once a year, while among residents of mountain communities, this figure did not exceed 32.6%. In the younger age group, such visits were mostly initiated by parents, while in the older age group, the motivation of the child prevailed. However, even among adolescents, visits to the dentist were not systematic, which indicates an insufficient culture of preventive care.

The obtained data indicate that the hygienic behaviour of children in the Zakarpattia region is formed unevenly under the influence of age, gender, and socio-geographical factors. The differences identified between the groups not only reflect varying levels of access to dental services but also demonstrate the influence of the social environment on the development of a culture of prevention. The most vulnerable remain younger schoolchildren, especially boys from mountainous areas, who have low levels of hygiene skills combined with limited access to dental care. This risk structure requires targeted intervention at the level of local educational and medical programmes, with an emphasis on early hygiene education, raising parental awareness and creating conditions for regular preventive screening in groups of children.

The relationship between clinical indicators and behavioural risk factors. To assess the relationship between the clinical condition of the oral cavity and the hygienic behaviour of children, a correlation analysis was performed, which determined the strength and direction of statistical relationships between the main indices of dental status (DMF, OHI-S) and the level of preventive activity, assessed by questionnaire scores. Figure 1 shows the dynamics of correlation coefficients in three age groups, which demonstrated a gradual strengthening of the inverse relationship between behavioural and clinical indicators with increasing age of children.

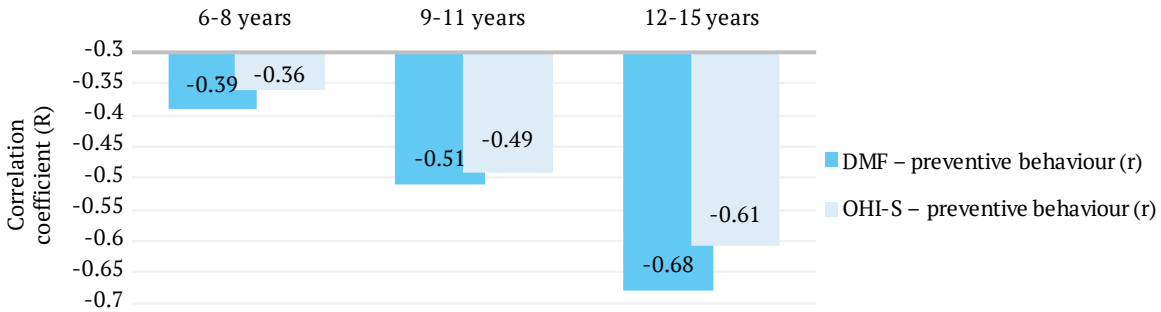

Figure 1. Correlations between clinical indicators (DMF, OHI-S) and preventive behaviour in children of different ages
Note: r – correlation coefficient, reflecting the strength and direction of the statistical relationship between clinical indicators and the level of preventive behaviour
Source: compiled by the authors

The results demonstrated that in the younger age group (6-8 years), the relationship between preventive behaviour and clinical indices was weak (r = -0.39 for DMF; r=-0.36 for OHI-S). This is attributed to the fact that the hygiene skills of children of this age are still developing, and the performance of daily procedures is largely controlled by parents. At this age, the clinical condition of the oral cavity is determined mainly by family factors such as care, eating habits and the level of awareness of adults, rather than the child's own behaviour. In the middle age group (9-11 years), the strength of correlations increased to r = -0.51 (DMF) and r = -0.49 (OHI-S), indicating the formation of stable hygiene habits and the beginning of a conscious attitude towards one's own dental health. Children of this age are already more likely to perform hygiene procedures on their own, and the regularity of brushing their teeth and using fluoride toothpaste is directly reflected in a decrease in the level of caries intensity and contamination of tooth surfaces. The most pronounced correlations were observed among adolescents (12-15 years old), where the coefficients reached r = -0.68 for DMF and r = -0.61 for OHI-S ($p < 0.01$). This indicates that in older school age, preventive behaviour becomes the leading factor that directly determines the clinical condition of teeth and gums. Teenagers who regularly performed hygiene procedures had significantly lower rates of tooth decay and better oral hygiene. The strengthening of the connection with age reflects the transition from external control to internal motivation, i.e., hygienic behaviour transforms from a habit supported by adults to a conscious element of the individual lifestyle. The generalised indicator for the entire sample confirmed the existence of a stable inverse relationship between clinical indices and the level of preventive activity: r = -0.62 for DMF and r = -0.58 for OHI-S ($p < 0.01$). Therefore, as the questionnaire score for preventive behaviour increases, the intensity of caries decreases and oral hygiene improves.

Interpretation of these results showed a clear trend: at a younger age, the clinical condition of teeth is determined mainly by environmental and social factors, while in adolescence, individual behaviour is primary. This pattern confirms the significance of early formation of hygienic habits and systematic preventive education of primary school children, which provides the basis for stable dental health in adolescence. Thus, the analysis showed that behavioural risk factors are closely related to clinical indicators of dental status. The strengthening of this relationship with age indicates the growing role of personal responsibility in maintaining oral hygiene. This highlights the need to move from occasional educational activities to systematic programmes for the formation of a culture of hygiene among children and adolescents in the region.

Assessment of the effectiveness of existing preventive measures and directions for their improvement. The effectiveness of existing prevention programmes was assessed based on the results of a questionnaire, which made it possible to determine the extent to which various social institutions (the family, school and medical institutions) are involved in shaping children's hygiene habits. To systematise the data, a comparative analysis of the level of implementation of the main areas of prevention within these three components was conducted (Table 5).

Table 5. Cross-sectional assessment of the effectiveness of preventive measures among children in Zakarpattia region (rated on a scale of 0-3)

Prevention	Family	School	Medical personnel
Hygiene education	1.5	1.5	2
Screenings	1	0.5	2.5
Hygiene skills control	1.2	1	2
Information basis	1.8	1.5	1.8
Access to hygiene products	1.3	1	1.5

Source: compiled by the authors

As shown in Table 5, the highest level of effectiveness of preventive measures was recorded in the medical sector, particularly in the areas of preventive examinations (2.5 points) and hygiene education (2.0 points). This demonstrated the central role of medical professionals in maintaining children's dental health, as they have the professional knowledge and diagnostic tools and can provide practical demonstrations of proper oral care. However, such activities are mainly concentrated in urban polyclinics, while in mountainous areas the participation of medical personnel is sporadic due to staff shortages, the remoteness of settlements and a lack of resources. As a result, the prevention efforts of medical institutions are not systematic and are often limited to treatment episodes when children already have clinical signs of caries.

The family link demonstrated an average level of effectiveness (1.3-1.8 points) with a predominance of information support (1.8 points) and hygiene education (1.5 points). Parents remain the primary agents of prevention, as they are the ones who shape their children's daily hygiene habits and monitor their implementation. However, the effectiveness of this influence varies significantly depending on the family's education, income and access to dental information. Rural and mountainous areas are characterised by less awareness of the role of fluoride, the correct duration of tooth brushing and the need for preventive visits, which is often combined with an underestimation of the problem of caries in deciduous teeth. At the same time, in families with higher socioeconomic status, parents are more probable to provide their children with quality hygiene products, which is reflected in lower caries intensity rates. Thus, the family is potentially a significant resource for prevention, but its effectiveness is limited by unequal access to information and material resources.

According to the assessment results, the school level proved to be the weakest (average effectiveness level of 0.5-1.5 points). The indicators are particularly low in the areas of preventive examinations (0.5 points) and hygiene

skills monitoring (1.0 points), which indicates a lack of systematic cooperation between educational institutions and medical services. In most schools, preventive activities are limited to one-off thematic lectures or "Health Days", without practical skills training and regular feedback. This creates a gap between the informational and behavioural levels of students' knowledge: they are aware of the benefits of dental care, but do not always follow the recommendations in practice. Another problem is the lack of an integrated monitoring system: schools do not keep records of preventive measures, do not record children's participation in hygiene programmes, and do not have a mechanism for interacting with local clinics. In most cases, the initiative depends on the enthusiasm of individual teachers or school medical workers, which reduces the consistency of such actions.

To systematise prevention in the educational environment, it is advisable to create a regulatory and organisational framework. It is recommended to develop a single set of regulations, the School Dental Prevention Programme, which will define the minimum scope of preventive measures, their frequency and the persons responsible for them. The programme should be integrated into the curricula for the subjects "Fundamentals of Health" and "Human Biology", and methodological support should be provided to teachers through participation in training courses organised jointly with medical specialists. It would be effective to create interdisciplinary teams consisting of a school doctor or nurse, a class teacher and a representative of the local dental service. This could provide not only regular lectures but also monitoring of hygiene and motivational talks with children and parents. It is also advisable to introduce a unified electronic database of school preventive measures, which can be used to monitor the implementation of programmes, evaluate their effectiveness and ensure feedback between schools and medical institutions.

The overall assessment of the three prevention components showed an average score of 1.5 points, which corresponds to a partially systemic level of functioning. The most critical area remains access to hygiene products, where all three components showed the lowest scores (1.3-1.5 points). This reflects a lack of social support programmes that would provide children in remote areas with free oral care kits. In addition, there is a lack of public information campaigns aimed at changing attitudes towards prevention as a daily necessity rather than a formal requirement. The results showed that the prevention system lacks a unified coordination framework. Families, schools and medical institutions operate separately, without a unified mechanism for information exchange and without clear algorithms for joint action. This disconnect reduces the effectiveness of even the best initiatives and leads to a loss of results at the stage of interagency interaction. To remedy the situation, it is advisable to create a unified regional strategy for dental prevention in children, which will include joint monitoring, standardised hygiene education programmes, a calendar of preventive examinations and an electronic record-keeping system.

Improvements can be achieved through cross-sectoral integration. Schools should become centres for regular hygiene monitoring, where teachers record children's participation in preventive programmes and coordinate cooperation with doctors. Medical staff should provide training for teachers and parents in basic oral health care skills, conduct outreach lectures and preventive examinations. Families should reinforce these skills through daily practice and positive reinforcement. A promising direction could be the creation of a regional digital platform called "Healthy Smile Zakarpattia", which would combine interactive educational modules, a system of reminders about preventive examinations, and the possibility of remote consultations with a dentist. For mountainous areas, it would be advisable to introduce mobile dental teams consisting of a doctor, hygienist and nurse, who would conduct examinations and lectures in schools twice a year, provide children with toothbrushing kits and demonstrate proper hygiene techniques. At the same time, mobile hygiene education programmes should be introduced to spread knowledge among parents even without the physical presence of specialists. Such steps will contribute to the formation of a unified preventive environment and reduce geographical disparities. Thus, a comprehensive assessment has shown that improving the effectiveness of dental prevention is only possible if a coordinated three-component system of "medicine-school-family" is created. Implementation of this system will help to establish a sustainable culture of hygiene, reduce the prevalence of caries among children, and lay the foundation for maintaining the dental health of the population of the Zakarpattia region in the long term.

DISCUSSION

The results of the clinical and questionnaire survey were used to comprehensively assess the dental health of children in the Zakarpattia region and determine the impact of behavioural, social and geographical factors. The analysis showed that the prevalence of caries and the level of oral hygiene have clear age, gender and territorial differences. Older children demonstrated improved preventive behaviour and lower caries intensity, while younger age groups showed higher dental risk. Gender differences were evident in the more consistent hygiene behaviour of girls, which is consistent with known psychological characteristics of self-organisation in the field of health.

The data obtained demonstrated distinct age and gender differences in the dental status of children. The DMF index increased from 2.12 ± 0.24 in the 6-8 age group to 4.36 ± 0.29 in adolescents aged 12-15, accompanied by a deterioration in hygiene status (from 1.49 to 2.06). A similar pattern was found by H. Das *et al.* [15], who proved that the increase in DMF among schoolchildren decreased by an average of 28% only under conditions of systematic school education, while with episodic programmes, the indicator remained consistently high. These data confirmed that the gradual increase in caries intensity observed in Transcarpathia was associated with insufficient consistency of preventive measures. R. Abbasova *et al.* [16] noted that the introduction of basic preventive methods (hygiene, fluoride prophylaxis) in early childhood reduced DMF by 25-30%, which is consistent with the trend towards higher values in older children in the study. T. Vaičiūnas *et al.* [17] showed that the average DMF level in post-Soviet countries was 3.8-4.0, which is close to the data obtained (3.92 in mountainous areas) and indicated the influence of similar socio-economic conditions. The study emphasised that it is

the lack of preventive infrastructure that is the key factor in regional differences, which was confirmed by the results of the study in Zakarpattia. Contrary to the conclusions of M. Glick *et al.* [18], which reported a downward trend in caries among children in highly developed countries thanks to nationwide strategies, the results obtained showed consistently high DMF and OHI-S scores in the mountainous regions of Ukraine. This indicated that without the integration of preventive programmes into the primary education and family medicine systems, it is impossible to overcome age-related accumulation of lesions.

Gender analysis revealed a stable advantage for girls in all clinical indicators: the average DMF was 3.22 ± 0.25 compared to 3.69 ± 0.28 in boys, and OHI-S 1.63 ± 0.10 versus 1.96 ± 0.12. This pattern is consistent with the data of F. Mlenga & E.G. Mumghamba [19], concluding that in Malawi, the frequency of regular tooth brushing among girls was 15-20% higher, and the DMF index was 0.5-0.7 points lower, which was explained by a greater adherence to preventive habits. Similar results were presented in a study by K.Y. Chandregowda *et al.* [20], where among children aged 6-10 years, the rate of twice-daily tooth brushing among girls reached 81.4%, while among boys it was only 64.9%. The difference directly correlated with lower caries intensity among girls. In contrast, A. Hemandez-Vasquez *et al.* [21] found no significant gender differences among children under 12 years of age in Peru, emphasising that in the absence of educational or social gaps, the influence of gender becomes insignificant. A study by K. Boustedt *et al.* [22] showed that systematic school hygiene education and individual preventive consultations can eliminate gender differences in the prevalence of early caries, reducing the incidence of lesions by 30%. The gender differences identified in the Transcarpathian region confirmed the universal mechanism of hygiene discipline formation: more consistent preventive measures among girls are accompanied by lower DMF and OHI-S scores, while boys remain a group at increased behavioural risk, especially in rural and mountainous areas.

Territorial analysis demonstrated a significant gap between urban children (DMF = 2.84 ± 0.22; OHI-S = 1.61 ± 0.10) and residents of mountain villages (DMF = 3.92 ± 0.29; OHI-S = 2.07 ± 0.14), indicating a pronounced socio-geographical gradient in dental health. A similar pattern was observed by R. Sava-Rosianu *et al.* [23], determining that the average DMF score among rural schoolchildren in Romania was 0.9 higher than among urban schoolchildren, which directly correlated with family income and access to preventive examinations. The results confirmed that in the mountainous regions of Transcarpathia, there is a similar relationship between social status and hygiene indicators, in particular, OHI-S above 2.0. A study by G. Tortora *et al.* [24] showed that children from peripheral communities in Italy had 35% worse hygiene indicators compared to their urban peers. The authors highlighted the lack of dental programmes in small settlements, which correlates with Ukrainian data. E. Štefanová *et al.* [25] found that in Slovakia, less than 40% of children underwent annual preventive examinations, which was accompanied by an increase in the average DMF to 4.1, which corresponds to the results for mountain schools in Transcarpathia (DMF = 3.92). A.R. Mareddy *et al.* [26] proved that even in socially vulnerable groups, regular use of electric or manual toothbrushes reduces DMF by 20-25%, which emphasised the importance of accessibility to hygiene products in mountainous areas. The territorial imbalance in dental status established in Transcarpathia reflects not only medical but also socio-economic determinants of health, which require targeted preventive interventions in remote communities.

Correlation analysis demonstrated a gradual strengthening of the inverse relationship between preventive behaviour and clinical indices with increasing age of children ($r = -0.39 \rightarrow -0.68$ for DMF; $r = -0.36 \rightarrow -0.61$ for OHI-S), reflecting a transition from external control to conscious self-regulation. According to L.F. Moghaddam *et al.* [27], behavioural factors determined about 60% of the variability in dental status, and among adolescents with high preventive scores, the DMF index was 1.5 units lower, confirming a similar trend in the Transcarpathian sample. As shown by I. Ciumeico *et al.* [28], the level of parental education directly correlated with the formation of children's hygiene habits: in families with higher education, the frequency of regular tooth brushing exceeded 80%, while in illiterate families it was only 52%. The study noted that short educational interventions for parents helped reduce the average DMF by 25%, confirming the significant impact of family educational resources on children's dental health. According to the results of A. Buckeridge *et al.* [29], parental choice of high-quality fluoride toothpastes was associated with lower DMF and OHI-S scores in children, and the difference between groups with different levels of education reached 1.2 units for DMF, confirming the importance of family awareness. According to the conclusions of Â.D. Nora *et al.* [30], sociodemographic determinants, in particular income level and place of residence, accounted for up to 40% of the difference in dental status between urban and rural children. The study demonstrated that low parental education levels in rural communities were a key predictor of high DMF scores, consistent with trends observed among children in the mountainous regions of Zakarpattia. A study by M. Recalde *et al.* [31] showed that short-term school prevention programmes reduced DMF by 15-20% by increasing children's knowledge and motivation, confirming the effectiveness of systematic learning in forming sustainable hygiene habits. This is also consistent with the data from M. Levkiv *et al*. [32], which emphasises the importance of educational strategies in shaping adolescents' oral hygiene behaviour. The results showed that the behavioural component is the leading factor in maintaining dental health in adolescence.

The assessment of the effectiveness of preventive measures showed an average integral level of 1.5 points, with the highest scores in the medical sector (2.5 points) and the lowest in schools (0.5-1.0 points). A study by J. Szöke & P.E. Petersen [33] demonstrated that in Central European countries where school prevention programmes operated without medical support, the average DMF level remained at 4.0, while under conditions of integration it decreased by half. L.F. Kaskova *et al.* [34] found that in European countries with unified state prevention programmes, the average DMF among 12-year-old children was 2.1, while in countries without coordinated prevention, it exceeded 4.0. The study also noted that the introduction of national monitoring systems made it possible to reduce

the proportion of untreated caries by almost 40%, which is fully consistent with the need to unify approaches within the regional system of Transcarpathia. N. Cenzato *et al.* [35] showed that territorial disparities in dental prevention directly reflect structural inequalities in the health care system, and that in rural areas, the effectiveness of hygiene programmes was 35% lower. The researchers also emphasised that in areas with low funding, the lack of dental education in schools led to an increase in the incidence of caries among children, confirming the relevance of similar trends in the mountainous areas of Transcarpathia. V. Bolchis *et al.* [36] demonstrated that the implementation of regionally adapted preventive programmes in Romania contributed to a 22% reduction in the average DMF among children aged 11-14. The study proved that the efficiency of these programmes increased when local communities, schools, and primary healthcare providers got involved, which shows that a comprehensive approach is needed for mountainous regions in Ukraine.

Summarising the results, the study determined that the dental health of children in the Zakarpattia region is determined by a combination of age, behavioural and territorial factors. With increasing age, there was an increase in the intensity of caries and a deterioration in hygiene, while a high level of preventive behaviour was accompanied by better clinical indicators. Girls and urban children showed more favourable results, confirming the influence of the social environment and established hygiene habits. The patterns identified are consistent with the results of other scientific studies, which also demonstrated the key role of preventive activities, educational programmes and cross-sectoral interaction in maintaining children's dental health.

CONCLUSIONS

A study of age, gender and regional characteristics of children's dental status showed a clear trend towards an increase in caries intensity with age: the average DMF index increased from 2.12 ± 0.24 in the 6-8 age group to 4.36 ± 0.29 among adolescents aged 12-15, accompanied by a deterioration in hygiene (OHI-S = 1.49 → 2.06). The dominance of component D in the index structure indicated late referral for dental care, while the proportion of filled teeth increased only in older children. The gender differences found (DMF = 3.22 ± 0.25 in girls versus 3.69 ± 0.28 in boys) indicated more developed hygiene discipline among girls. The territorial gap between urban children (DMF = 2.84 ± 0.22; OHI-S = 1.61 ± 0.10) and residents of mountain villages (DMF = 3.92 ± 0.29; OHI-S = 2.07 ± 0.14) confirmed the influence of socio-economic and infrastructural factors on dental health.

The results of the study of hygienic behaviour showed a pronounced age-related dynamic in the formation of preventive habits: regular brushing of teeth twice a day increased from 60% in children aged 6-8 to 85% in the 12-15 age group, the use of fluoride toothpaste from 54.1% to 78.3%, and the average score for preventive behaviour increased from 9.0 ± 2.4 to 11.4 ± 2.1. Girls demonstrated consistently higher hygiene activity (77% vs 69% among boys), indicating gender differences in behavioural patterns. Territorial differences (76.5% of urban children brushed regularly, compared to 63.0% of rural children) indicated limited access to hygiene products and information support in remote communities. The data confirmed that hygiene behaviour is influenced by age, gender and social environment.

Correlation analysis showed a statistically significant inverse relationship between preventive behaviour and clinical indicators: the correlation strength for DMF increased from r = -0.39 in the younger group to r = -0.68 in the older group, and for OHI-S from r = -0. 36 to r = -0.61 ($p < 0.01$). This indicated that as the level of hygienic activity increased, the intensity of caries decreased, and the condition of the oral cavity improved. The strengthening of the relationship with age demonstrated a transition from external parental control to conscious personal responsibility, which determines the need for early formation of sustainable preventive habits.

An assessment of the effectiveness of existing preventive measures revealed an average implementation level of 1.5 points on a three-point scale, with the highest scores in the medical sector (up to 2.5 points) and the lowest in schools (0.5-1.0 points). The family link provided partial information support (1.8 points) but did not have sufficient consistency in monitoring hygiene skills. The weakest component was the school, where preventive measures were sporadic. These results indicated the fragmentation of the preventive system and the need for a unified regional model of "medicine-school-family" that integrates educational, clinical and social components. For further research, it is advisable to expand the geography of the sample to include several areas with different levels of urbanisation and to evaluate the long-term effectiveness of integrated preventive programmes using digital monitoring tools.

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Профілактика стоматологічних захворювань у дітей різного віку на території Закарпатської області

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Анотація. Метою дослідження було охарактеризувати стан стоматологічного здоров'я дитячого населення Закарпатської області та визначити практичні шляхи оптимізації профілактичної роботи серед дітей. Дослідження проводилось у січні-червні 2025 року на базі Стоматологічного відділення Комунального некомерційного підприємства «Рахівська районна лікарня» Закарпатської області, охоплювало 240 дітей віком 6-15 років і передбачало клініко-аналітичний підхід із поєднанням обстеження, анкетування та статистичного аналізу взаємозв'язків між поведінковими та клінічними показниками стоматологічного здоров'я. Результати дослідження засвідчили, що середній показник карієс-інтенсивності зростав із 2,12 у віковій групі 6-8 років до 4,36 у підлітків 12-15 років, що супроводжувалося погіршенням гігієнічного стану від 1,49 до 2,06. У структурі індексу переважали зруйновані зуби – 1,50 у молодших, 2,58 у середніх і 3,02 у старших дітей, що відображає пізнє звернення за допомогою. Дівчата мали кращі результати (3,22 проти 3,69 у хлопців) і вищу частоту регулярного чищення зубів (77 % проти 69 %). Територіальний аналіз показав розрив: у міських дітей рівень карієсу становив 2,84, у гірських – 3,92, із гіршими показниками гігієни (2,07 проти 1,61). Лише 47 % міських дітей проходили профілактичні огляди, у гірських громадах – 32,6 %. Виявлено зворотний зв'язок між гігієнічною поведінкою та карієсом (r=-0,62), що підтвердив ключову роль поведінкових чинників у збереженні здоров'я. Отримані результати свідчать, що стоматологічне здоров'я дітей Закарпаття формується під впливом віку, статі, поведінкових звичок і територіальних умов, а ефективність профілактики залишається недостатньою через нерівномірність участі школи, сім'ї та медичної ланки у системі гігієнічного навчання. Практичне значення полягає у можливості використання даних місцевими органами охорони здоров'я, шкільними медичними службами та сімейними лікарями для планування регіональних програм профілактики карієсу та гігієнічного навчання дітей

Ключові слова: гігієна; здоров'я; карієс; фторована паста; чищення зубів; поведінкові чинники; віддалені гірські села

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Microbiocenosis in patients with acute tonsillitis influenced by smoking

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Abstract. Acute tonsillitis is a widespread disease, the course of which can be affected by the patient's smoking status, which leads to changes in the oropharyngeal microbiota. The purpose of the study was to evaluate the effect of smoking on the development of palatine tonsil microbiocenosis in patients with acute tonsillitis. The study included 54 patients who were divided into two groups: smokers (n = 26) and non-smokers (n = 28). The microbiological study included inoculating samples on various nutrient media, followed by identification of microorganisms by phenotypic methods. Microbiota density was estimated by counting colony-forming units. The Mann-Whitney U-test, Fisher's exact test, and principal component analysis were used for statistical analysis. Principal component analysis did not reveal a clear clustering of the samples, which indicated that there were no global changes in the tonsil microbiota depending on smoking status. However, selective shifts were found, and these included a significantly reduced colonisation density of *Corynebacterium* spp. ($p = 0.04$) and the exclusive presence of fungi of the genus *Candida* among smokers. Clinically, the groups did not differ in the severity of the disease on the Centor scale, but smokers were more likely to receive antibiotic therapy (30.8% and 10.7%) and had a higher incidence of respiratory infections (42.3% and 27.3%). The results showed that smoking does not change the overall structure of the tonsil microbiota in acute tonsillitis, but causes selective dysbiosis. This substantiated the need to consider the patient's smoking status to assess the risk of recurrent infection and develop more personalised approaches to prescribing antibiotic therapy

Keywords: bacteria; bacteriological analysis; diagnostic tests; viruses; microbiota; oropharynx

INTRODUCTION

Acute tonsillitis remains one of the most common respiratory tract infections, and the palatine tonsils, which are part of the Waldeyer-Pirogov ring, play a key role in shaping the immune response and serve as a barrier to pathogens [1]. Researchers are increasingly paying attention to the role of the mucosal microbiota as a critical factor in maintaining health and developing pathological conditions. As noted by J.L. Pathak *et al.* [2], the oral microbiome is in close interaction with the respiratory system, and its dysbiosis is an important factor in the development of respiratory diseases, which confirms the relevance of studying the tonsil microbiota in acute tonsillitis. The structure of the microbiota is significantly influenced by external factors, including smoking as one of the important stress factors [3]. It is important to note that the problem is not only traditional tobacco smoking, but also the impact of electronic cigarettes. Thus, the study by M. Al-Alawneh *et al.* [4] found an increased incidence of tonsillectomy among children exposed to e-cigarette aerosol. The researchers noted that even indirect exposure of children to aerosols of electronic devices is associated with pathological changes in lymphoid tissue, which increases the likelihood of the need for surgical treatment. The data obtained are particularly relevant in the context of the growing popularity of vaping among young people.

According to S. Cicchinelli *et al.* [5], exposure to tobacco smoke leads to changes that are manifested by a loss of bacterial diversity, a decrease in the number of commensal species (for example, genera *Corynebacterium* and *Streptococcus*) and the growth of opportunistic microorganisms. This effect was confirmed by studies of the oral microbiota. For example, the paper by G. D'Angiolella *et al.* [6] presented

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data according to which tobacco smoking significantly reduces the number of Gram-positive bacterial populations in saliva. Specifically, in the review analysed, a decrease in the diversity of Gram-positive bacterial species was recorded from 18 in non-smokers to 7 in smokers, indicating suppression of key species responsible for colonisation resistance. Based on the results of the literature review conducted by S. Cicchinelli *et al.* [5], the authors pointed out that these changes are systemic in nature, but they are most pronounced in places of direct contact with smoke. Research by X. Wang *et al.* [7] showed that both traditional cigarettes and electronic devices cause significant shifts in the microbial community of saliva, with e-cigarettes showing a unique exposure profile different from tobacco, but also leading to dysbiosis. These data are confirmed and detailed in the metagenomic study by S. Chattopadhyay *et al.* [8], which revealed clear signs of oral microbiota dysbiosis in smokers, characterised by increased colonisation of pathogens against the background of a decrease in the number of beneficial commensal species. These changes disrupt colonisation resistance and immune homeostasis of the mucous membranes, which can contribute to the chronisation of infectious processes.

According to O.I. Lemko *et al*. [9], any form of tobacco smoking, including alternative smoking, significantly increases the risk of developing respiratory infections. In their review, C. Jiang *et al.* [10] systematised data confirming the association between smoking and an increased risk of infectious diseases of various localisation, including respiratory infections, tuberculosis, and pneumonia. The paper described in detail the pathophysiological mechanisms of this phenomenon, which, in addition to dysbiosis, include damage to the ciliated epithelium, impaired mucociliary clearance, alveolar macrophage dysfunction, and weakened adaptive immunity. In particular, M. Hilty *et al.* [11] emphasised that smoking not only increases the likelihood of infection, but also worsens the course and results of treatment of infectious diseases. Experimental studies in mouse models have confirmed that exposure to cigarette smoke alters the composition of the oropharyngeal microbiota and reduces its diversity. T. Wüthrich *et al.* [12] in a comprehensive study demonstrated that exposure to cigarette smoke causes disorganisation of the microbiota, which, in turn, increases the severity of influenza A virus infection. An important aspect is that changes in the microbiota caused by smoking are long-lasting and can maintain a pathological condition even after stopping exposure to smoke. Dysbiosis caused by smoking leads to a violation of the functional state of the respiratory mucosa and increases the inflammatory response, creating favourable conditions for the development of a viral infection. The researchers provided direct evidence that changes in the microbiota caused by smoking are not only a concomitant phenomenon, but also an active participant in the pathogenesis of respiratory diseases, increasing their destructive potential.

However, despite the general recognition of the effects of smoking on the body, the question of what changes in the microbiota of the palatine tonsils occur during an acute inflammatory process under the influence of tobacco smoke remains poorly understood. Most existing studies focus on oropharyngeal microbiocoenosis in general or in health. The purpose of the study was to conduct a comparative analysis of the structure and density of the palatine tonsil microbiota in patients with acute tonsillitis, depending on their smoking status.

MATERIALS AND METHODS

The study included 54 patients with clinical signs of acute tonsillitis. The study included patients who visited family doctors at primary care centres in Ternopil with complaints of sore throat and high temperature. Verification of the diagnosis of acute tonsillitis was made according to the clinical protocol of primary, secondary (specialised), and tertiary (highly specialised) medical care for tonsillitis [13]. Exclusion criteria: chronic or recurrent tonsillitis, immunodeficiency conditions, cancer, autoimmune or severe concomitant pathology, pregnancy and lactation, recent surgical interventions, systemic glucocorticoid therapy, and refusal to participate in the study. Anamnestic data were collected through a survey, namely on antibiotic use (yes/no) and respiratory infections in 3 months (yes/no), smoking (yes/no). Based on the questionnaire, patients were divided into two groups: the smoking group (n = 26); the non-smoking group (n = 28). Clinical assessment was carried out according to the following criteria: pain intensity was assessed on a visual-analogue scale (VAS, 0-10 cm) in two states: rest and swallowing. The clinical severity of tonsillitis was determined on the Centor scale and its modification Centor/McIsaac (1-4 points).

Detection of pathogens was carried out using immunochromatographic tests (on the *Streptococcus* group A (Ecotest, China), influenza A/B viruses, adenoviruses, respiratory syncytial viruses (RSV), SARS-CoV-2 (Medbioalliance, Ukraine). Rapid immunochromatographic tests were purchased by patients and performed by a doctor. The positive result was evaluated in accordance with the manufacturer's instructions. Sterile swabs with Amis transport medium (manufactured by VOLES, Ukraine) were used for bacteriological research. The material was delivered at a temperature of +18...22 °C for two hours to the laboratory. The material was cultured on nutrient media: blood agar with 5% sheep erythrocytes "Sanimed" (Ukraine) streptococci, staphylococci and corynebacteria; mannitol salt agar "Farmaktiv" (Kyiv) as a selective medium for staphylococci; endo agar "Farmaktiv" (Kyiv) for the detection of Gram-negative representatives of the family Enterobacteriaceae; Sabouraud agar "Farmaktiv" (Kyiv) for the isolation of yeast-like fungi of the genus *Candida*. Identification of microorganisms was carried out using a complex of phenotypic methods, including Gram staining, biochemical tests (catalase, coagulase, lecithinase for Gram-positive cocci; Simmons citrate, indole, mobility for Gram-negative rods, "Farmaktiv", Kyiv), hemolysis results (blood agar with 5% sheep erythrocytes, "Sanimed-M", Kharkiv), and sensitivity to novobiocin, bacitracin and optoquine (LLC "Ukrmediasnab", Dnipro). The cultures were incubated under aerobic conditions at 37°C for 24 hours. Identification was performed according to the classical bacteriological protocols described by M. Goodfellow *et al.* [14], national guidelines and manuals on microbiological diagnostics by V.V. Minukhin *et al.* [15] and S.I. Klymnyuk *et al*. [16]. The number of colony-forming units (CFU) per 1 ml of an oropharyngeal smear sample suspended in a sterile transport medium was

determined to quantify the oropharyngeal microbiota. The results were expressed as the decimal logarithm (lg CFU/ml). Statistical data processing was performed using Python 3.11 software (Python Software Foundation, USA) using the scikit-learn, pandas, and numpy libraries in the Google Colaboratory environment. Initial data collection and structuring was performed in MS Excel 2010 (Microsoft Office 2010, USA). In addition, online services from Social Science Statistics (Social Science Statistics, Washington, Virginia, USA) were used for certain statistical calculations. Quantitative data were presented as the arithmetic mean ± standard deviation (m ± SD). The normality of the distribution was checked using the Shapiro-Wilk test. To compare quantitative indicators between groups, the Mann-Whitney U-test was used for data whose distribution deviated from the normal one. Fisher's exact test (at expected frequencies <5) was used to analyse categorical variables. The level of statistical significance was set at $p < 0.05$. Principal Component Analysis (PCA) was used to visualise and analyse multidimensional microbiological data. PCA is a method of reducing the dimension of data that allows identifying the main areas of maximum variability in a data set. Each primary component (PC) reflects a certain percentage of explained variance, which characterises the degree of influence of this factor on the overall data structure. The explained variance of the principal components was interpreted on the following scale: values <30% indicated a low influence of the factor on the data structure, 30-60% – on moderate influence, 60-80% – on significant influence, and >80% – on dominant influence. Heat maps were constructed to visualise the intensity of microbial colonisation across all samples. The study was conducted in accordance with the recommendations set out in the Convention on Human Rights and Biomedicine [17], considering the ethical principles set out in the Declaration of Helsinki [18], and in accordance with Order of the Ministry of Health of Ukraine No. 690 [19], as well as the requirements of the Bioethics Committee of the I. Horbachevsky Ternopil National Medical University of the Ministry of Health of Ukraine (protocol No. 81 dated 03.04.2025).

All patients were familiar with the study design and signed informed consent to participate in the study. The study is part of the research work of the Department of Microbiology, Virology and Immunology at the I. Ya. Horbachevsky Ternopil National Medical University of the Ministry of Health of Ukraine "Comprehensive study of microbiota, immune system, antibacterial resistance, and clinical and laboratory indicators for the diagnosis, prognosis, and development of therapy for human diseases" (state registration number 0125U000121). This study is a continuation of the previous research on the influence of smoking on oropharyngeal microcoenosis and evaluates differences (at the time of consideration of this paper in the journal, the study is not yet available in the public domain). A limitation of this study is the single-centre design and sample size, which may affect the generalisability of models.

RESULTS AND DISCUSSION

A comprehensive comparative analysis of clinical and anamnestic parameters was performed between two study groups: patients who smoke (Group 1, n = 26) and patients who do not smoke (Group 2, n = 28), with an established diagnosis of acute tonsillitis (Table 1).

Table 1. Comparison of basic clinical parameters between a group of smokers and non-smokers

Parameters	Group of smokers (n = 26)	Group of non-smokers (n = 28)	Statistical significance (p-value)
Body mass index (BMI)	24.76 ± 2.9	25.93 ± 3.5	0.2221, (p (x ≤ Z) = 0.111
VAS scale (sore throat at rest) (cm)	5.71 ± 1.09	5.71 ± 1.4	0.9011, (p (x ≤ Z) = 0.4506
VAS scale (pain when swallowing) (cm)	6.76 ± 1.22	6.82 ± 1.4	0.6939, (p (x ≤ Z) = 0.6531
Centor scale (score)	3.23 ± 0.68	3.21 ± 0.7	0.9157, (p (x ≤ Z) = 0.4579
Use of antibiotics throughout the month	30.76%	10.71	0.0675
Previous respiratory infections in the last 3 months	42.30%	27.27%	0.6455

Source: compiled by the author

The Centor/McIsaak clinical scale was used to objectively assess the severity of the disease. Statistical analysis of the results obtained did not reveal a significant difference between the groups ($p > 0.05$). The results showed the uniformity and comparability of the groups according to the key clinical criteria included in the scale, namely: the presence of high body temperature (above 38°C), the detection of exudate on the surface of the tonsils, the absence of coughing, and palpatory painful cervical lymph nodes. Anthropometric indicators also showed no statistically significant differences. In particular, the mean BMI values were similar in both groups, which was confirmed by the corresponding statistical criterion ($p = 0.222$). To quantify pain, a survey of patients was conducted using VAS. Analysis of pain intensity at rest and during the act of swallowing revealed no significant differences between patients who smoke and those who do not smoke ($p > 0.05$ for both types of pain). When analysing anamnestic data, it was found that the incidence of respiratory infections during the last three months was higher in the group of smokers (42.30%) compared to the group of non-smokers (27.27%). However, this difference did not reach the level of statistical significance ($p = 0.645$). An analysis of antibiotic treatment over the past month revealed a trend: antibiotic use was more frequent among smokers (30.76%) compared to 10.71% in non-smokers, with the p-value approaching the significance level ($p = 0.067$). In the group of smokers (n = 26), the vast majority of patients (22 people) used traditional cigarettes. The smoking intensity was 10.47 ± 4.0 cigarettes per day (range: 4-22 cigarettes). The remaining 4 patients in the group used e-cigarettes (vapes). According to the results of rapid diagnostics, the most common pathogen in the study

cohort was influenza (types A/B), which was diagnosed in 22% of patients. The detection rate of adenoviruses (18%) was only slightly lower, while Group A streptococcus was detected almost 2.5 times less frequently (9%) (Fig. 1).

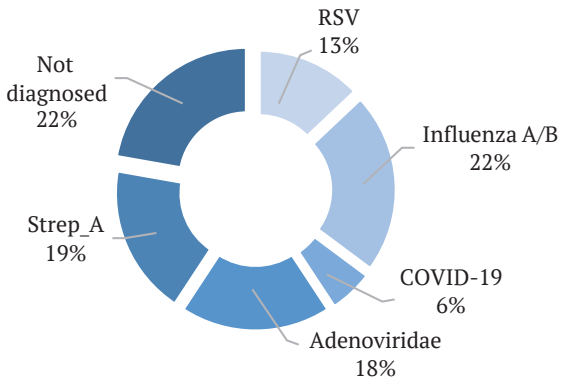

Figure 1. Results of immunochromatographic tests of the study cohort of patients with symptoms of acute tonsillitis
Source: compiled by the author

The remaining pathogens were found with a noticeably lower frequency: RSV – in 13% of cases (about half as often as influenza), and SARS-CoV-2 – only in 6% (almost 4 times less often than influenza). It is important to note that in 22% of those surveyed, the aetiology of the disease remained unknown, since the results of testing for all target pathogens were negative. Bacteriological examination of oropharyngeal smears confirmed the bacterial aetiology of acute tonsillitis in 10 of the 54 examined patients (18.51%). The detection rate of β-haemolytic Streptococcus spp.,, the main bacterial pathogen, was higher in the group of non-smokers (6 patients, or 21.4%) compared to the group of smokers (4 patients, 15.4%), but this difference did not reach statistical significance ($p > 0.05$). In addition to the target pathogen, routine microbiological analysis revealed a wide range of microorganisms that colonise the tonsil biotope. To systematise the detected microbiota, microorganisms were classified according to the type of metabolism and cell morphology. The vast majority of the identified species were aerobic and facultative anaerobic bacteria. Among them, Gram-positive cocci dominated, in particular, various species of Streptococcus (α-, β - and γ-haemolytic), *Staphylococcus aureus*, and coagulase-negative Staphylococcus spp. Gram-positive rods represented by genera *Corynebacterium* and *Rothia* were also present. Of the Gram-negative bacteria, they were identified as cocci (*Neisseria* spp., *Moraxella* spp.), and rods (*Klebsiella pneumoniae*, *Haemophilus* spp., *Enterobacter* spp.). Additionally, representatives of fungi of the genus *Candida* were found in the microbiota. PCA was used to assess the overall effect of smoking status on the structure of the tonsil microbiota. As shown in Figure 2, graphical representation of PCA results did not reveal a clear cluster distribution of patients' microbial profiles depending on smoking status.

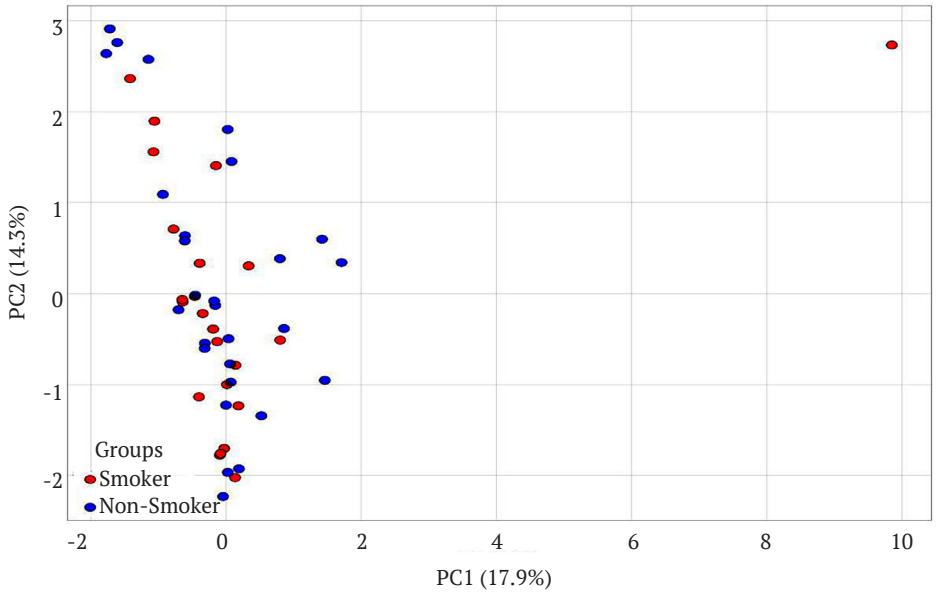

Figure 2. PCA analysis of the microbiome of patients with tonsillitis symptoms in smokers and non-smokers
Source: compiled by the author

The groups of smokers and non-smokers overlap significantly, which indicates that there is no global rearrangement of the microbiota under the influence of tobacco. It is important to note that the first two main components (PC1 and PC2) account for only 32.2% of the total variance (17.95% and 14.3%, respectively), which indicated that the smoking factor is not dominant in the development of microbiota composition, inferior to other individual factors. This conclusion was confirmed by the results visualised using a heat map (Fig. 3), which reflected the intensity of colonisation of individual microorganisms in each patient. The map did not show the development of separate clusters corresponding to the study groups. Individual microbial load profiles showed high variability among both smokers and non-smokers. A detailed comparative analysis of the colonisation density (CFU/mL) of individual microorganisms between the groups presented in Table 2 also found no statistically significant differences.

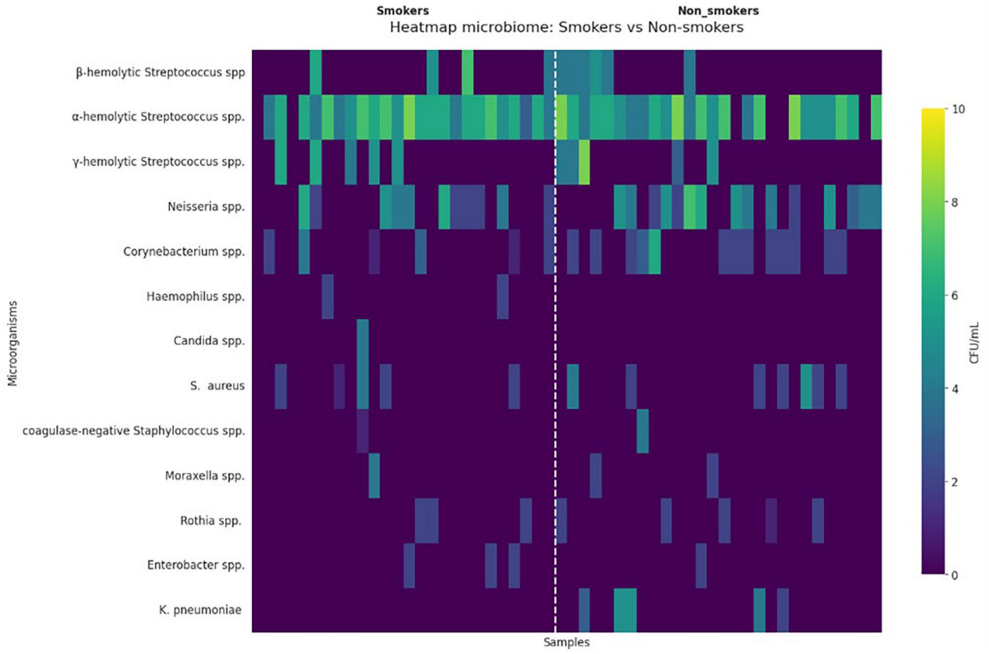

Figure 3. Heat map of the intensity of colonisation of isolated microbial isolates in the examined patients of the smoking and non-smoking groups

Source: compiled by the author

Table 2. Estimation of microbial colonisation density (CFU/mL) between a group of smokers and non-smokers

Microorganisms / Patient groups	Group of smokers (n = 26)	Group of non-smokers (n = 28)	Mann-Whitney U-test
α-haemolytic *Streptococcus* spp.	10^4-10^8	10^5-10^8	0.95
β-haemolytic *Streptococcus* spp.	10^7-10^4	10^4-10^5	0.48
γ-haemolytic *Streptococcus* spp.	10^6-10^4	10^5-10^8	0.82
Corynebacterium spp.	10^1-10^4	10^2-10^6	0.04
Neisseria spp.	10^2-10^6	10^2-10^7	0.28
S. aureus	10^1-10^4	10^2-10^5	0.55
Moraxella spp.	$<10^4$	$<10^2$	0.64
Haemophilus spp.	$<10^2$	10^3	0.50
Rothia spp.	$<10^2$	10^1-10^2	0.56
K. pneumoniae	-	10^2-10^5	-
Enterobacter spp.	$<10^2$	$<10^2$	0.28
Coagulase negative *Staphylococcus* spp.	$<10^1$	10^4	0.96
Candida spp.	10^4	-	-

Source: compiled by the author

Comparison of CFU/mL levels of individual isolates showed that the average densities of α-haemolytic Streptococcus spp. and *Neisseria* spp. were close between the groups ($p > 0.05$). A significant increase in colonisation with *Corynebacterium* spp. was observed among non-smokers ($p = 0.04$). In turn, *Candida* spp. were found only among smokers, which may indicate a local decrease in mucosal colonisation resistance in this group. Overall, the results show that smoking does not alter the global taxonomic profile of the tonsil microbiota, but may contribute to selective changes in the colonisation density of individual representatives, potentially associated with an increased risk of secondary infections or dysbiosis.

The results obtained in the study helped to deepen our understanding of the effect of smoking on the oropharyngeal microbiota in acute tonsillitis. Comparison of the data with the results of other studies revealed both similar trends and important differences, which may indicate the specific effects of smoking during acute infection. The key conclusion of the study was the lack of a global rearrangement of the tonsil microbiota under the influence of smoking. PCA did not reveal a clear cluster distribution between the groups, suggesting that smoking status is not the dominant factor determining the overall taxonomic composition of the microbiota at the time of acute illness. This result is partially consistent with a large-scale study by J. Wu *et al.* [20], which also found no global changes in the composition of the oral microbiota in smokers under health conditions. However, the author's study, conducted in an active infection setting, demonstrated that exposure

to smoking is not a decisive factor in determining the initial clinical severity. This result may be conditioned by the fact that severe inflammation serves as a powerful factor that masks and unifies the microbial environment, levelling the individual effects of smoking. Importantly, a weak explanation of the overall variance (only 32.2% was explained by PC1 and PC2) confirmed the multivariate aetiology and the presence of numerous, as yet unidentified, determinants that form the patient's microbial profile.

The lack of clear separation of microbial profiles by smoking status can be explained by the high individual variability of the oropharyngeal microbiota. As noted by J.T. Nearing *et al.* [21], this variability is a fundamental characteristic of a healthy microbiome. Separate analysis by bioinformatic approaches performed by J.H. Moon & J.H. Lee [22] also confirmed a significant level of diversity in the composition of the healthy oral microbiota. The study by L.L. Bach *et al.* [23] found that the oropharynx microbiota, despite the presence of a stable nucleus, is characterised by significant interpersonal differences and certain temporal dynamics. This finding of temporal variability in the oral microbiota was confirmed by E. Vogtmann *et al.* [24]. Thus, the significant contribution of individual non-communicable factors (such as genetic characteristics, diet, hygiene, and a history of concomitant diseases) can be so significant in the development of the microbial profile that the influence of an individual factor, even such a significant one as smoking, is levelled against the background of general variability. This is especially pronounced in the context of acute infection, which itself is a powerful stress and unifying factor for the microbiota [25].

Although the overall structure of the microbiome did not undergo major statistically significant changes, the selective shifts identified by the researcher are potentially clinically significant. Specifically, the significantly lower microbial colonisation of *Corynebacterium* species in smokers ($p = 0.04$) confirmed its known role as an indicator of a healthy microbiome and may indirectly indicate the dysbiotic effect of tobacco smoke. An even more revealing finding was the discovery of yeast fungi of the genus *Candida* spp. only in the group of patients who smoke. These results showed that smoking, without radically changing the overall structure, selectively modifies the niche, creating a favourable environment for colonisation of specific, potentially pathogenic microorganisms. This is consistent with the findings of L. Bach *et al*. [26], which showed that smoking reduces the stability of the pharyngeal microbiota and promotes selective growth of individual taxa. Similarly, a systematic review by N.L.M. Senaratne *et al*. [27] noted that various forms of tobacco can lead to specific shifts, in particular, promote the growth of yeast fungi of the genus *Candida*. A possible mechanism is that tobacco smoke damages the mucosal epithelium and suppresses local immune mechanisms, reducing colonisation resistance and opening niches for such microorganisms.

An important aspect of this study was the use of the Centor/McIsaac scale for an objective assessment of the severity of the disease. The results showed that, despite the identified microbiological and clinical differences, the groups of smokers and non-smokers were homogeneous according to the key clinical criteria included in this scale. Statistical analysis revealed no significant differences in Centor scores between the groups ($p > 0.05$), and in parameters such as the presence of exudate on the tonsils, body temperature >38°C, no cough, and soreness of the cervical lymph nodes. This showed that the increased risk of complications and more frequent administration of antibiotics to smokers is not associated with a more severe clinical picture at the time of treatment, but is a consequence of other mechanisms. These data were confirmed by T.E. Klug *et al*. [28], who proved that smoking is an independent risk factor for paratonsillar abscess, and this effect was not associated with changes in the microbial spectrum. Thus, it can be assumed that the effect of smoking is realised not because of the deterioration of clinical manifestations of pharyngitis, but because of the suppression of local immune mechanisms and violation of the barrier function of the mucous membrane, which creates conditions for the development of complications even with a standard clinical picture.

The clinical correlation of the identified microbiological trends may be the difference in antibiotic use observed in this study. Although it did not reach a strict level of significance ($p = 0.067$), the frequency of their use among smokers was almost three times higher (30.76% vs 10.71%). The study by E.A. Saliba-Gustafsson *et al.* [29] indicated that clinical factors such as the presence of exudate on the tonsils are key to deciding whether to prescribe antibiotics for respiratory infections. The large-scale study by M.B. Steinberg *et al.* [30] demonstrated that smoking is an independent risk factor, as smoking patients are 20-30% more likely to receive antibiotics. This suggests that in addition to objective clinical signs, smoking status may influence drug decision, possibly due to the expectation of a more severe or prolonged course of infection. In particular, K. Ahmadi *et al*. [31] noted that the mechanisms underlying this may be impaired mucociliary clearance, stimulation of biofilm formation, and suppression of local immunity under the influence of tobacco smoke.

Moreover, the long-term impact of such treatment should be considered: a recent meta-analysis by I. Adamu *et al*. [32] showed that prescribing antibiotics for respiratory infections increases the risk of future consultations. Thus, it can be assumed that there is a cyclicity in which smoking contributes to infections that lead to more frequent use of antibiotics, which, in turn, can increase the tendency to future diseases. This cycle may partly explain the higher incidence of respiratory infections among smokers that was observed in the study (42.30% vs 27.27%), and which was confirmed in global estimates in the paper by F. Sitas *et al*. [33], 22.5% of deaths from respiratory infections were associated with smoking.

For the key pathogen, β-haemolytic Streptococcus spp.,, there was no statistically significant difference in the frequency of its detection between the study cohorts of patients, although there was a numerical advantage among non-smokers (21.4% vs 15.4%). This trend correlated with data by I. Brook & A.E. Gober [34], who observed microbiological changes after smoking cessation. It can be hypothetically assumed that in a healthy state, smoking suppresses competitive microflora, potentially creating a niche for colonisation by pathogens. However, in the context of an acute inflammatory process, this primary dysbiotic effect can be eliminated due to the intense immuno-inflammatory load that dominates the local mechanisms of microbial competition.

Thus, the study concluded that in acute tonsillitis, smoking does not lead to a global change in the tonsil microbiota, which is confirmed by the lack of clear clustering of samples by smoking status when analysing the main components. However, it manifests itself at a more subtle, selective level, contributing to dysbiotic shifts such as a decrease in the level of *Corynebacterium* spp. and colonisation with *Candida* spp. These selective shifts are likely associated with a decrease in local immune defences and changes in mucosal properties under the influence of tobacco smoke, which, in turn, may lead to clinical trends towards more frequent prescribing of antibiotics and respiratory infections in this category of patients.

CONCLUSIONS

The study demonstrated the complex and multi-level nature of the effect of smoking on the oropharyngeal microbiota in acute tonsillitis. Although the smoking factor does not lead to a global rearrangement of the microbiota, which was confirmed by the lack of a clear cluster division on the PCA graph and a low percentage of explained variance (32.2%), it causes selective dysbiotic shifts of clinical significance. There was a decrease in colonisation of *Corynebacterium spp.* ($p = 0.04$) – commensals associated with a healthy microbiota, and the exclusive presence of fungi of the genus *Candida* in smokers. This indicates a violation of the colonisation resistance of the mucous membrane, probably due to the suppression of local immune mechanisms under the influence of tobacco smoke.

The key fact was that despite the absence of significant differences in the clinical picture on the Centor and VAS scale between the groups, smokers showed clear trends towards more frequent use of antibiotics (30.8% and 10.7%; $p = 0.067$) and a higher incidence of respiratory infections in the anamnesis (42.3% and 27.3%). Therefore, smoking does not worsen the severity of clinical manifestations of tonsillitis, but creates a "hidden" dysbiosis, which probably underlies an increased tendency to relapse of infections and the need for antibiotic therapy. This indicated that tobacco exposure is realised mainly by inhibiting local immunity and disrupting microbial homeostasis, rather than by directly enhancing the inflammatory response. The data obtained highlighted the importance of taking smoking status into consideration when assessing the risks of complications and recurrent oropharyngeal diseases. Further studies with larger samples are needed to investigate the mechanisms by which selective shifts in the microbiota translate into clinical consequences.

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CONFLICT OF INTEREST

None.

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Мікробіоценоз у пацієнтів з гострим тонзилітом під впливом фактору куріння

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Анотація. Гострий тонзиліт є широко поширеним захворюванням, на перебіг якого може впливати статус куріння пацієнта, що призводить до змін у мікробіоті ротоглотки. Метою роботи було оцінити вплив куріння на формування мікробіоценозу піднебінних мигдаликів у пацієнтів із гострим тонзилітом. Дослідження охопило 54 пацієнти, які були розподілені на дві групи: курці (n = 26) та некурці (n = 28). Мікробіологічне дослідження включало культивування зразків на різних поживних середовищах з подальшою ідентифікацією мікроорганізмів за фенотиповими методами. Щільність мікробіоти оцінювали шляхом підрахунку колонієутворюючих одиниць. Для статистичного аналізу використовували U-критерій Манна-Уітні, точний тест Фішера та аналіз головних компонент. Аналіз методом головних компонент не виявив чіткої кластеризації зразків, що свідчило про відсутність глобальних змін у мікробіоті мигдаликів залежно від статусу куріння. Однак були виявлені вибіркові зміни, серед яких значно знижена щільність колонізації *Corynebacterium* spp. (p = 0,04) та виключно наявність грибків роду *Candida* серед курців. Клінічно, групи не відрізнялись за тяжкістю перебігу захворювання за шкалою Centor, але курці частіше отримували антибіотикотерапію (30,8 % та 10,7 %) та мали більшу частоту респіраторних інфекцій в анамнезі (42,3 % та 27,3 %). Отримані дані свідчили, що куріння не змінює загальну структуру мікробіоти мигдаликів при гострому тонзиліті, але викликає селективний дисбіоз. Це обгрунтовало необхідність врахування статусу куріння пацієнта для оцінки ризику рецидивуючого перебігу інфекції та розробки більш персоналізованих підходів призначення антибіотикотерапії

Ключові слова: бактерії; бактеріологічний аналіз; діагностичні тести; віруси; мікробіота; ротоглотка

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Differentiated tactics for surgical treatment of purulent sacroiliitis depending on the clinical and radiological stage under ASAS criteria

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Abstract. Purulent lesion of the sacroiliac joint (sacroiliitis) is a severe surgical pathology of the musculoskeletal system and requires surgical treatment in the department of purulent surgery. The purpose was to analyse the tactics of surgical treatment of purulent sacroiliitis in combination with infusion and antibacterial therapy depending on the clinical and radiological form of the disease. 27 patients with purulent sacroiliitis were studied. Patients were divided into forms: stage 2 ASAS – 40.7%, stage 3 ASAS – 33.3%, stage 4 ASAS (panarthritis) – 26.0%. Depending on the forms, patients received combination therapy: conservative treatment (antibiotics, blockades, infusions), economical or radical joint resection with drainage, bacteriological control, detoxification. 11 (40.7%) patients with synovitis who were treated only conservatively and 9 (33.3%) patients with arthritis who had additional economical resection fully recovered. Among 7 (25.9%) patients with panarthritis who underwent radical resection, 1 developed septic shock, which led to lethal outcomes, and 3 underwent repeated operations due to ligature fistulas. 25 (92.5 %) patients – complete recovery, 1 – periodic recurrences. It was found that treatment should consider the form of the disease; immediate resection in septic flow with bacterial control reduces chronisation and relapses, and the combined strategy is effective in avoiding complications, but requires early diagnosis and a multidisciplinary approach. The results obtained confirmed the feasibility of a differentiated approach to the choice of surgical tactics for the treatment of purulent sacroiliitis depending on the stage of ASAS, which can be considered when developing clinical protocols

Keywords: pelvic bones; antibiotic therapy; sacroiliac joint; panarthritis; septic complications

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INTRODUCTION

Treatment of purulent sacroiliitis in Ukraine is an pressing issue due to several objective factors, namely: the medical aspect – the disease is often not diagnosed timely, which leads to difficult treatment and long recovery; socio-economic context – in the conditions of war, pelvic injuries and infections have increased, which becomes a challenge for both military medicine and civilian hospitals. The disease often disguises itself as normal back pain, leading to late diagnosis, chronisation of the process, and long recovery, which requires differentiated treatment approaches. The lack of detailed statistics may indicate an underestimation of the problem due to limited diagnosis, insufficient knowledge of this pathology by surgeons, lack of experience in treating patients with purulent lesions of the pelvic bones, which with the rest leads to erroneous treatment tactics.

Purulent sacroiliitis is a severe surgical pathology of the musculoskeletal system that requires surgical intervention in the context of purulent surgery. According to M. He *et al.* [1], this is a rare complication that accounts for less than 1-2% of all cases of joint inflammation, most often occurring in immunocompromised individuals after pelvic injuries or intravenous drug use. Y. Wang *et al.* [2] analysed clinical, laboratory, and instrumental data from 135 patients with infectious sacroiliitis in China for the period 2008-2020, finding that 67% of cases were purulent, and a biopsy controlled by computed tomography (CT) provided positive results in identifying pathogens such as *Staphylococcus aureus* and *Malassezia* in 87% of cases, emphasising the need for a biopsy to differentiate spondyloarthritis. The researchers noted higher rates of bone marrow erosion and oedema when performing magnetic resonance imaging (MRI) studies for purulent and tuberculosis forms compared to brucellosis, which improves early diagnosis in patients with fever and increased erythrocyte sedimentation rate (ESR). M.R.M. Rishard *et al*. [3] described a case of purulent sacroiliitis in the postpartum period in a 25-year-old woman caused by *Streptococcus agalactiae*, where timely diagnosis by MRI and bacteriological seeding enabled the appointment of successful antibiotic therapy (cefotaxime and metronidazole) with joint support by corset and traction, preventing chronisation and demonstrating the role of a multidisciplinary approach in avoiding long-term complications such as pain. Y. Tokuyama *et al.* [4] considered a case of purulent sacroiliitis caused by *Salmonella schwarzengrund*, in a young healthy woman without immunodeficiency, where interventional radiology to drain the sacroiliac abscess in combination with antibiotics (meropenem, vancomycin, later levofloxacin) provided a complete recovery in 38 days, highlighting the potential for extraintestinal infections with *Salmonella* even in immunocompetent individuals. The presence of an untreated pathological focus in the acute period leads to a chronic course of the disease with frequent exacerbations over many years. As noted by O.O. Kopchak [5], the long-term existence of pathological pain contributes to the stable chronisation mechanisms, which complicates further diagnosis and therapeutic approaches. Similar observations were also confirmed by V. Tankut *et al.* [6], emphasising that untimely or incomplete correction of pain can lead to its persistence and repeated aggravations, even in specific clinical groups, such as pregnant women.

A. Al-Mnayyis *et al.* [7] described radiological diagnostic methods, in particular MRI as the gold standard for detecting early bone marrow oedema and effusion, and CT for detailed assessment of erosions and sclerosis, which are critical for differentiating the pyogenic form from other aetiologies such as brucellosis or tuberculosis, allowing timely aspiration for microbiological confirmation. Although over-the-counter medications such as nonsteroidal anti-inflammatory drugs (NSAIDs) and acetaminophen have shown moderate efficacy in reducing pain and disability in chronic lower back pain, they often did not affect inflammatory lesions of the sacroileal joints, highlighting the need for a comprehensive approach with antibiotics and surgery for infectious cases, as noted by J. Peck *et al*. [8]. Analysis of these sources showed that early imaging and aetiological differentiation are key to avoiding chronisation. Without timely instrumental imaging, such as SPECT or contrast MRI, diagnosis is often delayed, leading to destructive changes in the joint [9].

The purpose of the study was to evaluate the effectiveness of differentiated tactics of surgical treatment of purulent sacroiliitis depending on the clinical and radiological stages according to the ASAS criteria to optimise results, reduce the risk of chronisation of the process, relapses, and septic complications.

MATERIALS AND METHODS

A retrospective analysis was conducted of medical records of patients hospitalised between 2021 and 2024 in the bone and purulent infection unit of Municipal Non-Profit Enterprise “City Hospital No. 9” in Zaporizhzhia for purulent sacroiliitis. The study was conducted in accordance with the international standards of the Declaration of Helsinki World Medical Association [10], European Commission [11] and ethical principles approved by the local ethics committee of Zaporizhzhia State Medical and Pharmaceutical University (Protocol No. 8 of August 17, 2023). All patients have given written informed consent to the use of their clinical data for scientific purposes. The criteria for including patients were: consent to the use of clinical data, confirmed diagnosis of purulent sacroiliitis, availability of complete medical documentation. The exclusion criteria were: refusal to use clinical data, patients with incomplete medical documentation, lack of a confirmed diagnosis (for example, lack of CT/MRI data or microbiological studies).

The stages of the study included: 1) selection and collection of data from medical records; 2) statistical analysis of demographic, clinical and aetiological indicators; 3) evaluation of the effectiveness of treatment based on clinical criteria; 4) presentation of generalised results and illustrative clinical case to demonstrate the typical course of the disease. In addition to the generalised analysis, a significant clinical case was presented as an illustration of the typical course of the disease and the effectiveness of the treatment strategy, in compliance with the recommendations of the CARE guidelines [12]. Data sources included retrospective analysis of medical records, including medical history, CT, MRI, microbiological studies, laboratory tests, and operating protocols. During X-ray examination to assess the degree of sacroiliitis, the criteria of the Assessment of SpondyloArthritis international Society

(ASAS) according to J. Sieper *et al.* [13] were applied, in particular, the modified New York criteria for the classification of radiographic changes, adapted for the differentiation of infectious processes from inflammatory forms (Table 1).

Table 1. Radiological classification of sacroiliitis proposed by ASAS

Stage	Characteristics
Stage 0	Normal, no changes (or only soft tissue oedema).
Stage 1	Initial narrowing of the joint space, suspicious changes (blurred edges).
Stage 2	Minimal anomalies, erosions, sclerosis, narrowing of the joint space.
Stage 3	Significant erosions, bone lintels, partial ankylosis.
Stage 4	Complete ankylosis, overgrowth of the joint space.

Source: J. Sieper *et al.* [13]

In cases of doubt about the aetiology, ASAS criteria were used as an auxiliary tool to exclude autoimmune causes based on radiological signs, such as erosion and ankylosis. Data were collected from hospital archives without interfering with patient treatment. To evaluate the effectiveness of treatment, the following criteria were used: clinical improvement (pain reduction, normalisation of body temperature, improved mobility); laboratory parameters (normalisation of ESR, C-reactive protein, negative results of bacteriological cultures); radiological data (reduction of signs of inflammation on CT/MRI); and the absence of relapses for at least 6 months after discharge. Effectiveness was considered achieved when at least 80% of positive changes were achieved according to these criteria. Anamnestically, all 27 patients in the study were previously treated either in surgical, gynaecological, or neurological and trauma departments for complications of the underlying disease without a positive result. Distribution of patients by gender: women – 15 (55.5%), men – 12 (44.5%). The average age of patients was 32.4 years. Distribution of patients by aetiological factors: 7 (25.9 %) women – transferred postpartum sepsis with subsequent localisation of the process in the sacroiliac joint and gynaecological diseases, in 8 (29.6%) patients haematogenic osteomyelitis of the pelvic bones, in particular, the ilium was complicated by sacroiliitis, in 4 (14.8%) patients septic phenomena developed against the background of drug addiction, in 6 (22.2%) cases of the disease the root cause could not be established.

RESULTS AND DISCUSSION

The authors identified 3 clinical and Radiological forms of purulent sacroiliitis, which to a certain extent correspond to the classification described above: purulent non-specific unilateral synovitis, radiological stage 2 according to ASAS in 11 (40.7%) patients; purulent non-specific arthritis with destruction of articular cartilage (osteoarthritis), radiological stage 3 according to ASAS in 9 (33.3%) cases; purulent arthritis with destruction of cartilage and extra-articular bone formations – bodies ilium and sacrum (panarthritis), stage 4 radiological ASAS in 7 (26.0%) patients. Patients with the first two forms of the disease were hospitalised in the acute period with a clinic of severe purulent inflammation, which was characterised by severe fibrillation (39-40°C), tachycardia, chills, severe pain syndrome of the sacroiliac junction, with radiation in the *n.ischiadicus*, forced position of the lower limb (flexion and adduction in the hip joint) on the affected side. The course of the disease in patients with the third form of sacroiliitis was chronic in nature with frequent episodes of exacerbations, during one of which they were hospitalised. Purulent abscesses manifested elastic, low-painful fluctuation and were localised in the groin area and at the level of the gluteal fold, and in the chronic course – in the medial areas of the thigh. X-ray signs corresponded to the characteristics given in the classification up to complete destruction of the joint with the disappearance of the joint space. In some cases, foci of destruction and osteoporosis formed with areas of sclerosis around the joints, and destruction of the body and wing of the ilium, lateral masses of the sacrum, sacral foramen with the presence of large and small sequesters. Fistulas of various localisation were observed in 8 (29.6%) patients (Table 2).

All patients received complex therapy in a surgical hospital. The method of treatment depended on the form of the disease and aetiopathological characteristics. Conservative treatment was given to 11 (40.7%) patients with purulent non-specific unilateral synovitis. It was based on bed rest on the shield, intraosseous anti-inflammatory prolonged blockades, which included lidocaine 2% – 4.0 mL and the osteotropic antibiotic lincomycin 300 mg (1 mL) with a total course of 5-7 injections with a frequency of once every two days. Antibacterial therapy began with empirical therapy based on the use of drugs active according to the spectrum of potential pathogens and was primarily directed to methicillin-resistant staphylococci with the appointment of vancomycin. If gram-negative flora was suspected, ceftazidime with ciprofloxacin, amikacin with ceftazidine, and carbapenems were used intravenously for 14 days. Ceftriaxone, cefotaxime, and inhibitor-protected penicillins (piperacillin/tazobactam) were administered when seeding *E. coli* or *Proteus* spp. If bacteriological testing revealed coagulase-negative staphylococcus with a high level of resistance to many antibiotics, patients were given vancomycin and teicoplanin.

Table 2. Results and features of patient treatment according to the form of the disease

Form of the disease (ASAS stage)	Number of patients (%)	Treatment type	Key elements of therapy	Results and notes
Purulent non-specific unilateral synovitis (stage 2)	11 (40.7%)	Conservative	Bed rest, intraosseous blockages, empirical antibiotic therapy, infusion therapy.	Successful relief of acute inflammation; no need for surgery.

Table 2. Continued

Form of the disease (ASAS stage)	Number of patients (%)	Treatment type	Key elements of therapy	Results and notes
Purulent non-specific arthritis with destruction of articular cartilage (stage 3)	9 (33.3%)	Surgical (economical joint resection), conservative	Resection, postoperative infusion therapy, antibiotic therapy depending on the pathogen.	Successful recovery after resection; focus on preventing hypervolaemia and hypokalaemia.
Purulent arthritis with destruction of cartilage and extra-articular bone formations (panarthritis, stage 4)	7 (26.0%)	Surgical (joint resection, drainage), conservative	U-shaped/window resection, removal of affected tissue, drainage, antibiotic therapy depending on the pathogen.	Wound healing by primary tension in all patients; chronic course with relapses.

Source: systematised by the authors

Due to inflammation, the body's physiological metabolism is disrupted, pathological products accumulate, and intoxication increases. All this deepens the course of the purulent-inflammatory process, contributes to the spread of infection and, accordingly, requires intensive infusion therapy. The daily volume of infusion therapy in patients was 20-25 mL/kg of the patient's body weight. Depending on the severity, the treatment lasted from 5 to 20 days. First, an albumin solution was administered, which has high oncotic pressure and caused a directed flow of fluid from the tissues into the vessels. After that, Ringer's crystalloid solution was administered intravenously by drip. It made up for the lack of fluid in the cells and intercellular space. At the final stage, rheopolyglucin and rheosorbylact were used, which have detoxification and rheological properties. 5-10 mL of 2.4% eufillin was added to the above solutions to enhance renal circulation and stimulate diuresis. Solutions were heated to 35-36°C with the rate of administration of drugs with high osmotic activity of 15-20 mL/min, crystalloids 25-35 mL/min.

Economical resection of the sacroiliac joint was performed in 9 (33.3%) patients with purulent non-specific arthritis and signs of articular cartilage destruction. In the postoperative period, patients were prescribed infusion therapy, which included 5% glucose solution, at the rate of 10 mL/kg of body weight, insulin, B vitamins (1 mL) and C (3-5 mL), trental (5 mL), cardiac glycosides, 3% potassium chloride solution (1.0 mL/kg) to prevent hypokalaemia. Next, Ringer's solution was administered intravenously at the rate of 5-7 mL/kg of body weight. An increase in intravascular volume by extracting fluid from the cellular and extracellular spaces provided subsequent administration of rheopolyglucin. The infusion rate is 5-7 mL/min. At this stage, to prevent hypervolaemia and hemodilution, patients were administered mannitol at a dose of 0.5-0.8 g/kg of body weight and 2-3 mL of Lasix to stimulate diuresis. Infusion therapy was completed with the introduction of 5-10% albumin solution at a dose of 1-3 mL/kg, at a rate of 5-10 mL/min. The average duration of such forced actions depended on the patient's condition and was up to 10 days.

Antibacterial therapy in the postoperative period depended on the pathogen. Patients with isolated *S. epidermidis*, *S. aureus*, *Streptococcus* spp. were prescribed cefepime – 2 g IV infusion every 12 hours or ceftriaxone – 2 g IV infusion every 24 hours + amikacin – 20 mg/kg IV (diluted in 100 mL of saline solution). Patients with Gram-negative *Entrobateriaceae*, *P. Aeruginosis* were prescribed Cefazolin 2 g IV infusion every 8 hours or oxacillin 2 g IV infusion every 4 hours + amikacin – 20 mg/kg IV (diluted in 100 mL of saline) or gentamicin – 5 mg/kg (diluted in 100 mL of saline).

In patients who were diagnosed with purulent panarthritis of the sacroiliac joint – 7 (25.9%) cases, surgical intervention was performed depending on the location of fistulas. In the absence of fistulas or their location only in the sciatic region, U-shaped or window resection of the joint was performed. Joint elements, affected bone tissue were removed, sacral openings were opened, and the roots of the horse's tail were removed up to the sacral canal. An additional incision was made in the projection of the iliac wing for the purpose of revising the pelvic cavity. In the presence of pus, active drainage was established through a resection hole in the joint into the pelvic cavity. In the postoperative period, the wounds were washed using drainage tubes with antiseptic solutions (decasan, chlorhexidine) by drip method. Drains were removed on Day 5. Targeted antibiotics were administered intravenously for 14 days (depending on the results of a bacteriological examination). In all patients, the wounds healed by primary tension. On average, patients stayed in the hospital for 4 weeks.

Intraoperatively, one patient was found to have a purulent process spreading within the middle third of the thigh, which required additional opening of abscesses followed by drainage. According to the data by A.R. Rezaei *et al.* [14] and C. Hinson *et al.* [15], which were confirmed by the results of studies by A. Bucataru *et al.* [16], inflammatory processes rapidly affect cell spaces, which leads to the development of various purulent accumulations in the pelvic area, extraperitoneal space, and lower extremities. The deep location of the pelvic bones, combined with a large number of muscles, prevents direct external drainage of pus near the focus of osteomyelitis. As a result, pus migrates over distances, involving the main vascular and nerve plexuses, which provokes a range of complications.

In the postoperative period, wounds were washed through drains with antiseptic solutions of decasan or chlorhexidine, in a volume of up to 5 litres by drip method around the clock. Drains were removed depending on the condition of the wounds and the nature of the discharge. Bacteriological cultures from wounds were inoculated every 7-10 days. At 3-4 weeks of treatment, cultures from wounds were negative. The main complication when performing sacroiliac joint resection may be damage to the superior sciatic artery. The authors did not observe such complications, since they always planned its projection, which allowed performing interventions outside this zone. In the postoperative period, there was a violation of independent urination for 4-5 days in 3 (33.3%) patients, a delay in defecation in 2 (22.2%) patients. In the future, the function of

the pelvic organs was fully restored. The pain in my back disappeared 3-4 weeks after the operation. In the immediate postoperative period, 1 (3%) patient died with bilateral damage to the sacroiliac joint, which was complicated by septic shock and manifestations of multiple organ failure. 3 (11.1%) patients were re-operated on for ligature fistulas. Long-term results were observed in 26 (96.2%) patients aged 2 to 4 years. A patient who refuses surgical treatment was periodically hospitalised in the department with an exacerbation of the process. The remaining 25 (92.5%) patients had no complains.

The positive results of treatment of 11 patients using conservative methods with an emphasis on empirical antibacterial therapy (vancomycin, ceftazidime, ciprofloxacin) and intensive infusion detoxification are consistent with the literature data, where antibiotics remain the basis for the treatment of infectious sacroiliitis, especially in the early stages, in order to prevent the spread of infection. For example, in the retrospective multicentre study by M. Hermet *et al.* [17], 39 adult patients with infectious sacroiliitis have been shown to be effective with conservative antibiotic treatment in 70-80% of cases without complications, while surgery is reserved for abscesses or osteomyelitis.

For patients with purulent arthritis (stage 3 according to ASAS), where articular cartilage destruction was observed, economical resection of the sacroiliac joint in combination with postoperative infusion and antibacterial therapy ensured the elimination of the inflammatory process in all 9 cases. This approach was justified by the literature data, so L.S. Briongos-Figuero *et al*. [18] emphasised the need for surgical intervention in case of destructive changes to prevent chronisation of the process and to reduce the risk of sepsis. In a recent multicentre study of infectious sacroiliitis in children and adults, M. Cahueque *et al.* [19] noted that surgical rehabilitation with abscess drainage improves prognosis in patients with extensive infection, reducing the risk of relapse by up to 10-15%.

The results of treatment of patients in the group with panarthritis (stage IV according to ASAS criteria) who underwent radical resection with opening of purulent abscesses, drainage and antiseptic lavage emphasise the risks of septic complications, especially in bilateral lesions, which is confirmed by contemporary studies: in the case of *Salmonella*-associated infectious sacroiliitis of postgastroenteritis origin, timely surgical intervention with antibiotics is key to preventing multiple organ failure. Long-term results showed the advantages of radical treatment over symptomatic treatment, which prevents a chronic course with frequent exacerbations. However, the presence of complications such as ligature fistulas and pelvic organ dysfunction indicates the need for improved techniques, including prevention of vascular damage and enhanced bacteriological control. No less important in the successful outcome of treatment is the possibility of early instrumental diagnosis. Thus, W. Feki *et al.* [20] focused on the role of timely use of MRI and CT, which reduces the frequency of chronic forms. Data by I.K. Venher *et al*. [20] also emphasised that systemic disorders, in particular, endothelial dysfunction and increased coagulation activity in patients with connective tissue dysplasia, can significantly increase the risk of postoperative thrombotic complications, which requires careful monitoring and prevention. In general, the data confirmed the relevance of complex treatment of purulent sacroiliitis in the context of purulent surgery, with an emphasis on aetiopathogenetic factors such as postpartum sepsis or haematogenic osteomyelitis, and highlighted the need for a multidisciplinary approach to improve treatment outcomes.

To illustrate the course of purulent sacroiliitis and evaluate the effectiveness of the treatment methods used, a clinical example is given that reflects the manifestations of the disease characteristic of this pathology. Patient R., 29, was hospitalised in the department with complaints of sharp pain in the right sacroiliac joint and right hip. According to the patient, he fell ill seven days ago, when after hypothermia there was pain in the pelvis and an increase in temperature to 39.0°C. On examination, the patient had sharp pain over the right sacroiliac joint and the presence of a fistula with purulent contents. Severe swelling of the right thigh. Movement in the right hip joint was restricted due to pain. Body temperature – 38.5°C. In the general blood test, leukocytosis was 14 · 10x9/L, ESR – 45 mm/h, procalcitonin – 2.2 ng/mL. Computed tomography showed a significant expansion of the joint space with signs of destruction of the articular surface of the right sacroiliac joint (Fig. 1, 2).

Figure 1. CT scan image of a patient with destruction of the sacroiliac joint on the right side
Source: photo by the authors obtained during an instrumental examination

Figure 2. Photographic image of a 3D CT model Lesion of the sacroiliac joint
Source: photo by the authors obtained during an instrumental examination

During contrast CT, contrast fluid spread through the fistula to the sacroiliac joint. On the day of hospitalisation, the patient was prescribed empirical antibacterial therapy with vancomycin intravenously 500 mg, diluted with 10 mL of water for injection twice a day. For detoxification therapy, rheosorbilact was used intravenously at 200 mL twice a day for three days. To improve blood circulation, the patient received intravenous drip of pentoxifylline 2% solution at 5.0 mL diluted in 200.0 mL of saline solution for 10 days. A diagnostic puncture of the soft tissues of the right thigh was performed, during which pus was extracted. After preoperative preparation, surgical rehabilitation of the purulent focus with "window" resection of the sacroiliac joint and opening of purulent abscesses in the right thigh area was performed (Fig. 3).

In the postoperative period, the wounds were constantly washed with antiseptics by the installation of through drainage tubes (Fig. 4). The complex treatment, including drug therapy and dressings with active flushing of drainage tubes, contributed to wound healing. The patient was discharged in a satisfactory condition for further rehabilitation.

Figure 3. Resection of the right sacroiliac joint and opening of purulent abscesses between the muscles along the back of the thigh
Source: photo by the authors obtained during surgical treatment

Figure 4. Postoperative wounds with installed drainage tubes
Source: photo by the authors obtained during a clinical examination

The results of treatment are consistent with the data of studies that have emphasised the effectiveness of a combined approach to purulent sacroiliitis. Compared to another clinical case described by X. Li *et al.* [22], purulent sacroiliitis caused by methicillin-sensitive *S. aureus* in a 29-year-old healthy woman with no risk factors, where empirical intravenous therapy for 4 weeks without surgery resulted in complete clinical recovery, but with persistent changes on MRI for months, similar to the case described above, involving antibiotics and infusion therapy with an emphasis on microbiological confirmation to avoid chronicity. Other publication by D. Colatutto *et al.* [23] was based on the outcome of treatment of two patients with post-COVID sacroiliitis, showed spontaneous improvement in symptoms when taking NSAIDs, but with persistent bone marrow oedema visualised on MRI for almost a year, highlighting the role of long-term monitoring and the possible impact of long-term viral persistence on the immune response, which resonates with the author's observations on the need for a multidisciplinary approach to prevent septic complications.

These sources have shown that early imaging (MRI/CT) and adapted therapy (starting from 4 weeks of antibiotics) reduce the risk of sepsis, although in some cases they lead to a chronic process. Therefore, the emphasis on timely microbiological diagnostics and correction of treatment in accordance with the results obtained plays a key role in the favourable prognosis. In addition, these clinical examples demonstrated the need for individualisation of therapeutic tactics, because with successful clinical recovery, long-term residual changes in MRI data are possible, which require extended supervision and multidisciplinary support.

CONCLUSIONS

Analysis of literature sources and obtained clinical data indicates that when choosing the method of treatment of

purulent sacroiliitis, it is necessary to consider various forms of joint damage and surrounding tissues, since the disease can manifest itself in both aseptic and purulent forms with varying degrees of severity. It was found that the severe condition of patients, when the disease becomes septic in nature with signs of intoxication, fever and severe pain in the lower back, is a direct indication for immediate resection of the sacroiliac joint and the opening of purulent abscesses. The study emphasised that in such cases, constant bacteriological monitoring is necessary to determine the antibiotic resistance of microorganisms, which allows adapting therapy and avoiding the spread of infection. In addition, the analysis of clinical cases proved that the delay in surgical intervention significantly increases the risk of chronisation of the process, contributing to the development of persistent inflammatory changes and complications, such as abscesses or osteomyelitis. Therefore, early intervention with bacteriological control optimises treatment outcomes, reducing the likelihood of relapses and improving the prognosis for patients.

A combined strategy that combines antibiotic therapy with surgical techniques such as drainage and resection has been found to avoid long-term complications, including chronic pain, joint dysfunction, and systemic septic manifestations. Clinical guidelines based on case reviews indicate the importance of an individual approach, depending on the aetiology (e.g. bacterial, tuberculosis, or other specific), with an emphasis on conservative methods for the early stages and surgery for purulent forms. Overall, systematic analysis has shown that timely diagnosis using MRI, CT, and laboratory tests is key to success, minimising the invasiveness of interventions and improving patients' quality of life. Prospects for further research include the need for high-quality randomised clinical trials to establish clear diagnostic and treatment protocols, comparison of conservative methods (antibiotics with drainage) with minimally invasive surgical techniques such as joint arthroscopy, identification of potential in the study of new antibiotics considering the growth of resistance, and the role of biomarkers for early identification of septic forms.

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Диференційована тактика хірургічного лікування гнійного сакроілеїту залежно від клініко-рентгенологічної стадії за ASAS

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Анотація. Гнійне ураження крижово-клубового суглоба (сакроілеїт) є тяжкою хірургічною патологією опорно-рухового апарату та вимагає оперативного лікування в умовах відділення гнійної хірургії. Метою було проаналізувати тактику хірургічного лікування гнійного сакроїлеїту в комплексі з інфузійною та антибактеріальною терапією залежно від клініко-рентгенологічної форми захворювання. Досліджено 27 пацієнтів з гнійним сакроїлеїтом. Розподіл пацієнтів відбувся за формами: II стадія ASAS – 40,7 %, III стадія ASAS – 33,3 %, IV стадія ASAS (панартрит) – 26,0 %. В залежності від форм пацієнти отримували комбіновану терапію: консервативне лікування (антибіотики, блокади, інфузії), економна або радикальна резекція суглоба з дренуванням, бактеріологічний контроль, дезінтоксикація. 11 (40,7 %) пацієнтів з синовітом, які лікувались лише консервативно та 9 (33,3 %) пацієнтів з артритом, які мали додатково економну резекцію, повністю одужали. Серед 7 (25,9 %) пацієнтів з панартритом, які перенесли радикальну резекцію, у 1 розвинувся септичний шок, що призвело до летальних наслідків, 3 – перенесли повторні операції через лігатурні нориці. 25 (92,5 %) пацієнтів – повне одужання, 1 – періодичні загострення. Виявлено, що лікування повинно враховувати форму захворювання; негайна резекція при септичному перебігу з бакконтролем зменшує хронізацію та рецидиви, а комбінована стратегія ефективна для уникнення ускладнень, але потребує ранньої діагностики та мультидисциплінарного підходу. Отримані результати підтвердили доцільність диференційованого підходу до вибору хірургічної тактики лікування гнійного сакроілеїту залежно від стадії за ASAS, що може бути враховано при розробці клінічних протоколів

Ключові слова: кістки тазу; антибіотикотерапія; крижово-клубовий суглоб; панартрит; септичні ускладнення

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Features of adipokine-mediated myocardial injury in patients with ST-segment elevation myocardial infarction

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Abstract. The aim of the study was to determine the features of adipokine-mediated myocardial injury in patients with ST-elevation myocardial infarction and excess body weight/obesity by assessing the relationship between leptin levels and metabolic disturbances with the severity of atherothrombosis and the severity of the course of acute coronary syndrome according to laboratory and instrumental data. A single-centre prospective cohort study was conducted, which included 120 patients with ST-segment elevation myocardial infarction, who were divided into three groups according to the body mass index: group 1 – excess body weight (25.0-29.9 kg/m², n = 42); group 2 – obesity (⩾ 30 kg/m², n = 34); group 3 – normal body mass index (18.5-24.9 kg/m², n = 44). In the obesity group, the highest concentrations of leptin (57.27 ± 4.1 ng/mL) and troponin I (4.09 ± 4.33 ng/mL) were found, which significantly exceeded the indicators of the other groups (ANOVA $p < 0.001$). A strong positive relationship was established between the body mass index and leptin ($r = 0.87$; $p < 0.001$) and between leptin and troponin I ($r = 0.46$; $p = 0.008$), which indicated the functioning of a single adipokine-apoptotic axis in the context of myocardial injury. Instrumental methods confirmed a more severe nature of myocardial damage in obesity: lower left ventricular ejection fraction (46.3 ± 6.2%), higher left ventricular mass index (131 ± 22 g/m²), increased wall thickness, the greatest elevation of the ST segment (4.88 ± 2.10 mm; ANOVA $p = 0.013$), higher frequency of three-vessel lesion (28.6%), and maximal values according to the SYNTAX scale (24.5 ± 8.9 points; $p < 0.001$). Multiple regression analysis confirmed that the body mass index ($\beta = 0.42$; $p < 0.001$), SYNTAX ($\beta = 0.36$; $p = 0.004$), and reduced ejection fraction ($\beta = -0.33$; $p = 0.008$) are independent predictors of increased levels of troponin I

Keywords: obesity; excess body weight; leptin; acute coronary syndrome; coronarography; ejection fraction; body mass index

INTRODUCTION

ST-elevation myocardial infarction (STEMI) remains a leading cause of mortality, and concomitant obesity and other comorbid conditions form a proatherogenic and proinflammatory phenotype that deepens ischemic and reperfusion injury. Adipose tissue under metabolic dysfunction produces adipokines (leptin, resistin) and cytokines that contribute to endothelial dysfunction, thrombus formation, activation of caspases, and death of cardiomyocytes. Despite the available data from modern scientific research, the study of the relationship between adipokine levels and the nature of atherothrombosis and the degree of myocardial injury in STEMI according to instrumental diagnostic data remains relevant.

Recent studies on adipokine-dependent myocardial injury emphasised the persistent increase in obesity among adults worldwide up to 2022, which highlighted the importance of obesity-related myocardial injury for public health. As indicated in the work of O.Ye. Labinska [1] a clear association was established between obesity and the occurrence of cardiovascular diseases due to the fact that adipose tissue produces more than 100 adipokines, which include interleukins, prostaglandins, tumour necrosis factor alpha, leptin, adiponectin, angiotensinogen, resistin. Certain chemokines expressed by adipose tissue, including caspase-9, play an important role in attracting inflammatory leukocytes to adipose tissue, which is a key link in the development of obesity-associated inflammatory processes. According to the results of the study by V.M. Zhebel & O.L. Starzhynska [2], oxidative stress plays a special role in acute coronary syndrome (ACS), in particular, it is the lead-

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ing link in the pathogenesis of reperfusion injury of the myocardium. The products of free radical oxidation can initiate processes of cardiomyocyte death and be responsible for 50% of the final size of the necrotic area in ACS, as well as the occurrence of reperfusion arrhythmias and systolic microvascular dysfunction.

The involvement of leptin in inflammatory processes underlying atherosclerosis has raised interest in its potential as a biomarker of cardiovascular diseases, particularly among the authors A. Ismaiel *et al.* [3], who noted that previous studies demonstrated a positive correlation between increased leptin levels and the development of ischemic heart disease (IHD) and, as a consequence, ACS. It is known that elevated leptin levels in patients with ACS and concomitant metabolic syndrome may indicate that leptin may serve both as a biomarker and a potential therapeutic target for risk stratification and treatment of patients with STEMI. At the same time, in the work of B. Du *et al.* [4], it is emphasised that during the period of myocardial ischemia the process of apoptosis occurs slowly; however, after the transition to the reperfusion phase, oxidative stress, inflammatory reactions, and mitochondrial damage intensify, leading to activation of death receptors such as TNF-R and Fas. This activation triggers both external (through caspase-9, caspase-8, caspase-3) and internal (through cytochrome c) pathways of apoptosis.

Translational reviews by S.H. Liu *et al*. [5] confirmed that chronic hyperleptinemia in obesity promotes inflammation, fibrosis, autonomic dysregulation, and metabolic remodelling, thereby creating susceptibility to unfavorable postischemic remodelling of the myocardium. However, due to the phenomenon of the "obesity paradox", in acute vascular catastrophes obesity plays a positive role in greater adaptive mechanisms during ischemia and hypoxia of the myocardium. G. Ndrepepa *et al*. [6] demonstrated that leptin derived from epicardial or pericardial adipose tissue induces apoptosis of cardiomyocytes and disrupts myocardial homeostasis, which provides a plausible paracrine link between regional obesity and the biology of infarction. In particular, the study by T. Vilariño-García *et al*. [7] described that in most cases hyperleptinemia is associated with adverse cardiovascular outcomes. In fact, leptin may be produced by the heart itself to function as an autocrine/paracrine factor. Nevertheless, documented cases in rodent studies indicated that animals with leptin deficiency may exhibit a cardioprotective effect. This protection is attributed to coronary artery vasodilation, activation of endothelial nitric oxide synthase, and activation of endothelial progenitor cells. The findings of R.A. Byrne *et al*. [8] within the structure of the European recommendations of 2023 indicated that the morphological characteristics of the coronary arteries after STEMI are significantly altered by cardiometabolic comorbid conditions and systemic inflammation, despite advances in primary percutaneous coronary intervention (PCI) and supportive pharmacotherapy.

The longitudinal cohort study by L. Liu *et al.* [9] demonstrated that lower levels of adiponectin and higher levels of leptin are independently associated with higher levels of residual cholesterol and its progression, and that atherogenic features are closely related to plaque burden and vulnerability. According to the results of the study by D. Skrypnik *et al.* [10], an elevated serum leptin level is significantly associated with IHD. Due to the growing amount of scientific evidence, leptin has begun to be considered not as a marker but as a trigger of IHD, mediating atherosclerotic processes independently of traditional cardiovascular risk factors and of body weight status. Higher serum leptin concentrations were associated with arterial stiffness and an increased number of stenotic coronary arteries in patients with IHD. Acute myocardial infarction also significantly increases leptin concentration in the blood. Dysregulation of leptin metabolism has a negative impact on the heart, affecting cardiac remodelling, contractile function, and cardiac metabolism. In addition, leptin enhances platelet activation in patients with IHD and alters the morphology of the left ventricle [11].

In the work of J. Wang *et al*. [12], it is reported that a significant correlation was found between leptin and several indicators related to heart rate, arterial pressure, peripheral vascular resistance, the pumping and contractile function of the heart, as well as pulmonary ventilation function. The angiographic complexity and spread of disease in ACS are more consistently associated with high-risk clinical profiles. K. Skalsky *et al.* [13] identified numerous predictors of multivessel disease, including dyslipidemia, renal dysfunction, and a history of heart failure, factors that often coexist with obesity.

Aim of the study – to evaluate the effect of obesity and overweight on adipokine-dependent mechanisms of myocardial damage in patients with ST-segment elevation myocardial infarction.

MATERIALS AND METHODS

A single-centre prospective cohort study was conducted from 2022 to 2025, covering 120 hospitalised patients with ST-segment elevation myocardial infarction at the Zaporizhzhia Regional Clinical Hospital. Diagnosis, reperfusion strategy, and inpatient treatment were carried out in accordance with the recommendations of R.A. Byrne *et al.* [8] and the national unified clinical protocol of the Ministry of Health of Ukraine [14]. The study protocol No. 10 dated 18.09.2022 received approval from the institutional ethics committee, and written informed consent was obtained from all participants before enrollment. The study was conducted in accordance with the Declaration of Helsinki [15].

Inclusion criteria were patient age from 18 to 90 years, the presence of confirmed ST-elevation myocardial infarction according to symptoms, typical ischemic chest pain, ST-segment elevation on 12-lead electrocardiography (ECG), and elevated levels of high-sensitivity cardiac troponin I, availability of general clinical laboratory data, and performance of echocardiography. All patients underwent primary percutaneous coronary intervention as the reperfusion method. A mandatory condition for inclusion was the signing of informed consent to participate in the study. Exclusion criteria included myocardial infarction without ST-segment elevation, decompensated chronic renal or hepatic insufficiency, acute surgical pathology of non-cardiac origin, active inflammatory diseases, confirmed sepsis, malignant neoplasms, or refusal to participate in the study.

All patients were stratified according to body mass index (BMI) in accordance with the generally accepted classification according to the Centers for Disease Control and

Prevention [16]: group 1 included patients with overweight (25.0-29.9 kg/m², n = 42), group 2 included patients with obesity (≥ 30.0 kg/m², n = 34), and group 3 represented the control group with normal BMI (18.5-24.9 kg/m², n = 44). Standard 12-lead electrocardiograms were recorded at admission to determine the infarct-related artery, to quantify cumulative ST-segment elevation, and to detect reciprocal changes or rhythm disturbances. The degree of ischemic injury was assessed using an ECG-based injury index representing the total sum of ST elevation in all affected leads.

Transthoracic echocardiography was performed within 24-48 hours after hospitalisation using standard two-dimensional and Doppler imaging techniques. Left ventricular end-diastolic and end-systolic volumes were measured, and ejection fraction was calculated using the modified biplane Simpson method. In addition, the thickness of the interventricular septum (IVS) and the posterior wall of the left ventricle, as well as the left ventricular myocardial mass index, were assessed. All patients underwent coronary angiography to identify the infarct-related artery, to assess the type and morphology of coronary lesions, and to evaluate blood flow before and after the intervention according to the Thrombolysis in Myocardial Infarction (TIMI) scale [17]. The number of affected vessels and the complexity of coronary artery disease were quantified using the SYNTAX score [18] calculated by a specialised scoring calculator. Optimal reperfusion was defined as achieving TIMI 3 flow after PCI.

Statistical analysis included tests for normality of data distribution using the Shapiro-Wilk test and for homogeneity of variances using Levene's test. For comparisons among the three BMI groups, one-way analysis of variance (ANOVA) with Tukey's post-hoc test was applied for normally distributed variables, while the Kruskal-Wallis test with Dunn's correction was applied for non-parametric data. For comparisons between two groups, an unpaired t-test or the Mann-Whitney U test was used, as appropriate. Correlations between variables were assessed using Pearson or Spearman coefficients, with a two-tailed p-value < 0.05 considered statistically significant. Statistical analysis was based on measurement of mean values and standard deviation across the three groups. Anthropometric data (age, height, weight, sex), laboratory indicators (quantitative troponin I level, immunoassay data via ELISA assessing levels of caspase-9 and leptin), and instrumental findings (electrocardiographic data – ST elevation amplitude in leads; echocardiographic data – ejection fraction by Simpson, left ventricular wall thickness, IVS; coronary angiographic data – degree of stenosis of the left coronary artery, circumflex artery, left anterior descending artery, and right coronary artery) were evaluated. To determine independent predictors of high-sensitivity cardiac troponin I levels, a multiple linear regression model was constructed, including BMI, leptin, caspase-9, age and sex as covariates. All statistical analyses were performed using Statistica 13 and Microsoft Excel 2016.

RESULTS AND DISCUSSION

Demographic and clinical-anamnestic characteristics. The mean age of the patients included in the study was 64.9 ± 12.86 years. There are no significant differences in this indicator were found stratified by BMI: in the excess body weight (EBW) group, the mean age was 65.36 ± 12.64 years; in the obesity group, 63.85 ± 11.83 years; and in the control group, 65.27 ± 14.03 years. Preliminary analysis using the Shapiro–Wilk test demonstrated no significant deviations from the normal age distribution in all three groups ($p > 0.05$), and Levene's test showed homogeneity of variances ($p > 0.05$), allowing the use of ANOVA. The difference between the mean age values across the BMI groups did not reach statistical significance ($p > 0.05$), indicating the comparability of the samples by age.

Gender analysis revealed marked age differences between men and women. In all three groups, male patients were statistically significantly younger than female patients. The parametric t-test was used to compare age between genders. In particular, in the first group, the mean age of men was 58.96 ± 10.45 years, whereas that of women was 75.75 ± 8.23 years (a difference of 16.79 years, $p < 0.01$ according to the unpaired t-test). In the second group, the mean age of men was 60.08 ± 11.62 years versus 72.90 ± 6.28 years in women (a difference of 12.82 years, $p < 0.02$), and in the third group, 59.69 ± 13.35 years in men and 73.33 ± 10.93 years in women (a difference of 13.64 years, $p < 0.02$). In terms of sex distribution, the sample was generally characterised by a predominance of men – 76 individuals vs 44 women. The proportion of men increased in parallel with rising BMI: in the excess body weight group – 61.9%, in the obesity group – 70.6%, and in the control group – 59.1%. Gender-age data of the participants were presented in Figure 1.

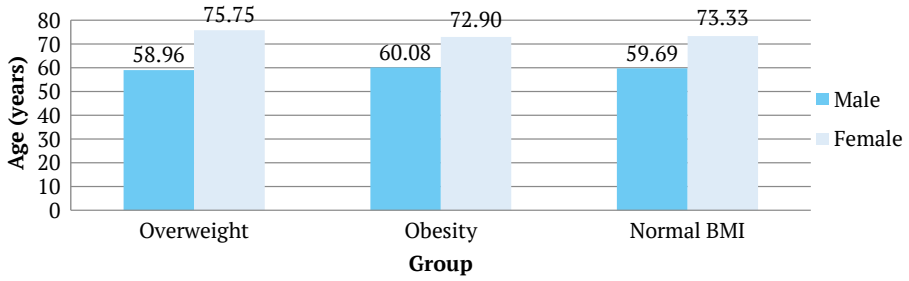

Figure 1. Gender-age characteristics of the sample by groups

Source: author's research

Analysis of sex distribution among the three groups using Pearson's χ^2 test showed no statistically significant differences ($\chi^2 = 3.98$; df = 2; $p = 0.13$). An additional trend test demonstrated only a tendency toward an increasing proportion of men with rising BMI ($p \approx 0.08$), which did not reach the threshold for statistical significance. Pairwise

comparisons of proportions (using χ^2 or Fisher's exact test, depending on expected frequencies) likewise revealed no significant differences between individual groups ($p > 0.29$). At the same time, for the obesity group, elevated relative odds for male sex were calculated (OR = 1.67; RR = 1.19) compared with the control group, reflecting a clinically noticeable, although statistically nonsignificant, tendency toward a higher proportion of men in this cohort.

Biochemical parameters and adipokine profile. Biochemical profiling demonstrated a pronounced metabolic gradient between the groups. The mean leptin concentration was 36.60 ± 2.9 ng/mL in group 1, 57.27 ± 4.1 ng/mL in group 2, and 28.92 ± 2.5 ng/mL in the control group. With acceptable values ($p > 0.05$), one-way ANOVA was used for between-group comparison, which revealed statistically significant differences in mean leptin levels among the three groups ($p < 0.001$). Subsequent Tukey post-hoc analysis showed that leptin levels in the obesity group were significantly higher compared with both the control group and the EBW group ($p < 0.05$ for both comparisons), and patients with EBW also had higher values compared with controls ($p < 0.05$). The mean troponin I levels across the groups were as follows: group 1 – 3.46 ± 2.17 ng/mL, group 2 – 4.09 ± 4.33 ng/mL, group 3 – 2.54 ± 2.19 ng/mL. Correlation analysis demonstrated a strong positive relationship between leptin and BMI ($r = 0.87$; $p < 0.001$), and a moderate positive relationship between leptin and troponin I ($r = 0.46$; $p = 0.008$).

Caspase-9 concentrations mirrored the leptin gradient: maximal values in the obesity group, intermediate values in the EBW group, and minimal values in the normal BMI group. Correlation analysis showed an exceptionally strong positive relationship between leptin and caspase-9 ($r \approx 0.99$; $p < 0.001$), indicating their parallel increase within a single adipokine-apoptotic axis. Comorbid conditions were represented predominantly by arterial hypertension (AH) and type 2 diabetes mellitus (T2DM). The prevalence of AH was 73.3%, and that of T2DM was 19.8%, consistent with the typical profile of patients with STEMI. Comparison of AH and T2DM frequencies between BMI groups using the χ^2 test did not show statistically significant differences ($p > 0.05$), although the proportion of such conditions was slightly higher in the obesity group.

ECG and echocardiographic parameters. ECG analysis revealed differences reflecting the degree of ischemic and reperfusion injury of the myocardium. The QRS ECG complex duration in patients with obesity was 101 ± 13 ms, whereas in the control group it was 92 ± 10 ms. According to results of the unpaired t-test, QRS ECG complex prolongation in the obesity group was statistically significant ($p = 0.016$). The magnitude of ST-segment elevation – a key marker of acute ischemia – also differed substantially between BMI groups. The mean values were as follows: 3.46 ± 1.23 mm in the EBW group, 4.88 ± 2.10 mm in the obesity group, and 3.22 ± 1.89 mm in the normal BMI group. The maximal recorded ST-elevation values were 6.8 mm in a patient with obesity, 5.3 in a patient with EBW, and 5.1 mm in the control group.

The Shapiro-Wilk test showed no significant deviations from normal distribution of ST elevation in any group ($p > 0.05$), and Levene's test confirmed comparable variance ($p > 0.05$). This allowed the use of one-way ANOVA, which demonstrated statistically significant between-group differences ($F = 4.62$; $p = 0.013$). Subsequent Tukey post-hoc testing showed that patients with obesity had significantly higher ST-elevation compared with the control group ($p = 0.009$) and with the EBW group ($p = 0.018$). No statistically significant difference was found between the EBW group and the control ($p = 0.74$). Correlation analysis demonstrated a positive association between the degree of ST elevation and biochemical markers of myocardial injury and metabolic stress: troponin I ($r = 0.57$; $p = 0.003$) and leptin ($r = 0.42$; $p = 0.015$). For these variables, Pearson's correlation coefficient was applied, given the approximate normality of distributions and linearity of relationships. The presented statistical findings were shown in Figure 2 in the form of box plots. Box plots showed median values (horizontal line), interquartile ranges (boxes), and range (whiskers).

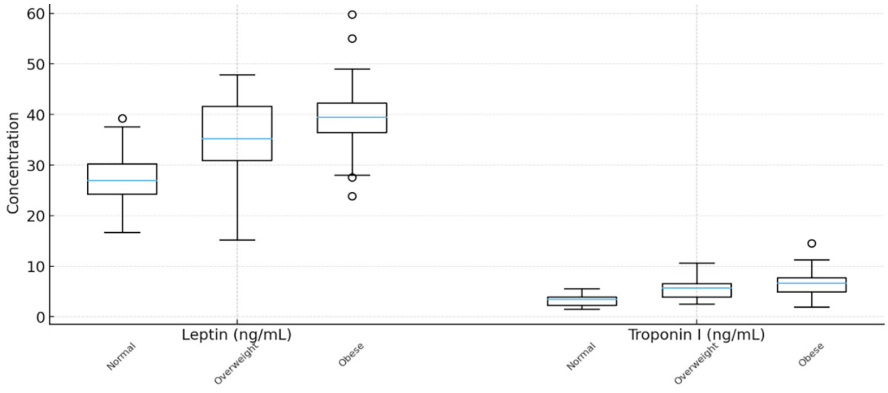

Figure 2. Distribution of serum leptin and cardiac troponin I levels across BMI categories in patients with STEMI
Source: author's research

Echocardiographic data confirmed progressive deterioration of systolic function and structural myocardial remodelling with increasing BMI. The left ventricular ejection fraction (LVEF) was 46.3 ± 6.2% in patients with obesity, 51.8 ± 5.9% in individuals with EBW, and 55.9 ± 5.6% in the control group. The Shapiro-Wilk test confirmed normal distribution of LVEF, and Levene's test indicated homogeneity of variances ($p > 0.05$), allowing the use of ANOVA. Between-group differences in LVEF were statistically significant ($p < 0.001$), and Tukey post-hoc analysis

demonstrated a consistent decrease in LVEF from the control group to EBW and further to obesity (all $p < 0.05$ in pairwise comparisons). Parallel to the decline in LVEF, an increase in the left ventricular mass index (LVMI) was observed: 131 ± 22 g/m² in the obesity group, 112 ± 17 g/m² in the EBW group, and 97 ± 14 g/m² in the control group ($p < 0.001$ by ANOVA). A similar pattern was observed for left ventricular wall thickness: IVS – 11.3 ± 1.2 mm in the obesity group, posterior wall – 11.4 ± 1.3 mm, with statistically significant differences compared with the other two groups ($p < 0.001$). All calculated echocardiographic parameters are presented in the summary diagram shown in Figure 3.

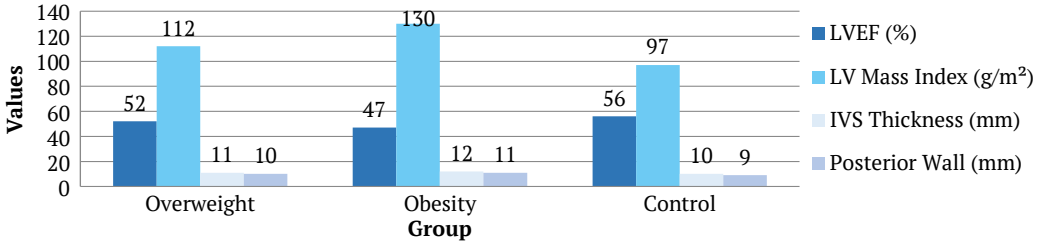

Figure 3. Echocardiographic parameters: LVEF, LVMI, posterior wall thickness, IVS across study groups
Source: author's research

Correlation analysis demonstrated inverse associations between LVEF and leptin ($r = -0.47$; $p = 0.009$), indicating that each incremental rise in leptin concentration was accompanied by a measurable reduction in systolic performance. A similarly strong negative relationship was identified between LVEF and BMI ($r = -0.58$; $p < 0.001$), with regression analysis showing that a 1 kg/m² increase in BMI was associated with an average 0.6-0.8% decrease in LVEF. Moreover, multivariate modelling confirmed that both BMI ($\beta = -0.52$; $p < 0.001$) and leptin ($\beta = -0.39$; $p = 0.014$) independently contributed to the decline in ejection fraction, explaining nearly 42% of the total variance in LVEF. These findings clearly demonstrated that rising body weight and adipokine dysregulation exert a quantifiable negative impact on left ventricular systolic function in patients with acute coronary syndrome.

Angiographic and reperfusion parameters. According to coronary angiography findings, multivessel disease was more frequently recorded in patients with obesity. The incidence of triple-vessel disease was 28.6% in the obesity group, 19.1% in the EBW group, and 15.9% in the control group ($p = 0.042$ according to Pearson's χ^2 test), indicating a greater prevalence of diffuse atherosclerotic involvement in obesity. The mean SYNTAX score, reflecting the anatomical complexity and extent of coronary atherosclerosis, was significantly highest in the obesity group. Based on the angiographic data obtained after coronary angiography, the SYNTAX score values were 24.5 ± 8.9 in patients with obesity, 18.7 ± 7.2 in individuals with EBW, and 14.2 ± 5.6 in the control group ($p < 0.001$ by ANOVA). Tukey post-hoc analysis demonstrated significant differences among all three groups ($p < 0.05$), confirming a progressive increase in anatomical complexity of coronary artery disease with rising BMI.

Correlation analysis revealed a strong positive association between the SYNTAX score and leptin level ($r = 0.64$; $p < 0.001$). The correlation coefficient between SYNTAX and BMI was $r = 0.71$ ($p < 0.001$). These correlations indicate a close interplay between the metabolic and anatomical components of atherosclerosis. Reperfusion parameters according to the TIMI scale showed that preprocedural blood flow TIMI 0-1 was more frequently observed in patients with obesity (78.6%) compared with the control group (63.6%), although these differences did not reach statistical significance according to the χ^2 test ($p > 0.05$). Restoration of full coronary blood flow TIMI 3 after primary PCI was 85.7% in the obesity group, 91.0% in the EBW group, and 93.2% in the control cohort.

Multivariable determinants of myocardial injury. To integrate the obtained data, a multiple linear regression analysis was performed with troponin I concentration as the dependent variable. According to the analysis, BMI showed $\beta = 0.42$ ($p < 0.001$), the SYNTAX score $\beta = 0.36$ ($p = 0.004$), and reduced LVEF $\beta = -0.33$ ($p = 0.008$). These factors represented independent predictors of troponin I level, and the constructed model explains 63% of the total variance of this indicator ($R^2 = 0.63$). This indicated that metabolic (BMI), anatomical (SYNTAX score), and functional (LVEF) parameters jointly contribute to the extent of myocardial necrosis in STEMI. A summary of the multivariable statistical analysis and linear regression results for predictors of troponin I levels was presented in Table 1.

Table 1. Multiple linear regression for determinants of adipokine-mediated myocardial injury and troponin I

Predictor	β coefficient	Standard error	p-value
BMI (kg/m²)	0.42	0.08	<0.001
SYNTAX score	0.36	0.10	0.004
LVEF (%)	–0.33	0.11	0.008
Leptin (ng/mL)	0.29	0.09	0.013
Caspase-9 (pg/mL)	0.25	0.08	0.021
Age (years)	0.10	0.06	0.18
Low-Density Lipoprotein Cholesterol (mmol/L)	0.12	0.07	0.14

Source: author's research

The obtained results indicated that even with a similar mean age across BMI groups, men with STEMI manifest the disease at a substantially younger age than women. Age-related trends point to an earlier manifestation of STEMI in patients with obesity in this study, which is consistent with the findings of D. Demirci *et al.* [19], who reported that patients with ACS and severe obesity were younger than those with ACS in the classes of class I obesity, EBW, and normal weight (52.8 ± 9.9 versus 55.3 ± 10.9, 56.8 ± 11.4, and 61.4 ± 14.2, respectively; $p < 0.001$). BMI showed a strong inverse linear association with earlier age of first ACS. Patients with EBW, class I obesity, and severe obesity experienced their first ACS episode earlier than normal-weight patients by 3.9, 6.1, and 7.7 years, respectively ($p < 0.001$).

In the study by A.J. Fischer *et al.* [20], similar gender and age trends in STEMI were confirmed. Women accounted for 32.8% of STEMI cases (n = 5714). They were older than men (women: median 74 years, interquartile range [IQR] 22; men: 60 years, IQR 19). Among 11,629 patients with STEMI in the study by J. Schmucker *et al.* [21], 2.3% had severe obesity. These patients were more frequently women and were on average 8.6 years younger than normal-weight patients (57.8 ± 12 versus 66.4 ± 14 years, $p < 0.01$). In author's study, the identified metabolic gradient (increasing leptin, troponin I, and caspase-9 with rising BMI) confirms that obesity forms an unfavourable prognostic STEMI phenotype. The strong correlation of leptin with BMI and troponin, as well as the nearly linear association between leptin and caspase-9 ($r \approx 0.99$), supports the concept of adipokine-mediated myocardial injury through activation of mitochondrial apoptosis.

In the study by O.Ye. Labinska [1], the serum leptin level upon hospital admission in patients with STEMI and normal body weight was 6.65 ± 0.55 ng/mL, in individuals with STEMI and EBW – 16.01 ± 1.73 ng/mL, and in patients with STEMI and class I-III obesity – 38.64 ± 3.1 ng/mL. In patients with EBW and obesity, these values were significantly higher than in normal-weight individuals. Similar findings were reported in the by A. Ismaiel *et al*. [3], where leptin levels were measured in serum or plasma and compared between patients diagnosed with ACS and healthy controls. The pooled analysis of leptin levels resulted in a mean difference of 10.508 ng/mL (95% CI 3.670-17.346). Significant heterogeneity was also observed, with $I^2 = 98.63\%$ and a p-value < 0.001.

ECG findings (greater ST elevation and QRS prolongation in patients with obesity), combined with higher troponin I levels, reflect a larger volume of ischemic and necrotic myocardial injury. The positive correlations between ST elevation, troponin I, and leptin indicate a link between metabolic inflammation and the electrical manifestations of acute myocardial necrosis. Echocardiographic data (reduced LVEF, increased LVMI, thickening of left ventricular walls) are consistent with the pattern of concentric hypertrophy and maladaptive remodelling in obesity. In this context, earlier studies by I.O. Yastremska [22] have shown that endothelial dysfunction and oxidative stress substantially aggravate myocardial injury in acute myocardial infarction, especially when combined with metabolic syndrome, highlighting the pathogenic relevance of metabolic-vascular interactions. The inverse correlations between LVEF and leptin, as well as LVEF and BMI, support the hypothesis of dose-dependent systolic dysfunction worsening against the background of hyperleptinemia and metabolic stress, and align with the findings of O.Ye. Labinska [1], where it was shown that as body weight increased, there was a tendency toward reduced LVEF in patients with obesity (group III) compared with those of normal weight and EBW ($p1\text{-}2 = 0.69$, $p1\text{-}\text{–}3 = 0.32$, $p2\text{-}3 = 0.57$). Among patients with obesity, left ventricular dimensions were significantly larger compared with the control group ($p1\text{-}2 < 0.05$).

In the study by K. Puchałowicz *et al.* [23], the mean levels of adiponectin, leptin, and resistin were 5.25 ± 3.22 μg/mL, 15.3 ± 17.9 ng/mL, and 7.81 ± 3.28 ng/mL, respectively. Significantly higher adiponectin levels were observed in patients with heart failure. The authors also reported an association between adiponectin and echocardiographic parameters. Author's data demonstrated a different pattern: although adiponectin was not directly assessed, patients with obesity exhibited substantially higher levels of leptin and caspase-9, accompanied by reduced LVEF and increased LVMI. Whereas adiponectin played a central role in the work of K. Puchałowicz *et al*., in this study the dominant factor was hyperleptinemia, which is more characteristic of obesity and exerts a stronger proinflammatory effect.

According to coronary angiography results in the study by O. Labinska *et al.* [24], multivessel coronary artery lesions were significantly more common in individuals with EBW and obesity. In patients with obesity, hemodynamically significant lesions were most frequently localised in the mid-segment of the left anterior descending artery ($p < 0.05$), and there was also a tendency toward more frequent chronic occlusions ($p = 0.08$). Author's results align with these findings, indicating that the higher frequency of triple-vessel involvement, higher SYNTAX scores in the obesity group, and strong correlations between SYNTAX, BMI, and leptin demonstrated that obesity is associated not only with a more severe course of ACS but also with anatomically more complex and diffuse coronary artery disease.

According to the data reported by K. Samak *et al*. [25], serum leptin levels were significantly higher in patients with high SYNTAX scores compared with those with low and intermediate scores ($p < 0.05$). A positive association was identified between serum leptin concentrations and the SYNTAX score. Individuals classified into the high SYNTAX score category were significantly older (61.8 ± 10.63 years) and exhibited a higher body mass index (38.5 ± 7.04 kg/m²) compared with patients in the intermediate (54.8 ± 9.62 years; 34.9 ± 5.19 kg/m²) and low (48.8 ± 9.36 years; 32.9 ± 5.4 kg/m²) SYNTAX score groups. In parallel, leptin concentrations increased progressively with rising anatomical complexity of coronary artery disease. Specifically, mean serum leptin levels were highest in the high SYNTAX group (12.6 ± 5.34 ng/mL), exceeding those observed in the intermediate (9.6 ± 3.3 ng/mL) and low (7.5 ± 2.66 ng/mL) SYNTAX score groups.

In the study by K. Samak *et al*. [25], it was shown that patients with a high SYNTAX score had markedly elevated leptin levels (12.6 ± 5.34 ng/mL) compared with the intermediate- and low-risk groups (9.6 ± 3.3 ng/mL and 7.5 ± 2.66 ng/mL, respectively). Furthermore, the SYNTAX score correlated with leptin, as well as with age, BMI, and traditional cardiovascular risk factors. In this study, a similar relationship between metabolic and anatomical

alterations was observed. The SYNTAX score was higher in patients with obesity (24.5 ± 8.9) compared with those with EBW (18.7 ± 7.2) and normal weight (14.2 ± 5.6), $p < 0.001$. The correlation between the SYNTAX score and leptin was $r = 0.64$ ($p < 0.001$), and the correlation between the SYNTAX score and BMI was $r = 0.71$ ($p < 0.001$). When comparing author's findings with those of K. Samak *et al.*, author's results demonstrated even stronger statistical associations, which may be attributed to the more acute course of STEMI and more pronounced adipokine activation.

Despite this, the achievement of TIMI 3 flow after PCI in most patients across all groups indicates preserved effectiveness of contemporary reperfusion strategies, although microvascular disturbances in obesity may contribute to the "no-reflow" phenomenon and suboptimal restoration of tissue perfusion. Comparable results were demonstrated in the study by A. Mohamed [26], where the frequency of the no-reflow phenomenon in the visceral obesity group included 62 cases in which angiographic flow was less than TIMI III (89.9%), while no cases of angiographic no-reflow were observed in the non-visceral group. Regarding coronary vessel involvement in both groups, single-vessel disease was identified in 24.6% of patients in the obesity group versus 86.4% in the control group. Multivessel disease was found in 75.4% of patients in the obesity group versus 13.6% in the control group. Thus, there was a statistically significant difference between the two groups, with $p = 0.0005$. Leptin, acting through the Ob-Rb receptor, activates proapoptotic signaling pathways (Bax, caspase-9), promotes endothelial dysfunction, reduces the bioavailability of nitric oxide, and enhances the expression of adhesion molecules, thereby exacerbating ischemic and reperfusion injury [3].

The integration of biochemical, echocardiographic, and angiographic data in this study provides a comprehensive pathophysiological understanding of adipokine-mediated myocardial injury. Obesity creates a chronic proinflammatory and proapoptotic environment that predisposes the myocardium to enhanced damage during acute ischemic stress. Upregulation of caspase-9 in patients with obesity and STEMI is likely the result of sustained mitochondrial injury induced by hyperleptinemia and oxidative imbalance. The entirety of the obtained findings allows obesity to be viewed not as a "background" comorbidity but as an active pathogenic factor within the context of adipokine-mediated myocardial injury, determining the depth of myocardial damage in STEMI. The concept of the "obesity paradox", in which some individuals with EBW demonstrate better early survival after myocardial infarction, requires reconsideration: author's data indicate that during longer follow-up, apoptosis, fibrosis, and remodelling predominate, ultimately worsening long-term outcomes.

CONCLUSIONS

The results of this study clearly demonstrated that EBW and obesity are key modifiers of the extent of myocardial injury in ST-elevation myocardial infarction, exerting their influence through adipokine- and apoptosis-mediated mechanisms. Patients with obesity had significantly higher leptin levels (F ANOVA, $p < 0.001$), and Tukey post-hoc testing confirmed significant differences among all groups (all $p < 0.05$). A strong positive correlation was demonstrated between leptin concentration and BMI ($r = 0.87$; $p < 0.001$), as well as between leptin and caspase-9 ($r \approx 0.99$; $p < 0.001$), indicating the formation of a potent adipokine-apoptotic axis. Parallel increases in troponin I ($r = 0.46$; $p = 0.008$) further confirmed that leptin-mediated metabolic activation is closely linked to the degree of cardiomyocyte necrosis.

Instrumental methods were consistent with the biochemical findings and demonstrated progressive myocardial remodelling with increasing BMI. LVEF declined along the gradient "control → EBW → obesity" (ANOVA $p < 0.001$; all Tukey comparisons $p < 0.05$), whereas LVMI and wall thickness were significantly higher in the obesity group ($p < 0.001$). Higher ST-segment elevation ($F = 4.62$; $p = 0.013$) and its correlations with troponin I ($r = 0.57$; $p = 0.003$) and leptin ($r = 0.42$; $p = 0.015$) further emphasised the more pronounced ischemic burden in patients with obesity. Angiographic findings also confirm greater severity of atherothrombotic disease in obesity: the frequency of triple-vessel disease reached 28.6% ($p = 0.042$), and the mean SYNTAX score was significantly highest in this group (24.5 ± 8.9; ANOVA $p < 0.001$; Tukey $p < 0.05$). Substantial correlations between SYNTAX and leptin ($r = 0.64$; $p < 0.001$), as well as SYNTAX and BMI ($r = 0.71$; $p < 0.001$), confirmed a close link between metabolic inflammation and the anatomical complexity of atherosclerotic disease.

Thus, the results confirmed that obesity is not a passive background condition but an active pathophysiological factor that amplifies ischemic myocardial injury through leptin-induced inflammation, increased oxidative stress, and caspase-9 activation. Adipokine dysregulation forms the basis for a more severe course of STEMI, deeper myocardial necrosis, more pronounced systolic dysfunction, and more complex coronary involvement. Promising therapeutic directions for modifying adipokine-mediated myocardial injury may include leptin-receptor inhibitors, mitochondrial-stabilising agents (mitochondria-targeted cardioprotectors), antiapoptotic agents (caspase-9 blockers), and therapies aimed at reducing systemic inflammation (IL-6 antagonists). Future research may focus on validating these mechanisms in larger cohorts and evaluating pharmacological interventions capable of reducing adipoinflammatory and apoptotic burden on the myocardium.

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CONFLICT OF INTEREST

None.

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Особливості адипокін-опосередкованих процесів ушкодження міокарда у пацієнтів з інфарктом міокарда з елевацією сегмента ST

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Анотація. Метою дослідження було визначити особливості адипокін-опосередкованого ушкодження міокарда у пацієнтів з інфарктом міокарда з елевацією сегмента ST та надмірною масою тіла/ожирінням шляхом оцінки зв'язку рівнів лептину й метаболічних порушень із вираженістю атеротромбозу та тяжкістю перебігу гострого коронарного синдрому за лабораторними та інструментальними даними. Проведено одноцентрове проспективне когортне дослідження, яке включало 120 пацієнтів з інфарктом міокарда з підйомом сегмента ST, які були поділені на три групи за індексом маси тіла: група 1 – надмірна вага (25,0-29,9 кг/м², n = 42); група 2 – ожиріння (⩾ 30 кг/м², n = 34); група 3 – нормальний індекс маси тіла (18,5-24,9 кг/м², n = 44). У групі ожиріння виявлено найвищі концентрації лептину (57,27 ± 4,1 нг/мл) та тропоніну I (4,09 ± 4,33 нг/мл), що достовірно перевищували показники інших груп (ANOVA p < 0,001). Встановлено сильний позитивний зв'язок між індексом маси тіла та лептином (r = 0,87; p < 0,001) та між лептином і тропоніном I (r = 0,46; p = 0,008), що свідчило про функціонування єдиної адипокін-апоптотичної осі у контексті ушкодження міокарду. Інструментальні методи підтвердили більш тяжкий характер ураження міокарда при ожирінні: нижча фракція викиду лівого шлуночка (46,3 ± 6,2 %), вищий індекс маси лівого шлуночка (131 ± 22 г/м²), збільшена товщина стінок, найбільша елевація сегмента ST (4,88 ± 2,10 мм; ANOVA p = 0,013), вища частота трисудинного ураження (28,6 %) та максимальні значення за шкалою SYNTAX (24,5 ± 8,9 балів; p < 0,001). Множинний регресійний аналіз підтвердив, що індекс маси тіла (β = 0,42; p < 0,001), SYNTAX (β = 0,36; p = 0,004) та знижена фракція викиду (β = –0,33; p = 0,008) є незалежними предикторами підвищення рівня тропоніну I

Ключові слова: ожиріння; надлишкова маса тіла; лептин; гострий коронарний синдром; коронарографія; фракція викиду; індекс маси тіла

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Clinical and functional effectiveness of nuclear magnetic resonance therapy in the comprehensive treatment of the early stages of gonarthrosis

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Abstract. Gonarthrosis (deforming osteoarthritis of the knee joints) is one of the most common degenerative-dystrophic disorders of the musculoskeletal system, which significantly reduces patients' quality of life and leads to persistent impairment of the functional activity of the lower limbs. In the early stages of the disease, the search for effective, non-invasive and scientifically substantiated therapeutic approaches is particularly important, especially those capable of influencing the regeneration of cartilage and bone tissue structures, reducing pain, and slowing the progression of degenerative changes. The aim of this study was to conduct a clinical assessment of the feasibility of using nuclear magnetic resonance as a therapeutic adjuvant in patients with early-stage gonarthrosis and to determine its effect on the dynamics of key clinical indicators. Within the framework of the study, the results of the comprehensive use of nuclear magnetic resonance therapy alone and in combination with basic treatment methods were analysed in 47 outpatients diagnosed with gonarthrosis. The study group included 19 men (40.4%) and 28 women (59.6%). Evaluation was carried out using indicators of pain intensity, range of motion in the knee joint, functional activity, and the overall clinical condition of the patients. It was established that the inclusion of nuclear magnetic resonance therapy in the treatment programme contributed to significant and sustained clinical improvement. After completion of the treatment course, 80.9% of patients demonstrated a marked reduction in pain and improved mobility, 14.9% showed a moderate positive outcome, while the absence of a pronounced effect was recorded in only 4.2% of cases. The practical value of the obtained results lies in the fact that nuclear magnetic resonance therapy may be regarded as an effective, safe and promising method of conservative treatment for patients with degenerative-dystrophic lesions of the knee joints, capable of complementing traditional treatment approaches and enhancing their therapeutic effect

Keywords: osteoarthritis; knee joint; degenerative changes; cartilage tissue; functional status of patients

INTRODUCTION

Osteoarthritis of the knee joint is one of the most common degenerative diseases of the musculoskeletal system, leading to chronic pain, reduced functional activity and significantly reduced quality of life. Despite the availability of various treatment methods, there are very few effective approaches that affect early pathogenetic mechanisms and inhibit the progression of structural changes in joint tissues. This fact necessitates the search for new, safe and scientifically sound therapeutic strategies. Current scientific research is focused on finding physical methods of influence, in particular magnetic resonance technologies, to modify biological processes in cartilage and bone tissues.

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In the period 2017-2024, active research began on the possible use of MBST® nuclear magnetic resonance for therapeutic purposes. In a study by A. Mann *et al*. [1], scientists analysed the effect of low-intensity nuclear magnetic resonance therapy (NMRT) on the regeneration of dorsal root ganglion neurons in culture. The authors investigated whether NMRT is capable of modulating the behaviour of Schwann cells and neurons, in particular their proliferation, gene expression and neurogenesis processes. The results indicated that NMRT stimulates the proliferation of Schwann cells without changing their phenotype and significantly enhanced neuron survival, neurite formation, and differentiation. In addition, the environment obtained from Schwann cells after NMRT itself promoted the growth and survival of neurons. Thus, the study pointed to the potential ability of NMRT to accelerate peripheral nerve regeneration and highlighted the prospects for its further study as an adjunctive non-invasive therapy.

The study by V. Thöni *et al*. [2] presented an experimental analysis of therapeutic nuclear magnetic resonance (tNMR), the essence of which is that the method was divided into three separate components – tNMR itself, sweep field, and radiofrequency mode – to determine their contribution to cellular effects. As a result, it was found that each mode causes specific changes in reactive oxygen species levels, lactate metabolism, and proliferation indices. The authors concluded that tNMR affects processes dependent on proton gradients, indicating a possible enhancement of the proton motive force of cells. A narrative review by M. Žnidarič *et al*. [3] included an analysis of the potential of molecular biophysical stimulation therapy (MBST), in particular NMRT, in the treatment of chronic musculoskeletal disorders. The authors emphasised the fact that traditional treatments for osteoporosis and osteoarthritis have limited effectiveness and are mainly aimed at reducing pain or increasing bone mass. MBST has been shown to have a safe and non-invasive effect on cartilage regeneration, improving bone tissue quality and reducing symptoms in chronic musculoskeletal disorders, including back pain, making it a promising technology for conservative treatment.

A study by N. Huels *et al*. [4] showed a statistically significant reduction in pain in dogs with osteoarthritis of the elbow joint. Even though this was a veterinary model, the results are important because the pathogenesis of osteoarthritis in animals is similar to that in humans. A scientific review by D. Bichsel *et al.* [5] revealed significant heterogeneity in clinical recommendations for the treatment of hip and knee osteoarthritis, indicating the lack of a universal approach and the need for more standardised evidence-based treatment algorithms. Scientists L.O. Dantas *et al*. [6] summarised the key areas of physical therapy for gonarthrosis, emphasising the importance of exercise, load control and multimodal strategies, the effectiveness of which has been confirmed by clinical data. A study by T. Paolucci *et al*. [7] demonstrated that a new physiotherapy approach leads to a statistically significant reduction in pain and improvement in joint function after just a few weeks of therapy. This discovery is important for the development of effective treatment strategies for this disease. A brief communication by S. Onuora [8] drew attention to the phenomenon of "hyalinisation" as a potential marker of regeneration, opening up new diagnostic guidelines. This phenomenon may become an important tool for monitoring tissue repair processes and evaluating the effectiveness of therapeutic methods. The monograph by K.P.H. Pritzker & H.K. Gahunia [9] presented a summary of the mechanisms of homeostasis, ageing and cartilage degeneration, emphasising the combined role of mechanical stress, inflammatory mediators and cellular metabolism disorders.

Thus, in summary, modern clinical and experimental studies have shown that nuclear magnetic therapy shows promising results in reducing pain, improving joint function, modulating inflammatory mechanisms, and stimulating regenerative processes. The aim of the study was to investigate the clinical and functional efficacy of NMRT in the complex treatment of early stages of gonarthrosis.

MATERIALS AND METHODS

The study was conducted using a combined retrospective-prospective model. Initially, a retrospective analysis of patients' medical records from 2019-2021 was carried out, which made it possible to determine the main clinical characteristics of disease progression and the outcomes of previously applied treatment methods. This was followed by prospective observation of patients who underwent a course of nuclear magnetic resonance therapy, with the aim of assessing the dynamics of clinical status and structural changes in the knee joint. Histological, clinical, radiological, and statistical methods were used in the study. Histological analysis was focused on investigating degenerative-dystrophic changes in the knee joint in rats and assessing morphological signs of the regenerative capacity of cartilage tissue under the influence of nuclear magnetic resonance therapy. The clinical approach involved evaluation of treatment outcomes in patients with early stages of knee osteoarthritis after completion of an NMRT course. Radiological examination made it possible to monitor structural and functional changes in the knee joint at early stages of gonarthrosis during the course of treatment.

During the study, clinical outcomes of the use of NMRT alone and in combination with other treatment methods were analysed in 47 patients diagnosed with gonarthrosis who were receiving outpatient care at the "VinProfiMed" Rehabilitation Centre in Vinnytsia. The group included 19 men (40.4%) and 28 women (59.6%). The mean age of the examined patients was 60.4 years (range 28-77 years). Inclusion criteria were patients diagnosed with deforming osteoarthritis of the knee joints (gonarthrosis) stages I-III. Exclusion criteria included stage IV gonarthrosis, the presence of metal implants, and oncological diseases.

The study was conducted in accordance with international ethical standards. The provisions of the Declaration of Helsinki and the recommendations of the European Commission were observed. Approval from the local ethics committee was obtained prior to the start of the study in accordance with Protocol No. 7 dated 16 September 2021. All participating patients signed informed consent forms for participation in the study and for the processing of their medical data. Potential participants were invited from the patient database of the "VinProfiMed" Medical and Rehabilitation Centre or applied independently. A clinical examination by an orthopaedic trauma specialist was performed, eligibility according to inclusion and exclusion criteria was verified, and medical history was collected (duration of symptoms, previous therapeutic interventions,

comorbidities). Before the initiation of therapy, each patient underwent clinical pain assessment (Visual Analogue Scale, VAS); evaluation of joint function (Lequesne Index or WOMAC, if available); psycho-emotional screening (HADS or PHQ-9, if indicated); knee joint radiography in standard projections to determine disease stage; MRI or ultrasound where indicated to clarify the condition of cartilage, menisci, and periarticular structures; and laboratory tests (complete blood count, C-reactive protein, biochemistry) when clinically required.

These data were used as baseline values for subsequent comparisons. The next stage involved assignment of the therapeutic programme and group allocation. Allocation of patients to the "cartilage" or "bone" NMRT programme was based on clinical and instrumental findings (predominantly cartilage pathology or signs of bone involvement/aseptic necrosis) and individual indications. Subsequently, the treatment protocol (intervention) was determined. The cartilage programme consisted of daily NMRT sessions lasting 60 minutes for seven consecutive days (one course) and was applied to 40 patients. The bone programme consisted of daily NMRT sessions lasting 60 minutes for nine days and was applied to six patients. One patient sequentially completed both programmes, first the cartilage programme and then the bone programme.

During each session, vital signs (blood pressure, heart rate), patients' subjective sensations, and any adverse events or discomfort were recorded. Concomitant (combined) therapy was provided. Thirteen patients received intra-articular injections of hyaluronic acid (the interval between the last injection and the start/end of NMRT was documented); one patient received cell-based therapy, and one patient underwent spa and health resort treatment. All these interventions were documented and taken into account in the analysis as potential covariates. Assessment of effectiveness was repeated immediately after completion of the course and at follow-up examinations at 3 and 6 months. At each stage, clinical scales (VAS, Lequesne/WOMAC), physical examination (presence of swelling, range of motion), and radiological or instrumental methods – when planning long-term follow-up (MRI/ultrasound) – were used to evaluate structural changes.

Treatment was carried out using the certified MBST® system, which generates low-intensity magnetic fields with resonant characteristics adapted for therapeutic effects on cartilage and bone tissue. Ultrasound examinations were performed using expert-class devices, and radiographic examinations were carried out on digital X-ray systems in accordance with medical equipment standards. Statistical analysis was conducted using descriptive statistics; depending on the type of data, the t-test, Mann-Whitney U test, χ^2 test, or their non-parametric equivalents were applied. A p value of < 0.05 was considered statistically significant. Medical data were stored in the centre's secure electronic registry with restricted access and in paper form (patients' medical records). Anonymised datasets with assigned patient codes were used for analysis. Study limitations included a small sample size, variability in the intensity of concomitant treatment in some patients, the absence of randomisation, and the lack of a control group, which may affect the interpretation of causal relationships.

RESULTS AND DISCUSSION

Osteoarthritis is among the most prevalent disorders of the musculoskeletal system and is accompanied by the development of chronic pain syndrome, leading to disability, significantly impairing patients' quality of life and constituting a serious public health problem. For a long time, this pathology was regarded exclusively as a consequence of natural ageing processes; consequently, treatment was predominantly symptomatic, while preventive approaches remained largely overlooked. Research by I. Mařík *et al*. [12] demonstrated that resonant vibration of the molecular structures of cartilage and bone tissue stimulates the proliferation of chondroblasts and osteoblasts, activates the synthetic function of chondrocytes, and reduces proteoglycan degradation. Energy accumulated by cells under the influence of external factors modifies cellular metabolism by enhancing protein expression, ion transport, and the activation of signalling cascades [2].

NMRT is based on the principles of diagnostic magnetic resonance imaging and relies on the phenomenon of nuclear magnetic resonance. Under the influence of a static magnetic field, hydrogen protons in the body align parallel to the field lines, forming a net magnetic moment. A radiofrequency pulse delivered at the appropriate precessional frequency via a coil induces their transition to a higher energy level, after which, during relaxation, the absorbed energy is emitted. The energy transferred to tissues exerts a therapeutic effect [13]. Exposure parameters (field strength, resonant frequency, and procedure duration) are selected individually, taking into account the localisation and stage of the degenerative–dystrophic process. The settings are recorded on chip cards, from which the information is automatically read by the device control unit [14]. To facilitate a clearer understanding of the physical principles and therapeutic potential of the method, its main mechanisms of action are summarised (Table 1).

Table 1. Main mechanisms of action and parameters of NMRT

Component	Description/Characteristics	Therapeutic significance
Physical principle	The phenomenon of nuclear magnetic resonance: precession of hydrogen protons in an external magnetic field and resonant absorption of energy.	Mobilisation of intracellular processes, restoration of energy balance.
Primary fields	Static (0.4-2.35 mT); alternating electromagnetic (17-100 kHz); sinusoidal alternating (stabilising).	Creation of resonance conditions, stimulation of cellular metabolism.
Equipment	Twelve independently controlled coils, orthogonal configuration, local coil for the affected joint.	Formation of a three-dimensional therapeutic field.
Biological effect	Stimulation of chondroblast and osteoblast proliferation; activation of the synthetic function of chondrocytes; reduction of proteoglycan degradation; modulation of ionic transport across membranes.	Restoration of cartilage tissue, reduction of inflammation and pain syndrome.

Table 1. Continued

Component	Description/Characteristics	Therapeutic significance
Safety	Induction 10,000 times lower than that used in diagnostic MRI.	Absence of harmful effects, possibility of repeated treatment courses.

Source: compiled based on I. Mařík *et al.* [12]

The study analysed the effectiveness of NMRT in 47 patients with gonarthrosis who were receiving outpatient treatment at the "VinProfiMed" Rehabilitation Centre in the city of Vinnytsia. The study group was characterised by a wide spectrum of clinical forms of the disease (Fig. 1).

In order to expand and strengthen the analytical nature of the results, patients were divided into subgroups according to age, gender, disease stage, and NMRT programme (Table 2). This division allows for a more accurate assessment of the differentiated effect of therapy and identification of the characteristics of response to treatment in different categories of patients.

This distribution and its analysis demonstrated a tendency toward an increased effect in younger patients, women, and in the early stages of the disease; the combination of NMRT with additional treatment methods shows a synergistic positive effect. Immediately after completing the course of treatment, most patients noted positive changes (Table 3). According to the survey, 38 patients (80.9%) noted a significant reduction or complete disappearance of pain in the affected joint. Seven patients (14.9%) reported moderate improvement, and two patients (4.2%) did not experience significant changes.

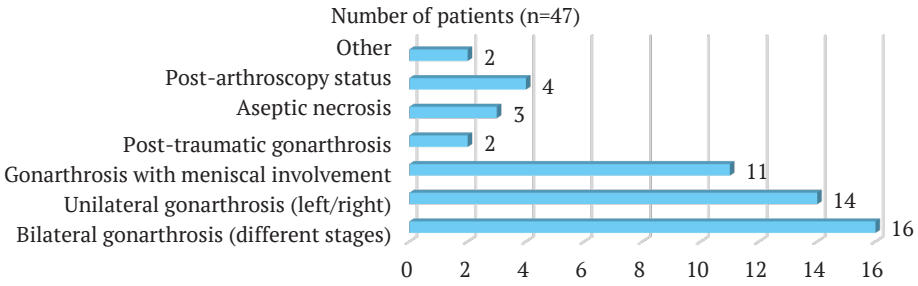

Figure 1. Distribution of patients by diagnosis
Source: compiled by the authors based on the results of a clinical study

Table 2. Distribution of patients into subgroups by age, gender, disease stage, and NMRT programme

Subgroup	Number of patients	Significant improvement, %	Moderate improvement, %	No change, %
Age ⩽50 years	18	88	11	1
Age >50 years	29	76	17	7
Women	25	84	12	4
Men	22	77	18	5
Stage I-II	21	90	10	0
Stage III	26	73	15	12
NMRT standard programme	30	80	15	5
NMRT programme + additional treatment	17	82	12	6

Source: compiled by the authors based on the results of a clinical study

Table 3. Clinical results of treatment

Result	Number of patients (n=47)	Percentage (%)
Significant improvement	38	80.90
Moderate improvement	7	14.90
No change	2	4.20

Source: compiled by the authors based on the results of a clinical study

Among the main complaints reported by the patients were pain (constant and movement-related), restricted mobility in the affected joint(s), and swelling. After completion of the NMRT course, the majority of patients noted a reduction in pain intensity, improved mobility, and resolution of swelling. Patients who received additional treatment (intra-articular administration of hyaluronic acid) demonstrated a relatively more pronounced and rapid positive effect, which can be explained by the synergistic action of different therapeutic modalities. In patients with aseptic necrosis and osteoporosis who received a bone-targeted programme, subjective improvement was also observed, indicating a positive effect of NMRT not only on cartilage but also on bone tissue.

Analysis of the questionnaire-based assessment methods showed that, after completing the NMRT course, patients experienced a statistically significant reduction in pain intensity and an improvement in joint functional status. The dynamics according to the VAS and Lequesne indices were positive and indicated a substantial decrease in pain severity and mobility limitation, thereby confirming the clinical effectiveness of the therapy. Follow-up examinations at 3 and 6 months after the NMRT course demonstrated the persistence of the therapeutic effect: pain intensity remained reduced at a level of 2.8-3.2 points, while anxiety and depression scores according to the HADS scale remained at 7.0-7.5 and 6.0-6.7, respectively (Table 4).

Table 4. Dynamics of clinical indicators in patients at 3 and 6 months after the NMRT course

Indicator	Before treatment (M ± SD)	After 3 months (M ± SD)	After 6 months (M ± SD)	p-value
VAS (pain)	6.8-7.2	3.0-3.4	2.8-3.2	<0.05
HADS – anxiety	9.0-10.2	7.2-7.5	7.0-7.3	<0.05
HADS – depression	8.2-9.1	6.5-6.9	6.0-6.7	<0.05
Lequesne index (function)	8.5-9.3	5.0-5.4	4.8-5.1	<0.05

Source: compiled by the authors based on the results of a clinical study

This fact indicates the long-term positive effect of NMRT on the physical and psycho-emotional state of patients. The changes detected were statistically significant ($p < 0.05$), which is consistent with the data presented in Table 5.

Table 5. Clinical and psycho-emotional outcomes of treatment in patients with gonarthrosis (n = 47)

Indicator	Before treatment (mean ± SD)	After the NMRT course (mean ± SD)	Change	p-value
VAS (pain)	6.8 ± 1.2	3.4 ± 1.0	↓ 3.4	<0.05
Lequesne index (function)	11.2 ± 2.1	7.1 ± 1.9	↓ 4.1	<0.05
HADS – anxiety	10.1 ± 3.4	7.2 ± 2.8	↓ 2.9	<0.05
HADS – depression	9.3 ± 3.1	6.5 ± 2.5	↓ 2.8	<0.05
PHQ-9	12.4 ± 4.2	8.1 ± 3.7	↓ 4.3	<0.05

Note: the arrow '↓' indicates a decrease in values, which indicates improvement; $p<0.05$ – statistically significant dynamics
Source: compiled by the authors based on the results of a clinical study

Thus, it has been demonstrated that a course of NMRT has a positive effect not only on pain and joint function, but also on the psycho-emotional state of patients. According to Table 2, there was a significant reduction in pain intensity as measured by the VAS and an improvement in function (Lequesne index); a decrease in levels of anxiety and depression according to HADS and in depressive symptoms according to PHQ-9; a synergistic positive effect of NMRT on both the physical and psycho-emotional state of patients is clearly evident. Consequently, the obtained results indicate a comprehensive positive impact of NMRT, which includes not only a reduction in pain intensity and improvement in functional activity, but also a decrease in the psycho-emotional burden that accompanies the course of gonarthrosis. A substantial limitation in clinical practice is the absence of objective *in vivo* methods for measuring bone strength, osteoid quality, and cartilage integrity. This complicates the assessment of therapeutic effectiveness and leads to the predominant use of indirect or subjective criteria, which always carries the risk of a "placebo effect". In this context, observations on the use of NMRT are of particular value.

As a result of the discussion, experimental studies have demonstrated the effect of NMRT on the proliferation and viability of chondrocytes and osteoblasts, accompanied by cartilage tissue regeneration and stimulation of bone formation. Clinical observations have confirmed a reduction in pain intensity in osteoarthritis and a decrease in fracture incidence in osteoporosis. Despite extensive experience with its use, this method has not yet been widely implemented in standard medical practice. Thus, the presented clinical observation, together with the results of numerous experimental and clinical studies, confirms the significant potential of NMRT in the treatment of osteoarthritis and osteoporosis. However, the results of certain experimental and preclinical studies do not provide sufficient grounds to recommend NMR as an effective treatment for post-traumatic osteoarthritis at the current stage of research development, as the data demonstrated only moderate and heterogeneous changes in the expression of individual microRNAs, which cannot form a clear mechanistic vector capable of ensuring cartilage tissue regeneration. It should also be noted that the identified molecular changes were not confirmed by corresponding clinical outcomes: the studies did not demonstrate a significant reduction in pain, improvement in function, or structural restoration of cartilage according to imaging criteria. Thus, this indicates that NMRT currently lacks a sufficient evidence base to be recommended as an effective treatment for post-traumatic osteoarthritis.

In the study by B. Steinecker-Frohnwieser *et al.* [15], the cellular effects of NMRT in osteoarthritis were investigated. The authors analysed the microRNA (miR) profile in healthy chondrocytes and in cells from patients with osteoarthritis after exposure to NMRT. It was shown that the therapy prevents a decrease in the levels of miR-106a, miR-27a, miR-34b, miR-365a, and miR-424, which play a key role in the regulation of cellular metabolism. Table 6 presented summarised data on the clinical effects of NMRT obtained from previous studies, demonstrating the main directions of the therapeutic impact of the method. The authors' research results are consistent with these trends

Table 6. Clinical effects of NMRT in gonarthrosis

Indicator	Study results	Clinical significance
Pain syndrome	Reduction in pain intensity according to the VAS by an average of 35-60% after a course of 5-10 sessions.	Relief of symptoms and an increase in the level of daily activity.
Joint functional status	Improvement on the WOMAC and Lequesne scales by 25-40%.	Increase in range of motion and improvement in gait.
Quality of life	Positive dynamics according to the EQ-5D and SF-36 questionnaires.	Psycho-emotional improvement and reduction in fatigue.
Inflammatory activity	Reduction of local swelling and a decrease in C-reactive protein concentration in some patients.	Modulation of the inflammatory process.
Cartilage tissue	In some patients, an increase in cartilage thickness (according to MRI and ultrasound) was observed after 2-3 courses of therapy.	Signs of chondroprotection and potential regeneration.
Need for NSAIDs	Reduction or complete discontinuation of NSAID use in 40-60% of patients after the course.	Lower risk of medication-related complications.
Tolerability and safety	No serious adverse effects were recorded; mild sensations of warmth or tingling in the treatment area were occasionally noted.	Possibility of safe use in the majority of patients.

Source: compiled based on H. Jansen *et al*. [16]

The obtained data indicated that NMRT exerts a multifactorial effect on cartilage and bone tissue cells by activating regenerative processes, modulating epigenetic and signalling mechanisms, and reducing inflammatory activity. At the same time, the problem of studying cellular changes under the influence of NMRT remains open and requires further in-depth investigation. The results were consistent with the conclusions of J. Tong *et al*. [17], who, in a scientific review, reported a significant reduction in pain, decreased stiffness, and improved physical function in patients with osteoarthritis. Similar to the study by G. L. Bagnato *et al*. [18], the present research demonstrated that combining NMRT with additional treatment methods produced a synergistic effect, whereby patients receiving hyaluronic acid injections showed more rapid and pronounced improvement. These findings underlined the importance of a combined approach in rehabilitation and are consistent with previous randomised controlled trials. In addition, S. E. Hashemi *et al*. [19] presented a study in which pulsed electromagnetic fields combined with physiotherapy significantly improved outcomes in patients with knee osteoarthritis, further emphasising the importance of individualising NMRT parameters, as applied in the present study. The meta-analysis by X. Yang *et al*. [20] confirmed the effectiveness of pulsed electromagnetic fields in improving pain, stiffness, function, and quality of life, which corresponds with the present findings regarding the duration of effect and the positive psycho-emotional impact of NMRT. These data allow the conclusion that the present results are consistent with existing evidence and expand upon it by providing detailed clinical observation of treatment effects lasting up to six months.

Separate reports addressed the long-term use of NMRT. In particular, D. Krpan & W. Kullich [21] described a clinical case of a dog with severe chronic osteoarthritis and hip dysplasia that underwent annual NMRT courses over a period of nine years. Sustained preservation of high motor activity and the absence of pain were observed, which the authors attributed to long-term application of the method. Thus, published data on the effectiveness of NMRT in osteoarthritis remain heterogeneous: some studies demonstrate clear clinical benefits, whereas others indicate the need for further research. A review of the literature nevertheless confirmed the clinical effectiveness of NMRT in the treatment of osteoarthritis. The review by J.K. Schmidt *et al.* [22] summarised trial results and confirmed the effectiveness of this technology in patients with various forms of osteoarthritis. The authors reported reduced inflammation, normalisation of cellular metabolism, and increased expression of extracellular matrix proteins. They also highlighted consistency in treatment duration (one hour per session) despite differences in the number of sessions (five to ten). All seven studies included in the review demonstrated a significant positive clinical effect. In six studies, reductions in pain, improvements in joint function, and enhanced quality of life were reported, while one study demonstrated improvement in the structural characteristics of articular cartilage according to ultrasound findings. Thus, NMRT contributes to a reduction in subjective symptom severity and positively affects objective markers of cartilage tissue regeneration. NMRT is an effective treatment method for osteoarthritis that provides a rapid clinical effect even in the presence of pronounced structural joint changes, which justifies its recommendation for use in later stages of the disease.

Thus, the results of the present study confirmed the conclusions of most previous authors while also extending them, demonstrating the promise of NMRT in the comprehensive treatment of patients with various clinical forms of gonarthrosis. Considering the favourable results of clinical and experimental studies, as well as its high safety profile, NMRT may be regarded as an innovative approach to the treatment of degenerative-dystrophic joint disorders. The method has potential as an adjunct to traditional pharmacological and physiotherapeutic interventions. At the same time, most existing studies have methodological limitations, including short follow-up periods, the absence of unified standards for the physical parameters of

electromagnetic fields, and small sample sizes. Data on the cellular mechanisms of action of NMRT remain limited.

CONCLUSIONS

Analysis of contemporary publications has demonstrated variability in the results of studies on the clinical effectiveness of NMRT in osteoarthritis, with a substantial proportion of research reporting a positive impact of this method on disease progression. Individual clinical observations and experimental studies have indicated the ability of NMRT to maintain the viability of cartilage and bone cells, reduce pain manifestations, and improve joint functional activity. In a clinical and experimental study, it was found that the use of NMRT in patients with early stages of gonarthrosis was associated with a pronounced positive clinical effect. The dynamics of patients' condition indicated improvement in functional parameters and a reduction in pain intensity in 80.9% of patients after completion of the treatment course; moderate improvement was observed in 14.9% of participants, while the absence of a therapeutic response was recorded in only 4.2% of cases, confirming the high effectiveness of the method.

Statistical analysis demonstrated that the effectiveness of NMRT therapy was significantly associated with baseline symptom severity and individual clinical characteristics of patients. The most pronounced changes were observed in patients with a shorter duration of symptoms and minimal structural abnormalities according to imaging findings. It was also confirmed that the therapeutic effect persisted for at least six months after completion of treatment, indicating a potentially prolonged action of the method. The study showed that NMRT can be effectively combined with traditional physiotherapy and pharmacological treatments, enhancing the overall effectiveness of comprehensive therapy.

The obtained data indicated that the inclusion of NMRT in rehabilitation programmes may reduce the need for analgesic medications and improve patients' quality of life. High safety, relative ease of application, and the absence of adverse effects make NMRT a promising non-invasive therapeutic technology capable of reducing the need for injection-based or surgical interventions. Thus, the conducted study confirmed the feasibility and clinical effectiveness of nuclear magnetic resonance therapy in the treatment of early stages of gonarthrosis. The results provided a scientifically substantiated basis for the further expansion of NMRT application in clinical practice and create a foundation for future randomised studies. Further research in this area should focus on determining optimal NMRT exposure parameters (frequency, duration, and individualisation of treatment courses) appropriate for specific patient profiles. In addition, it is important to investigate the relationships between biomechanical, morphological, and molecular changes in cartilage tissue under the influence of NMRT.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Клініко-функціональна ефективність ядерної магнітно-резонансної терапії у комплексному лікуванні початкових стадій гонартрозу

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Анотація. Гонартроз (деформуючий остеоартроз колінних суглобів) є одним із найпоширеніших дегенеративно-дистрофічних захворювань опорно-рухового апарату, що суттєво знижує якість життя пацієнтів та призводить до стійкого порушення функціональної активності нижніх кінцівок. На початкових стадіях перебігу патології особливо важливим є пошук ефективних, неінвазивних та науково обґрунтованих терапевтичних підходів, здатних впливати на регенерацію структур хрящової та кісткової тканин, зменшувати больовий синдром і сповільнювати прогресування дегенеративних змін. Метою даної статті було проведення клінічної оцінки доцільності застосування ядерно-магнітного резонансу як терапевтичного ад'юванта у пацієнтів із початковими стадіями гонартрозу та визначити його вплив на динаміку основних клінічних показників. У межах дослідження проаналізовано результати комплексного застосування ядерної магнітно-резонансної терапії окремо та у поєднанні з базовими методами лікування у 47 амбулаторних пацієнтів із діагнозом гонартроз. До дослідницької групи увійшли 19 (40,4 %) чоловіків та 28 (59,6 %) жінок. Оцінювання проводилося за показниками інтенсивності болю, обсягу рухів у колінному суглобі, функціональної активності, а також загального клінічного стану пацієнтів. Встановлено, що включення ядерної магнітно-резонансної терапії до програми лікування сприяло значному та стійкому клінічному покращенню. Після проходження курсу у 80,9 % пацієнтів відзначено виражене зменшення больового синдрому та покращення рухливості, у 14,9 % – помірний позитивний результат, тоді як відсутність вираженого ефекту зафіксовано лише у 4,2 % випадків. Практична цінність одержаних результатів полягає у тому, що ядерна магнітно-резонансна терапія може розглядатися як ефективний, безпечний та перспективний метод консервативного лікування пацієнтів із дегенеративно-дистрофічними ураженнями колінних суглобів, здатний доповнювати традиційні підходи лікування та посилювати їх терапевтичний ефект

Ключові слова: остеоартроз; колінний суглоб; дегенеративні зміни; хрящова тканина; функціональний стан пацієнтів

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