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Correspondence address: Ukraine, 61022, Kharkiv, Nauky Avenue, 4.
E-mail: ic.journal@knmu.edu.ua
as.shevchenko@knmu.edu.ua
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BIOCHEMICAL EVALUATION OF ANTI-INFLAMMATORY ACTION OF CELECOXIB AND CAFFEINE IN A FORMALIN PAIN MODEL IN RATS

Syrova G.O., Tishakova T.S., Savelieva O.V., Chalenko N.M.

Kharkiv National Medical University, Kharkiv, Ukraine

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ABSTRACT

Background. Inflammation is a reaction of living tissue on injury. Nowadays there is a wide spectrum of anti-inflammatory medications that are used for the treatment of many problems. But because their application is associated with a wide range of side effects, there is a need for the development of new pharmaceutical compositions to maximise patient safety.

Aim. To carry out biochemical evaluation of anti-inflammatory action of celecoxib in combination with caffeine on the biochemical markers of inflammation (sialic acids and ceruloplasmin) and to determine its anti-exudative action on formalin-induced paw edema in rats.

Materials and Methods. The study involved male Wistar Albino Glaxo (WAG) line rats, divided into six treatment groups: control, formalin-induced, celecoxib (5 mg/kg), caffeine (0.6 mg/kg), a combination of celecoxib and caffeine (5 mg and 0.6 mg/kg), and diclofenac sodium (8 mg/kg). Biochemical studies were carried out by using the blood serum samples of white laboratory rats (WAG line). Anti-inflammatory activity of celecoxib and its pharmaceutical composition with caffeine was studied using the formalin-induced paw edema model. The animals were divided into the same groups as in the Anti-Exudative Activity (AEA) study.

Results. It was shown, that composition of celecoxib and caffeine exerted higher anti-inflammatory activity versus celecoxib and it is efficient in relation to the exudation processes. Biochemical studies of celecoxib, caffeine and their composition on the level of sialic acid level and ceruloplasmin level in the blood serum as well as study of anti-exudative activity of the proposed composition have shown, that caffeine potentiates pharmacological activity of celecoxib in formalin-induced paw edema model.

Conclusion. The findings indicate that the combination of celecoxib and caffeine is a promising therapeutic option for inflammatory conditions.

Keywords: *anti-inflammatory drugs, anti-exudative action, biomarkers of inflammation.*

Introduction

Inflammation is a fundamental pathological process linked to various diseases. Anti-inflammatory drugs, both long- and short-acting, including non-steroidal and steroidal types, are employed for treating inflammatory conditions. These drugs vary in chemical structure and mechanism, primarily functioning through the inhibition of CycloOXygenase (COX) enzymes responsible for prostaglandin synthesis [1–4]. COX exists in three isoforms: COX-1 (protects gastrointestinal mucosa), COX-2 (inducible and associated with inflammation), and COX-3 (involved in fever regulation). Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) predominantly inhibit COX-2 to mitigate inflammation while minimizing COX-1-related side effects. The anti-inflammatory effects of NSAIDs are largely attributed to their inhibition of COX-2 activity, while the side effects, particularly gastrointestinal complications, are primarily due to COX-1 inhibition. Furthermore, NSAIDs can also influence the synthesis of leukotrienes and superoxide radicals, affecting cellular membrane activity, neutrophil aggregation, and lymphocyte function [5–8].

Celecoxib, a well-known COX-2 inhibitor, is widely used for pain management due to its efficacy and lower gastrointestinal side effects. It is effective for treating various conditions, including rheumatoid arthritis, dysmenorrhea, and migraine. Importantly, at therapeutic concentrations, celeco-

Corresponding Author:
Savelieva Olena V. – PhD of Pharmaceutical Sciences, assistant of the Department of Medical and Bioorganic Chemistry, Kharkiv National Medical University.
✉ Ukraine, 61022, Kharkiv, Nauki ave., 4.
E-mail: ov.savelieva@knmu.edu.ua

xib does not inhibit COX-1, which contributes to its favorable safety profile. However, its efficacy can be enhanced through combinations with adjuvants, such as caffeine [9–12]. Recent research indicates that caffeine can act as an adjuvant to NSAIDs, enhancing their anti-inflammatory and analgesic effects. Caffeine has been studied in conjunction with various NSAIDs, including coxibs, to improve therapeutic outcomes [12–19]. This study investigates the Anti-Exudative Activity (AEA) of a combination of celecoxib and caffeine, comparing it to individual components and the reference drug sodium diclofenac, as well as its effects on biomarkers of inflammation: Sialic Acids (SA) and Ceruloplasmin (Cp).

The **aim** of study was to carry out biochemical evaluation of anti-inflammatory action of celecoxib in com-bination with caffeine on the biochemical markers of inflammation (sialic acids and cerulo-plasmin) and to determine its anti-exudative action on formalin-induced paw edema in rats.

Materials and Methods

The anti-exudative activity was assessed using a formalin-induced paw edema model in male Wistar Albino Glaxo (WAG) rats weighing (300–350) g. The animals were acclimatized for 14 days under controlled vivarium conditions (at an air temperature of [23–25]°C with lighting set at 100 lx in the room and 20–40 lx in the cages). All studies were conducted according to the "General Principles of Ethical Conduct for Experiments on Animals" (Ukraine, 2001), which comply with the provisions of the European Convention "On Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" (Strasbourg, 1986).

Rats were divided into six treatment groups:

1. Control group (received a single intragastric dose of 3% starch mucus)

2. Formalin-induced group (a 2% formalin solution was injected subplantarly into the rat's hind paw, and a 3% starch mucus was given intragastrically);

3. Subplantar 2% formalin injection and a single intragastric dose of 5 mg/kg celecoxib as suspensions in 3% starch mucus;

4. Subplantar 2% formalin injection and a single intragastric dose of 0.6 mg/kg caffeine celecoxib as suspensions in 3% starch mucus;

5. Subplantar 2% formalin injection and a single intragastric dose of combination containing celecoxib (5 mg/kg) and caffeine (0.6 mg/kg) as suspensions in 3% starch mucus;

6. Subplantar 2% formalin injection and a single intragastric dose of 8 mg/kg sodium diclofenac) as suspensions in 3% starch mucus.

The treatments were administered intragastrically, and paw volume was measured before and after treatment using a digital plethysmometer (IITC Life Science, USA). Changes in rat paw volume at different time points were expressed in milliliters (mL). The AEA was calculated as a percentage inhibition of inflammation (PII) according to the following formula:

$$PII = \frac{V_c - V_o}{V_c} \times 100\% \qquad (1)$$

where:

V_c – paw volume in the control group minus initial paw volume before edema, mL;

V_o – paw volume after edema minus initial paw volume before edema, mL.

Biochemical studies were conducted using blood serum samples from white laboratory rats (WAG line). The anti-inflammatory activity of celecoxib and its pharmaceutical composition with caffeine was investigated using the formalin-induced paw edema model. The animals were divided into the same groups as in the AEA study.

The level of serum SA was measured using the "SialoTest" from the Research and Production Centre "Eco-Service". The procedure involved adding 1 mL of hydrolyzing agent to test tubes containing 2 mL of distilled water and 0.6 mL of blood serum samples. The solutions were mixed thoroughly and then placed in a boiling water bath for 5 minutes. Following this, the samples were centrifuged at 3000 rpm for 5 minutes to collect the supernatant.

0.4 mL of a color-producing reagent was added to 2 mL of the supernatant. This reactive mixture was incubated in a boiling water bath for 15 minutes, then cooled with tap water. After cooling, 2 mL of distilled water was added to each test tube, and the contents were mixed again. The absorbance was measured at 540 nm using a photocolorimeter. Sialic acid concentrations (CSA, mmol/L) were calculated based on absorbance values, using the following formula:

$$C_{SA} = \frac{A_{sam} \times C_{cal}}{A_{cal}} \qquad (2),$$

where:

A_{sam} – absorbance of the investigated serum sample;

C_{cal} – concentration of the calibrator (mmol/L);
A_{cal} – absorbance of the calibrator.

The conversion factor (K) was determined prior to each measurement using the formula:

$$K=2/A_{cal} \quad (3)$$

where:
A_{cal} – absorbance of the calibrator.

2 represents the concentration of sialic acids in the calibrator (mmol/L) [20].

Ceruloplasmin levels were measured using the Ravin method, where ceruloplasmin catalyzes the oxidation of p-phenylenediamine, yielding a purple product [34].

The reaction mixture comprised 1.58 mL of a 0.5M sodium acetate buffer solution (pH 5.5), 0.2 mL of freshly prepared 0.5% p-phenylenediamine dihydrochloride solution, and 0.02 mL of the serum sample. The mixture was incubated at 37°C in a water bath for one hour. To terminate the reaction, 0.2 mL of a 0.5% sodium azide solution was added. For control purposes, a control sample was prepared by adding 0.2 mL of sodium azide before the incubation.

Absorbance was measured at 530 nm, and ceruloplasmin concentration was calculated using a standard optical density coefficient:

$$C(Cp) = A_0 \times 5.83 \quad (4),$$

where:
C(Cp) – molar concentration of ceruloplasmin in the sample;
A_0 – optical density of ceruloplasmin in the sample.
5.83 – optical density coefficient according to Ravin's method, expressed in micromoles of active protein per liter (μmol/L) [21].

All procedures performed in this study complied with the regulations established by the State Pharmacological Center of the Ministry of Health of Ukraine [22]. Ethical guidelines, cost-effectiveness, and statistical considerations were taken into account when determining the number of animals and their allocation to the study groups [23]. All experiments were conducted in the afternoon, correlating with the circadian rhythms that influence the pharmacological parameters of the investigated drugs and their activities.

The findings were statistically analyzed using Statistica 6.0 (Statsoft, USA), employing the Student t-test to determine the significance of differences between groups.

Results

Our experimental studies on formalin-induced paw edema demonstrated that celecoxib (Group 3) achieved an Anti-Exudative Activity (AEA) of 50%, which was 6% higher than that of the reference drug, sodium diclofenac (Group 6). In comparison, the AEA of caffeine alone (Group 4) was markedly lower, at just [18.3–2.7]% times less than that of celecoxib. Interestingly, the addition of caffeine to celecoxib (Group 5) enhanced its AEA by 5% compared to celecoxib alone.

Based on these findings, the investigated drugs and proposed pharmaceutical composition can be ranked in terms of their AEA against formalin-induced paw edema in rats as follows. The composition containing celecoxib and caffeine (55.5%) is more effective than celecoxib (50%), which is more effective than sodium diclofenac (44%), which in turn is more effective than caffeine (18.3%).

To further substantiate our findings regarding the anti-exudative activity of the pharmaceutical composition and its individual components, we performed biochemical analyses of inflammatory markers. Specifically, we measured the levels of SA and Cp in rat blood serum after treatment for formalin-induced paw edema with the proposed pharmaceutical compositions and their components. These results were compared to those obtained with the reference drug, sodium diclofenac.

To further substantiate our findings regarding the anti-exudative activity of the pharmaceutical composition and its individual components, we performed biochemical analyses of inflammatory markers. Specifically, we measured the levels of SA and Cp in rat blood serum after treatment for formalin-induced paw edema with the proposed pharmaceutical compositions and their components. These results were compared to those obtained with the reference drug, sodium diclofenac.

The subsequent phase of the study focused on evaluating the effects of celecoxib, caffeine (as an adjuvant), their combination, and the reference drug sodium diclofenac on Cp activity in the blood serum of rats. A statistically significant increase in Cp levels was observed in Group 2, showing a 2.8-fold increase compared to the control group (Group 1). Following celecoxib administration (Group 3), Cp levels in the blood serum of rats decreased by 1.2 times compared to the formalin edema group (Group 2). This difference was statistically significant when compared to both the control

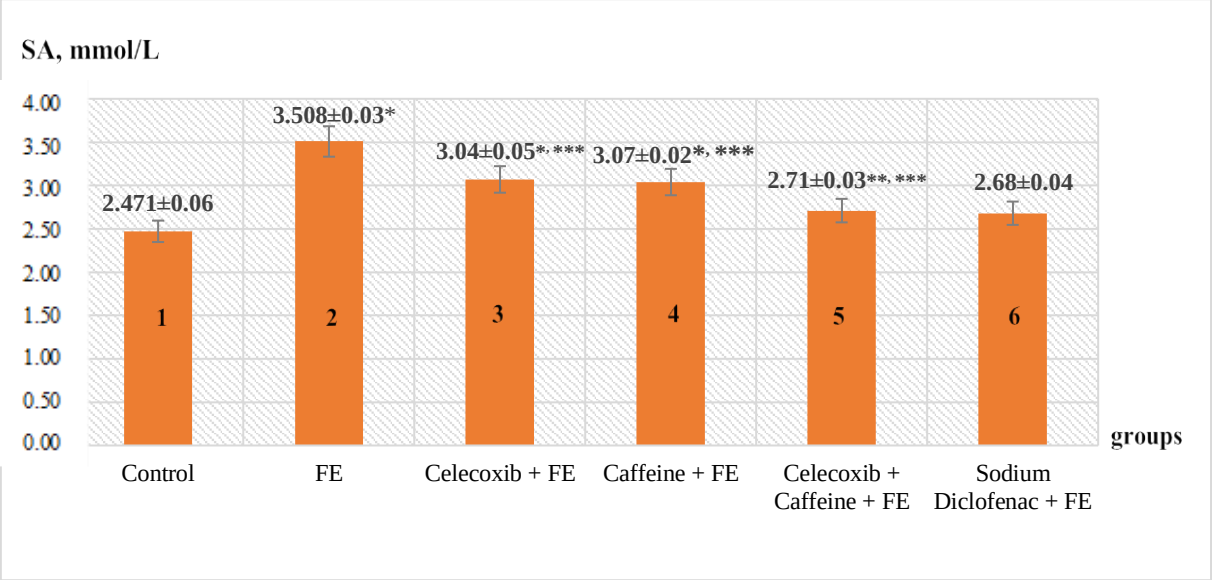

Fig. 1. Effect of celecoxib, caffeine, and their pharmaceutical composition on the SA level in rat blood serum in the formalin-induced paw edema model.

Note: difference between groups is shown as (mean ± standard error), all results are significant ($p<0.05$);
* – difference compared to the control group;
** – difference compared to the formalin edema group;
*** – difference compared to the formalin edema group;
**** – difference compared to the celecoxib and formalin edema group.

group (Group 1) and the sodium diclofenac group, although no significant difference was found between Groups 3 and 2.

In Group 4, the administration of caffeine resulted in a reduction of Cp levels in the rat blood serum by 1.6 times compared to the formalin edema group (Group 2), indicating a statistically significant difference from the results in Group 2. Moreover, caffeine effectively lowered the level of the inflammation marker ceruloplasmin in the formalin-induced inflammatory model. A statistically significant difference was observed in comparison with the control group but not in comparison with the sodium diclofenac group (Figure 2).

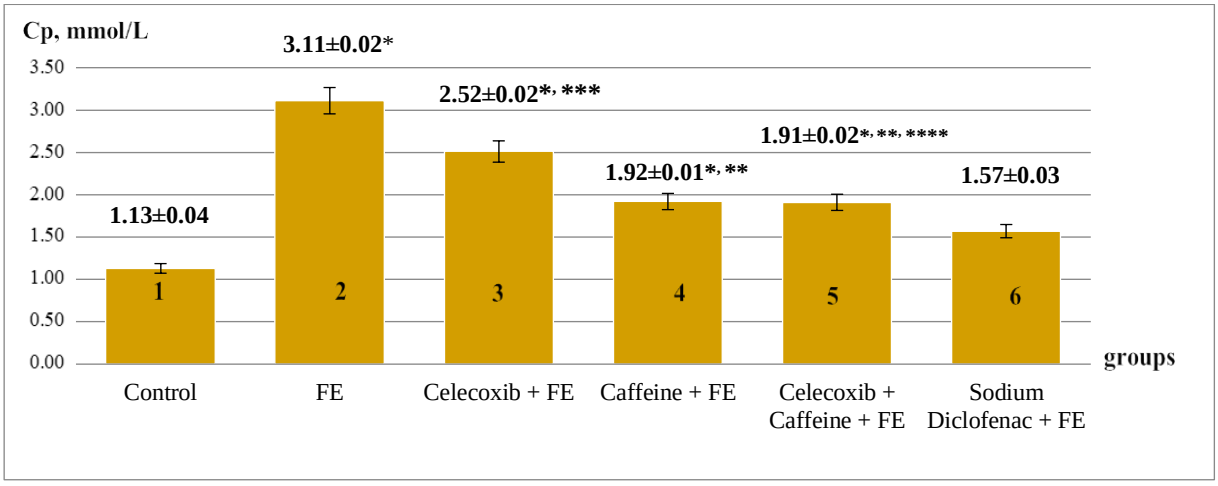

Fig. 2. Effect of celecoxib, caffeine, and their pharmaceutical compositions on the ceruloplasmin level in rat blood serum in the formalin-induced paw edema model.

Note: difference between groups is shown as (mean ± standard error), all results are significant ($p<0.05$);
* – difference compared to the control group;
** – difference compared to the formalin edema group;
*** – difference compared to the formalin edema group;
**** – difference compared to the celecoxib and formalin edema group.

Overall, the research demonstrated that caffeine (with an AEA of 18.3%) enhances the AEA of celecoxib (with an AEA of 50 %), and the proposed pharmaceutical composition of celecoxib and caffeine (with an AEA of 55.5%) is effective in mitigating exudative processes.

Acute-phase proteins, such as Cp, which belongs to the α-globulin group, are valuable biomarkers for diagnosing inflammatory diseases, as their levels increase during acute inflammation. This motivated our previous studies, which investigated the influence of coxibs on blood serum ceruloplasmin activity in rats using the formalin-induced edema model. Our findings established a positive effect of coxibs on Cp levels, with rofecoxib demonstrating greater efficacy than celecoxib.

It is well-known that one of the mechanisms by which NSAIDs exert their anti-inflammatory effects is through the inhibition of inflammatory responses, partly due to their ability to modulate oxidation and phosphorylation processes. Disruptions in the barrier properties of lipid membranes play a significant role in the development of inflammatory processes and pain syndromes. One major trigger for such disruptions is the activation of Lipid PerOxidation (LPO), which is regulated by the body's physiological antioxidant systems. A compromise in any of these protective mechanisms can lead to the activation of LPO.

During inflammation, ProstaGlandins (PGs) and leukotrienes are formed as a result of the enzymatic oxidation of arachidonic acid, leading to increased formation of free radicals that enhance LPO. Consequently, we studied the inhibitory effects of coxibs, particularly their pharmaceutical compositions with caffeine, on LPO processes. This was evidenced by a decrease in Conjugated Diene (CD) levels in the blood serum of rats subjected to formalin-induced edema.

Sialic acid is another important biomarker of inflammation. Sialic acids are normal components of all tissues and biological fluids in the human body and constitute a major part of glycoproteins and glycolipids. When freed from glycoproteins, sialic acids can inactivate certain bacterial and viral agents, which is why elevated sialic acid levels are observed in various pathological states characterized by inflammation.

In our earlier studies, we found that proposed pharmaceutical compositions of oxicams with caffeine affected serum sialic acid levels in rats. Additionally, we demonstrated that adjuvant caffeine positively impacts the anti-inflammatory activity of piroxicam and meloxicam, as evidenced by changes in sialic acid levels.

Biochemical investigations into the anti-inflammatory actions of celecoxib and caffeine revealed that both celecoxib (group 3) and caffeine (group 4) decreased sialic acid levels in the blood serum of laboratory animals relative to the model group (group 2). Statistically significant differences were observed between the treatment and control groups, confirming that the combination of celecoxib and caffeine significantly reduced sialic acid levels in relation to formalin-induced paw edema (group 2). In contrast, celecoxib alone (group 3) showed statistically significant similarities to both the reference drug and the intact control group.

The combination of celecoxib and caffeine (group 5) exhibited enhanced anti-inflammatory activity compared to celecoxib alone in formalin-induced rats. The pharmaceutical composition of celecoxib and caffeine (group 5) significantly reduced ceruloplasmin levels in both the model group (group 2) and the group treated solely with celecoxib (group 3). No statistically significant difference was noted between the results of the group treated with the reference drug and the control group.

Conclusion

The experimental studies of celecoxib, caffeine, and the proposed pharmaceutical compositions containing both agents in a formalin-induced paw edema model have demonstrated that caffeine enhances the anti-exudative activity (AEA) of celecoxib. The effectiveness of the investigated drugs and their composition, based on AEA, follows this order: the combination of celecoxib and caffeine is the most effective, followed by celecoxib alone, then sodium diclofenac, with caffeine being the least effective.

Therefore, we consider the pharmaceutical composition of celecoxib and caffeine to be effective in addressing exudation processes in this model.

Biochemical studies have shown that caffeine enhances the pharmacological activity of celecoxib by reducing sialic acid levels in blood serum. Based on their ability to reduce SA levels in blood plasma, the investigated drugs and their composition can be ranked as follows: the combination of celecoxib and caffeine is equally effective as sodium diclofenac, while celecoxib alone is as effective as caffeine.

Consequently, the proposed pharmaceutical composition containing celecoxib and caffeine is deemed effective in lowering sialic acid levels in rat blood serum in the formalin-induced edema model.

Furthermore, the results of biochemical studies indicate that caffeine acts as an adjuvant in reducing ceruloplasmin levels. In terms of reducing ceruloplasmin levels, sodium diclofenac is the most effective, followed by the combination of celecoxib and caffeine, which has the same effect as caffeine, while celecoxib alone is the least effective.

Overall, our findings demonstrate that the proposed pharmaceutical composition of celecoxib and caffeine possesses anti-inflammatory activity. We also see potential for further experimental and biochemical studies of this composition in zymosan- and carrageenan-induced edema models.

DECLARATIONS:

Disclosure Statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Statement of Ethics

The authors have no ethical conflicts to disclosure.

Data Transparency

The data can be requested from the authors.

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ACTIVATION OF IMMUNO-INFLAMMATORY RESPONSE IN PATIENTS WITH CORONAVIRUS DISEASE (literature review)

Skorokhodova N.O.

Zaporizhzhia State University of Medicine and Pharmacy, Zaporizhzhia, Ukraine

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ABSTRACT

The COVID-19 pandemic caused by the SARS-CoV-2 virus has become a global challenge. Community-acquired pneumonia associated with COVID-19 is still one of the most challenging medical problems. It is especially important to study the pathogenesis of Community-Acquired Pneumonia (CAP) and its relationship with various inflammatory processes that occur in the setting of coronavirus infection. The aim of this study was to analyze the pathogenesis of CAP that develops against the background of COVID-19, to study the mechanisms of immune response, inflammatory processes and their impact on the patient's body, and to identify possible approaches to the diagnosis and treatment of this disease. The following materials and research methods were used in the study: a review of scientific sources on the pathogenesis of CAP in COVID-19, the peculiarities of the immune response, cytokine storm and endothelial dysfunction in this pathology. The authors of the analyzed studies, in turn, used an analysis of inflammatory markers (C-reactive protein, D-dimer, cytokines). They report that patients with CAP developing against COVID-19 have activation of the neutrophil chain and a significant increase in the level of pro-inflammatory cytokines such as IL-6, IL-1β, TNF-α. These processes lead to the development of a severe inflammatory reaction in the lungs and diffuse alveolar damage, which in turn leads to the development of acute respiratory failure. It has been noted that excessive D-dimer release is a key indicator of the development of these complications. Prediction of severe forms of the disease based on the level of cytokines and other inflammatory markers can be an important tool for early detection of the risk of complications in patients. Thus, it was found that in order to improve the prognosis of patients, it is necessary to use methods of monitoring the level of inflammatory markers and individualise therapeutic strategies to correct immune system disorders.

Keywords: *community-acquired pneumonia, COVID-19, cytokine storm, D-dimer, immune response, thromboembolism.*

Introduction

The COVID-19 (COronaVIrus Disease 2019) pandemic has become a global challenge for healthcare systems and has led to an increase in the incidence of respiratory diseases. One of the most common and severe complications of COVID-19 is pneumonia, which can have a different course depending on the conditions of infection, physiological characteristics of the patient and the strain of the virus. Community-Acquired Pneumonia (CAP) associated with coronavirus infection is of particular interest because it occurs in patients outside of healthcare facilities and has different features compared to hospital-acquired pneumonia [1; 2].

Recent studies related to COVID-19 have focused on various aspects of respiratory complications, with pneumonia occupying a special place among them. Understanding the activation of the immuno-inflammatory response in patients with COVID-19-associated CAP may provide new information for predicting the severity of the disease and developing more effective treatment approaches [3–5].

The pandemic has drawn researchers' attention to the differences between hospital-acquired and CAP. CAP associated with coronavirus infection is distinguished by its specificity, as it occurs in patients who were not in medical facilities before

Corresponding Author:
Skorokhodova Natalia – DMedSc, Professor, Professor of the Department of Phthisiology and Pulmonology, Zaporizhzhya State Medical and Pharmaceutical University, Zaporizhzhya, Ukraine.
✉ Ukraine, 69035, Zaporizhzhia, Marii Prymachenko Blvd., 26.
E-mail: 555544ns@gmail.com

the onset of symptoms. This requires special attention to diagnostic and prognostic markers, such as neurohumoral indicators, which can help identify the course of the disease in the early stages [6; 7].

Studies on CAP in the context of COVID-19 emphasize the importance of assessing the immune-inflammatory response, which may be one of the key factors in the development of complications. In particular, it is important to assess the level of endothelial function markers, such as endothelin-1, which may indicate the degree of damage to the vascular system during COVID-19. This is especially relevant for patients with CAP [8; 9].

However, despite a significant number of studies on COVID-19 and its impact on the body, the immune-inflammatory response in patients with CAP remains insufficiently studied. Most studies focus on hospital-acquired pneumonia or general changes associated with COVID-19, without taking into account the specifics of CAP. Therefore, the study of the immunoinflammatory response in patients with CAP associated with COVID-19 may provide new data on the diagnosis and treatment of this disease [10; 11].

Analysis of the immunoinflammatory response in patients with community-acquired pneumonia associated with COVID-19 will allow us to better understand the mechanisms behind severe pneumonia.

The **aim** of this systematic review is to analyze and summarize the available data on the immune-inflammatory response in patients with CAP associated with COVID-19 and to identify the main mechanisms that explain these changes.

Materials and Methods

To study the pathogenesis of CAP in patients infected with SARS-CoV-2, a systematic review of the literature was conducted, including sources published in leading scientific databases, including PubMed, Scopus, GoogleScholar and Web of Science, which provide access to peer-reviewed articles and other scientific publications. The following key terms were used to search for articles: "neurohormonal changes in COVID-19 pneumonia", "sympathetic nervous system and COVID-19", "inflammatory markers in pneumonia", "renin-angiotensin system in COVID-19", "neurohormonal imbalance and pneumonia", "COVID-19 and cytokine storm". Synonyms and alternative terms were also used to expand the search query, including "inflammatory response", "adrenal hormones", "stress hormones and pneumonia", "neurotransmitter changes in pneumonia".

Research was focused on pathophysiological changes in the respiratory and cardiovascular systems. Levels of inflammatory markers, such as D-dimer, C-Reactive Protein (CRP) and cytokines, as well as the mechanisms of thromboembolic complications and pathological changes in lung tissue were studied.

Results

The immunoinflammatory response is a multilevel and complex biological process that integrates the mechanisms of innate and adaptive immunity to maintain the body's homeostasis in response to exogenous and endogenous threats. When these mechanisms are disrupted, various pathological conditions and diseases occur [11; 12].

This process is initiated by the recognition of Pathogen-Associated Molecular Patterns (PAMPs) or endogenous damage-associated signaling molecules (Damage-Associated Molecular Patterns, DAMPs). By means of specialized Pattern Recognition Receptors (PRRs), including Toll-Like Receptors (TLRs), NOD-Like Receptors (NLRs) and RIG-I-Like Receptors (RLRs). The activation of these receptors initiates signaling cascades, in particular NF-κB- and MAPK-dependent pathways, leading to transcriptional regulation of proinflammatory mediators such as TNF-α, IL-1β, IL-6, and other effector molecules of the inflammatory response [13–15].

Acute inflammation is accompanied by complex changes in the microcirculatory system, including increased vascular permeability, endothelial activation and expression of adhesive molecules, which in turn promotes leukocyte migration to the site of injury. The main effector cells of the acute inflammatory response are neutrophils, monocytes and macrophages, which phagocytose pathogens and secrete cytokines and chemokines (in particular IL-8, MCP-1) that regulate chemotaxis and activation of immune cells. Dendritic cells process and present antigens on Major Histocompatibility Complex (MHC) molecules, which is a very important component for the activation of adaptive immunity [16–18].

T-cell activation is mediated by signals from antigen-presenting cells (APCs) and the cytokine microenvironment. Th1 and Th17 cells contribute to a prolonged pro-inflammatory response through the production of IFN-γ, IL-17 and GM-CSF, which stimulate the activity of macrophages and granulocytes. CD8+ T cells exert a cytotoxic effect on infected or altered cells, thereby inducing apoptosis through the perforin-granzyme mechanism or the Fas/FasL-mediated pathway. B lym-

phocytes, under the influence of Th2 cell cytokines (IL-4, IL-5, IL-13), synthesize antibodies involved in the neutralization of pathogens, opsonization and activation of complement [19; 20].

Inflammatory mediators, which include the following substances: proinflammatory cytokines (TNF-α, IL-1β, IL-6), chemokines (CXCL8, CCL2) and lipid derivatives (prostaglandins, leukotrienes), play a key role in modulating the immune response. Prostanoids, synthesized from arachidonic acid under the influence of CycloOXygenases (COX-1, COX-2), regulate vascular changes, pain and fever, while leukotrienes are involved in stimulating leukocyte adhesion and migrations [21; 22].

Inflammation resolution involves the activation of mechanisms that limit the intensity and duration of the immune response, preventing the development of chronic inflammation and pathological tissue destruction. Anti-inflammatory cytokines such as IL-10 and TGF-β promote apoptosis of proinflammatory effector cells, macrophage polarization into the M2 phenotype and restoration of tissue architecture. The dysfunction of resolution mechanisms leads to chronic inflammation, which is associated with pathologies such as rheumatoid arthritis, inflammatory bowel disease, atherosclerosis, and neurodegenerative processes [23; 24].

In addition, the pathological immunoinflammatory response can mediate the mechanisms of neoplastic cell transformation, promoting the development of tumors by chronic stimulation of proliferative signaling pathways, inhibition of apoptosis and creation of an immunosuppressive microenvironment. For example, chronic inflammation caused by persistent viral infections or autoimmune disorders is an important factor in carcinogenesis, in particular in cases of hepatocellular carcinoma, colorectal cancer, and gastrointestinal tumors [25; 26].

Thus, the immunoinflammatory response is a fundamental component of the body's defense mechanisms, but its dysregulation can be a trigger for a wide range of pathological conditions. A deep understanding of the mechanisms of inflammation regulation is essential for the development of innovative therapeutic strategies aimed at modulating immune responses in inflammatory, autoimmune and oncological diseases. In the future, the study of immune-inflammatory mechanisms may contribute to the development of new biological therapies, including cytokine receptor inhibitors, specific antagonists of inflammatory mediators, and cellular immunotherapeutic approaches that can selectively regulate pathologically activated immune mechanisms [27; 28].

CAP associated with COVID-19 coronavirus infection is a serious pathological condition accompanied by profound immunoinflammatory disorders. SARS-CoV-2 causes a significant activation of innate and acquired immunity, which leads to an uncontrolled inflammatory process, an imbalance between proinflammatory and anti-inflammatory mechanisms, and secondary immunosuppression. These mechanisms result in complications such as Acute Respiratory Distress Syndrome (ARDS), thromboembolic events, and secondary bacterial infections [29; 30].

In COVID-19, the activation of the neutrophil chain is one of the key aspects of CAP pathogenesis. Neutrophils, which are effector cells of the early immune response, play a critical role in the body's response to pathogens. They are the first cells to migrate to the site of infection and provide the primary line of defense by phagocytozing viral particles and neutralizing pathogens through various mechanisms. However, in COVID-19, excessive activation of neutrophils can lead to increased inflammation and the development of serious complications, including severe pneumonia, which is accompanied by the development of ARDS [31; 32].

The initial stage of neutrophil activation is contact with viral particles that enter the body. Once the SARS-CoV-2 virus enters the epithelial cells of the respiratory tract, it initiates their interaction with Toll-like receptors (TLRs), which trigger a cascade of signals that lead to the activation of pro-inflammatory molecules. This, in turn, promotes the release of chemokines, in particular interleukin-8 (IL-8), which play a crucial role in the chemotaxis of neutrophils, facilitating their mobilization to the site of infection. The production of cytokines and chemokines increases vascular permeability, which allows neutrophils to migrate to the site of infection, where they perform their primary function of phagocytosis and neutralization of pathogenic agents. However, in COVID-19, there is an excessive release of these molecules, which is accompanied not only by local inflammation but also by systemic effects, including activation of thrombosis and endothelial dysfunction [33; 34].

Excessive activation of neutrophils can cause serious pathological consequences. They activate mechanisms that promote the production of Reactive Oxygen Species (ROS), serine proteases and

various pro-inflammatory molecules, such as tumour necrosis factor alpha (TNF-α), interleukin-1β (IL-1β) and interleukin-6 (IL-6), which in turn intensifies the inflammatory process and tissue damage. These reactions result in tissue damage, particularly in the lungs, where interstitial edema, fibrosis, and decreased gas exchange develop. One of the most destructive processes is the formation of neutrophil extracellular traps (NETs), which are a network of DNA that appears during neutrophil activation. These traps are capable of trapping viral particles, but also increase inflammation and tissue homeostasis, contributing to the development of chronic inflammation in the lungs [35; 36].

At the same time, other immune cells, in particular T-lymphocytes, dysfunction occurs, leading to an imbalance in the immune response. Excessively activated neutrophils can not only neutralize pathogens but also damage healthy tissues, which is the main cause of prolonged inflammation in the airways and the development of pulmonary fibrosis. Chronic infectious burden and inflammation can lead to prolonged changes in lung tissue, impairing the functionality of the respiratory system and significantly increasing the risk of developing secondary bacterial infections, which often complicate the course of COVID-19 [37; 38].

Another key pathogenetic mechanism is the "cytokine storm", which significantly affects the severity of CAP caused by SARS-CoV-2. This phenomenon, which involves uncontrolled and excessive release of proinflammatory cytokines, is one of the main factors that determine the progression of the disease and complications associated with COVID-19 pneumonia. Cytokines, which normally control the immune response and contribute to the effective fight against viral infections, cause tissue and organ destruction in COVID-19, which worsens the clinical condition of patients [39; 40].

The activation of the "cytokine storm" in COVID-19-induced CAP begins with the penetration of viral particles into the body, where they interact with Toll receptors, which initiates a cascade of immune responses. As a result, macrophages and dendritic cells are activated, which are the main participants in anti-viral immunity, leading to the release of significant amounts of pro-inflammatory cytokines, among which IL-6, TNF-α, IL-1β, and interferons play a special role. Under normal conditions, these molecules contribute to the effective destruction of viral particles, but in the context of COVID-19, their excessive release is out of control, leading to inflammatory lung damage and the development of pneumonia [41; 42].

The excessive release of cytokines, in particular IL-6, contributes to the development of interstitial inflammation in the lungs, which is the main feature of COVID-19-induced CAP. Cytokines activate fibroblasts and other cells, which causes lung swelling and fibrosis, disrupting their ability to exchange gas normally. In addition, the activation of pro-inflammatory molecules increases vascular permeability, which leads to interstitial edema, reduces the efficiency of blood oxygenation and creates conditions for the development of ARDS, which is a serious complication that can threaten the lives of patients [43; 44].

In addition, as a result of immune system hyperactivation, patients with CAP caused by COVID-19 have activation of the hemostatic system. Cytokines, in particular IL-6 and TNF-α, can initiate thrombosis, which leads to increased levels of D-dimers and the development of thromboembolic complications such as venous thromboembolism, deep vein and pulmonary thrombosis [45; 46].

An important factor that determines the severity and progression of the disease is the imbalance in the immune response in community-acquired pneumonia caused by COVID-19. The SARS-CoV-2 virus, when it enters the body, initiates a complex immune response, including the activation of innate and adaptive immunity. However, it should be noted that in the context of COVID-19, there is a significant imbalance between different parts of the immune system, which in turn leads to an excessive inflammatory response, disruption of normal tissue function and the development of serious complications [47, 48].

One of the aspects that exacerbates the imbalance of the immune response in COVID-19 is the disruption of the interaction between the immune system and the vascular endothelium. The SARS-CoV-2 virus interacts with Angiotensin-Converting Enzyme 2 (ACE2), which is expressed not only in lung epithelial cells but also in vascular endothelial cells. This leads to impaired endothelial function, activation of inflammatory processes, and increased vascular permeability, which contributes to the development of edema, thrombosis, and tissue damage [49; 50].

Hypoxia and inflammation are two interrelated processes that are important in the development of CAP caused by COVID-19. In this case, there is

not only a disruption of the normal functioning of the respiratory system due to the inflammatory process, but also the development of severe hypoxia, which occurs as a result of lung damage and impaired gas exchange [51; 52].

Hypoxia in COVID-19 is a consequence of progressive inflammation, which is accompanied by a violation of the alveolar capillary barrier and fibrin deposition in the interalveolar space. All of this, in turn, impairs the normal process of blood oxygenation, leading to a decrease in the level of oxygen in the tissues and the development of hypoxia. Under conditions of hypoxia, a number of adaptive mechanisms are activated, including increased lung ventilation, activation of the sympathetic nervous system, and changes in cell metabolism to provide the necessary oxygen level for vital organs [53; 54].

The inflammatory process is an integral part of the body's response to infection, which in the case of COVID-19 is amplified many times over due to viral invasion of vascular endothelial cells and alveolar epithelial cells. This inflammatory process is accompanied by the release of proinflammatory cytokines, including interleukins (IL-6, IL-1β), tumour necrosis factors (TNF-α) and chemokines that stimulate the recruitment and activation of neutrophils and macrophages. Such a "cytokine storm" contributes to the development of relative hypoxia, which increases inflammation and reduces the body's ability to fight infection [55; 56].

Hypoxia is an important component for further exacerbating inflammation, as it activates adaptive mechanisms, such as activation of hypoxia-inducible factor 1 alpha (HIF-1α), which triggers the transcription of genes that help the body survive in low oxygen conditions. However, it should be noted that in the case of severe COVID-19, these mechanisms can cause excessive inflammation, which leads to an uncontrolled body response and damage to lung tissue. All of the above increases the risk of developing pulmonary fibrosis, which is a common cause of prolonged hypoxia in patients after COVID-19 [57; 58].

Discussion

Our literature review indicates the importance of understanding the mechanisms of the immune-inflammatory response in COVID-19 to optimize therapeutic approaches and predict the course of the disease. A detailed study of the literature revealed that the activation of the neutrophil chain in COVID-19 is an important factor determining the course of pneumonia and the development of serious complications such as ARDS, thromboembolism, and chronic pulmonary inflammation. Understanding the mechanisms of neutrophil activation is important for the development of therapeutic strategies that can reduce the inflammatory response and prevent tissue damage [59; 60].

The "cytokine storm" in COVID-19-induced CAP also causes significant changes in the cardiovascular system. The development of myocardial dysfunction, arrhythmias, and cardiac performance disorders is observed as a result of the inflammatory process, including the activation of inflammatory molecules and reactive oxygen species. Such changes in the circulatory system significantly worsen the prognosis for patients and contribute to the development of multiple organ failure [61; 62].

The main goal of treatment of CAP caused by COVID-19 is to control the "cytokine storm". Treatment includes the use of anti-cytokine therapy (e.g., tocilizumab) and corticosteroids, such as dexamethasone. A balanced approach to the correction of the immune response is critical, as excessive suppression of the immune system can lead to an increased risk of infectious complications [63; 64].

The negative consequences of an imbalance in the immune response include not only overactivation of the innate immune system, but also underactivation of adaptive immunity. Disruption of the interaction between innate and adaptive immunity cells, in particular T-lymphocytes, which are responsible for the effective fight against viral infections, is observed in patients with severe COVID-19. A decrease in the function of T lymphocytes, especially T helper cells, which contribute to the activation of B lymphocytes and the production of antibodies, can lead to an ineffective immune response and a weakening of the body's ability to fight the virus [65; 66]. Inflammation that develops and is maintained in hypoxia may be one of the key factors in the development of respiratory failure in patients with COVID-19, especially in patients with severe CAP. Hypoxia and inflammation are not only the result of viral damage, but also the main factors that determine the severity and prognosis in patients with COVID-19. This process is also closely related to hypercoagulability. High levels of D-dimers and activated coagulation contribute to the formation of microthrombi in the lungs and other organs, which worsens the clinical picture and increases the risk of serious complications. Timely detection of hypoxia and inflammation can help to correct treatment, which includes the use of antiviral, anti-inflammatory

and anticoagulant drugs. The administration of these drugs will improve the outcomes of patients with severe CAP caused by COVID-19 [67; 68].

Thus, understanding the processes of activation of the immune-inflammatory response that occur in CAP in the context of SARS-CoV-2 infection can significantly improve approaches to treatment and prevention. Another important aspect is the modulation of the "cytokine storm", in particular the inhibition of IL-6. Drugs such as tocilizumab have proven effective in patients with high levels of this cytokine, which helps reduce the severity of the disease and improve prognosis. Special attention should be paid to studies that examine patterns of activation of the immune-inflammatory response in CAP against the background of COVID-19. The study of these mechanisms may open up new therapeutic opportunities to correct pathological changes in patients with COVID-19, in particular those with comorbidities that increase the risk of complications.

Conclusions

1. High levels of immune and inflammatory markers serve as an indicator of disease severity. In patients with CAP associated with COVID-19, elevated levels of key inflammatory markers were found.

2. Changes in immuno-inflammatory markers are significant indicators of disease severity and can be used for early diagnosis and monitoring of complications.

3. The need for a comprehensive approach to treatment. The results of many studies emphasize the need for a comprehensive approach to the treatment of patients with COVID-19, including not only antibiotic therapy and respiratory support, but also the correction of immune and inflammatory disorders.

Prospects for further research

Further research is needed to better understand the mechanisms of CAP in association with COVID-19, as well as to improve prognosis and treatment methods. In particular, it is important to study molecular markers associated with endothelial dysfunction and evaluate the effectiveness of new therapeutic approaches to correct neurohumoral disorders in these patients. Increased attention to monitoring immune and inflammatory markers and correcting neurohumoral disorders is an important step to improve the outcomes of patients with CAP associated with COVID-19.

DECLARATIONS:

Disclosure Statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Statement of Ethics

The authors have no ethical conflicts to disclosure.

Data Transparency

The data can be requested from the authors.

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ELECTROMYOGRAPHIC INDICATORS INVESTIGATION IN FEMALE ATHLETES ENGAGED IN POLE ACROBATICS

Zharova I.O., Antonova H.P.

National University of Physical Education and Sports of Ukraine, Kyiv, Ukraine

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ABSTRACT

Background. The sensorimotor system is a key component of general physical preparedness in athletes, especially in sports disciplines that require high levels of coordination and reaction speed. One such discipline is pole acrobatics, characterized by complex movements demanding high sensorimotor integration.

Aim. To determine the effects of regular pole acrobatics training on sensorimotor system response parameters and to identify asymmetries between the right and left sides of the body in female athletes.

Materials and Methods. The investigation was conducted using electromyography methods: specific H-reflexometry and nerve conduction velocity measurements. The study was carried out at the Research Institute of the National University of Physical Education and Sports of Ukraine. The study involved 20 women in the early (group 1) and middle (group 2) stages of mature adulthood who regularly practice pole acrobatics. Data analysis was performed using the Mann-Whitney U test and the Sign test.

Results and Conclusions. Statistically significant differences between groups in terms of reaction latency, signal amplitude, reaction duration, and the area under the compound muscle action potential curve (H-wave) curve were found. Specifically, differences were observed in the functional activity of the peripheral nervous system between the right and left sides of the body, as evidenced by a decrease in signal amplitude and changes in the area under the curve. The findings suggest that regular pole acrobatics training can have a significant impact on the sensorimotor system and functional asymmetry between the right and left sides of the body in female athletes. This study represents an important step in understanding the specific effects of pole acrobatics on the functional state of the nervous system, which can be utilized to optimize training programs and enhance athletic performance.

Keywords: *neural asymmetry, women athletes, electromyography*.

Introduction

The sensorimotor system is a key component of the overall physical preparedness of athletes, particularly in sports requiring high levels of coordination and rapid reaction speed [1; 2]. One such athletic discipline is pole acrobatics, characterized by complex movements that demand a high degree of sensorimotor integration [3]. However, there is insufficient research on how regular pole training affects the functional state of the sensorimotor system in female athletes. An analysis of the literature indicates that most studies focus on the general effects of physical exercise on the nervous system [4–6], without addressing the specific questions related to the influence of pole training on the parameters of the sensorimotor response. Moreover, contradictions exist regarding how regular training in this sporting activity may alter functional indicators such as reaction latency, signal amplitude, reaction duration, and the area under the curve H-wave [7]. rheumatoid arthritis, dysmenorrhea, and migraine. Importantly, at therapeutic concentrations, celeco-

Aim and Objectives of the Study

The aim of this study was to determine the impact of regular pole training on the sensorimotor response parameters in female athletes. To achieve this aim, the following objectives were set:

Corresponding Author:
Antonova Hanna P. – PhD Student at the Department of Physical Therapy and Occupational Therapy, National University of Physical Education and Sports of Ukraine, Kyiv.
✉ Ukraine, 03150, Kyiv, Fizkultury str., 1.
E-mail: antonovapolesport@gmail.com

1) evaluate reaction latency, signal amplitude, reaction duration, and the area under the curve of the compound muscle action potential of the H-wave (i.e. the area between the first positive and last negative phases of the potential) (hereinafter referred to as the "area under the curve") in female athletes who engage in pole training;

2) compare response parameters between the left and right arms upon stimulation at the wrist and elbow;

3) identify potential asymmetries in the functional activity of the arms associated with pole training.

Materials and Methods

The research was conducted using electromyography methods: specifically H-reflexometry and nerve conduction velocity measurements. The study was carried out at the Research Institute of the National University of Physical Education and Sports of Ukraine. The M-TEST 4 computerized electromyograph (manufactured by "DX-Systems", Ukraine) was used. The research involved two groups of female pole acrobats: Group 1 (10 women in the early stage of mature adulthood, aged 23–35 years) and Group 2 (10 women in the middle stage of mature adulthood, aged 36–48 years). Age, anthropometric characteristics and training experience of women of both groups are shown in *Tables 1* and *2*.

Table 1. Characteristics of women in Group 1

Characteristic (measurement units)	Value
Age (years)	23.5±10.5
Training experience (years)	6.7±4.9
Body mass (kg)	59.1±10.4
Height (cm)	168.5±18.5

Table 2. Characteristics of women in Group 2

Characteristic (measurement units)	Value
Age (years)	40.5±8.1
Training experience (years)	7.1±4.4
Body mass (kg)	61.1±9.9
Height (cm)	166.3±16.6

Calculations of the indicators were performed using Statistica version 10 (StatSoft, Inc., USA). During our study, data analysis was performed using the Mann-Whitney U test and the Sign test. Both statistical methods were employed to evaluate the significance of differences between groups and to test hypotheses about data distribution.

Mann-Whitney U test – nonparametric test compares two independent groups by ranking all observations and assessing whether their distributions differ in location; it is an alternative to the independent-samples t-test when normality cannot be assumed.

Sign test – nonparametric paired-sample test evaluates whether the median of differences between two related samples is zero by counting the number of positive and negative differences. It is particularly useful when the distribution of differences is unknown or when outliers may distort other tests.

Results

The results of the Mann-Whitney U test (*Tables 3–6*) showed that the p-value was below the set significance level ($p<0.05$), which led to the rejection of the null hypothesis of no differences between the groups. This indicates statistically significant differences in the data distribution between the two groups.

Overall, the results of the Mann-Whitney U test demonstrate that some parameters of the sensory system show statistically significant differences between female athletes of groups 1 and 2. In particular, under wrist stimulation, significant differences were observed in the area under the curve in the left arm ($U=22.0$, $p=0.037$) and signal amplitude in the right arm ($U=11.0$, $p=0.004$). Under elbow stimulation, a statistically significant difference was found in the area under the curve for the left arm ($U=21.0$, $p=0.031$). These findings may indicate changes in the functional activity of the peripheral nervous system due to the specific loads involved in pole training.

For the motor system, no statistically significant differences were detected in any of the parameters, which could suggest that the influence of age-related changes is less pronounced in the motor system compared with the sensory system. This may be attributable to adaptive mechanisms that maintain the effectiveness of motor functions even in the presence of age-related changes.

In summary, the Mann-Whitney U test results indicate statistically significant differences in certain sensory parameters between female athletes in the early and middle stages of mature adulthood. Specifically, significant differences were found in the area under the curve for the left arm ($p=0.037$) and signal amplitude in the right arm ($p=0.004$) when stimulating the wrist, as well as in the area under the curve for the left arm ($p=0.031$) when stimulating the elbow. These findings suggest potential alterations in peripheral nervous

Table 3. Results of sensory system response to wrist stimulation in adults in the early and middle stages of mature adulthood (Mann-Whitney U)

Parameter (measurement units)	Sum of ranks		U	Z	p
	Group 1	Group 2			
Left side of the body					
Reaction latency (ms)	97.50	112.50	42.50	-0.53	0.60
Signal amplitude (μV)	128.00	82.00	27.00	1.70	0.09
Reaction duration (ms)	124.00	86.00	31.00	1.40	0.16
Area under the curve (ms×mV)	133.00	77.00	22.00	02.08	0.04
Right side of the body					
Reaction latency (ms)	105.50	104.50	49.50	0.00	1.00
Signal amplitude (μV)	144.00	66.00	11.00	2.91	0.01
Reaction duration (ms)	117.50	92.50	37.50	0.91	0.36
Area under the curve (ms×mV)	117.50	92.50	37.50	0.91	0.36

Notes: U – Mann-Whitney U statistic;
Z – standardized Z value;
p – significance level.

Table 4. Results of sensory system response to elbow stimulation in adults in the early and middle stages of mature adulthood (Mann-Whitney U)

Parameter (measurement units)	Sum of ranks		U	Z	p
	Group 1	Group 2			
Left side of the body					
Reaction latency (ms)	85.50	124.50	30.50	-1.44	0.15
Signal amplitude (μV)	130.00	80.00	25.00	1.85	0.06
Reaction duration (ms)	113.50	96.50	41.50	0.60	0.54
Area under the curve (ms×mV)	134.00	76.00	21.00	2.15	0.03
Right side of the body					
Reaction latency (ms)	103.50	106.50	48.50	-0.08	0.94
Signal amplitude (μV)	130.00	80.00	25.00	1.85	0.06
Reaction duration (ms)	102.50	107.50	47.50	-0.15	0.88
Area under the curve (ms×mV)	108.00	102.00	47.00	0.19	0.85

Notes: U – Mann-Whitney U statistic;
Z – standardized Z value;
p – significance level.

Table 5. Results of motor system response to wrist stimulation in adults in the early and middle stages of mature adulthood (Mann–Whitney U)

Parameter (measurement units)	Sum of ranks		U	Z	p
	Group 1	Group 2			
Left side of the body					
Reaction latency (ms)	123.50	86.50	31.50	1.36	0.17
Signal amplitude (μV)	110.00	100.00	45.00	0.34	0.73
Reaction duration (ms)	83.50	126.50	28.50	-1.59	0.11
Area under the curve (ms×mV)	110.00	100.00	45.00	0.34	0.73
Right side of the body					
Reaction latency (ms)	118.50	91.50	36.50	0.98	0.33
Signal amplitude (μV)	96.00	114.00	41.00	-0.64	0.52
Reaction duration (ms)	110.00	100.00	45.00	0.34	0.73
Area under the curve (ms×mV)	100.00	110.00	45.00	-0.34	0.73

Notes: U – Mann-Whitney U statistic;
Z – standardized Z value;
p – significance level.

Table 6. Results of motor system response to elbow stimulation in adults in the early and middle stages of mature adulthood (Mann-Whitney U)

Parameter (measurement units)	Sum of ranks		U	Z	p
	Group 1	Group 2			
Left side of the body					
Reaction latency (ms)	95.50	114.50	40.50	-0.68	0.50
Signal amplitude (μV)	104.00	106.00	49.00	-0.04	0.97
Reaction duration (ms)	104.50	105.50	49.50	0.00	1.00
Area under the curve (ms×mV)	101.00	109.00	46.00	-0.26	0.79
Right side of the body					
Reaction latency (ms)	92.00	118.00	37.00	-0.94	0.34
Signal amplitude (μV)	108.00	102.00	47.00	0.19	0.85
Reaction duration (ms)	115.50	94.50	39.50	0.76	0.45
Area under the curve (ms×mV)	113.00	97.00	42.00	0.57	0.57

Notes: U – Mann-Whitney U statistic;
Z – standardized Z value;
p – significance level.

system activity related to the specific demands of pole training.

For the motor system, no statistically significant differences were identified, indicating that age-related changes may be less pronounced in the motor system than in the sensory system. Adaptive mechanisms could be maintaining motor function effectively despite age-related factors.

For the motor system, the Sign test was used, and calculations were performed on the combined group because there were no statistically significant differences between participants in the early and middle stages of mature adulthood (*Tables 7–12*).

Meanwhile, the Sign test revealed that, for most comparisons, there were no statistically sig-

Table 7. Motor system response to wrist stimulation in adults in the early and middle stages of mature adulthood: right vs. left side (Sign test)

Parameter (measurement units)	Number of mismatches	(v<V), %	Z	p
Reaction latency (ms)	17.00	47.06	0.01	1.00
Signal amplitude (μV)	20.00	45.00	0.22	0.82
Reaction duration (ms)	19.00	52.63	0.00	1.00
Area under the curve (ms×mV)	20.00	45.00	0.22	0.82

Notes: (v<V) – number of negative differences (mismatches) in the Sign test;
Z – standardized Z value; p – significance level.

Table 8. Motor system response to elbow stimulation in adults in the early and middle stages of mature adulthood: right vs. left side (Sign test)

Parameter (measurement units)	Number of mismatches	(v<V), %	Z	p
Reaction latency (ms)	20.00	25.00	02.01	0.04
Signal amplitude (μV)	20.00	50.00	-0.22	0.82
Reaction duration (ms)	20.00	50.00	-0.22	0.82
Area under the curve (ms×mV)	20.00	55.00	0.22	0.82

Notes: (v<V) – number of negative differences (mismatches) in the Sign test;
Z – standardized Z value; p – significance level.

Table 9. Sensory system response to wrist stimulation in adults in the early stage of mature adulthood: right vs. left side (Sign test)

Parameter (measurement units)	Number of mismatches	(v<V), %	Z	p
Reaction latency (ms)	10.00	70.00	0.95	0.34
Signal amplitude (μV)	10.00	10.00	2.21	0.03
Reaction duration (ms)	9.00	33.33	0.67	0.50
Area under the curve (ms×mV)	9.00	44.44	0.00	1.00

Notes: (v<V) – number of negative differences (mismatches) in the Sign test;
Z – standardized Z value; p – significance level.

Table 10. Sensory system response to wrist stimulation in adults in the middle stage of mature adulthood: right vs. left side (Sign test)

Parameter (measurement units)	Number of mismatches	(v<V), %	Z	p
Reaction latency (ms)	10.00	50.00	-0.32	0.75
Signal amplitude (μV)	10.00	30.00	0.95	0.34
Reaction duration (ms)	10.00	50.00	-0.32	0.75
Area under the curve (ms×mV)	9.00	55.56	0.00	1.00

Notes: (v<V) – number of negative differences (mismatches) in the Sign test;
Z – standardized Z value; p – significance level.

Table 11. Sensory system response to elbow stimulation in adults in the early stage of mature adulthood: right vs. left side (Sign test)

Parameter (measurement units)	Number of mismatches	(v<V), %	Z	p
Reaction latency (ms)	10.00	30.00	0.95	0.34
Signal amplitude (μV)	10.00	70.00	0.95	0.34
Reaction duration (ms)	10.00	30.00	0.95	0.34
Area under the curve (ms×mV)	10.00	30.00	0.95	0.34

Notes: (v<V) – number of negative differences (mismatches) in the Sign test;
Z – standardized Z value; p – significance level.

Table 12. Sensory system response to elbow stimulation in adults in the middle stage of mature adulthood: right vs. left side (Sign test)

Parameter (measurement units)	Number of mismatches	(v<V), %	Z	p
Reaction latency (ms)	10.00	20.00	1.58	0.11
Signal amplitude (μV)	10.00	50.00	-0.32	0.75
Reaction duration (ms)	9.00	44.44	0.00	1.00
Area under the curve (ms×mV)	10.00	60.00	0.32	0.75

Notes: (v<V) – number of negative differences (mismatches) in the Sign test;
Z – standardized Z value; p – significance level.

nificant differences between the left and right arms. However, one notable exception was reaction latency during elbow stimulation in the combined group, where a statistically significant difference emerged (p=0.044171). Additionally, there was a statistically significant difference in signal amplitude between the left and right arms during wrist stimulation in the early stage of mature adulthood (p=0.026857), which may point to asymmetric load distribution or adaptation patterns in pole acrobatics. These findings provide insights into how regular pole acrobatics training could influence both sensory and motor parameters in female athletes, emphasizing the need for targeted training strategies to address potential asymmetries and enhance overall performance.

Discussion

The Sign test analysis confirmed that no significant differences were found between left and right arm indicators in the motor system under wrist stimulation. The majority of our tests revealed no statistically significant differences between the two age groups, suggesting an absence of notable age-related changes in the motor system. A significant difference in reaction latency between the left and right arms was identified only under elbow stimulation (p=0.044171), which may indicate possible asymmetries in functional activity.

With respect to the sensory system, only one metric showed statistically significant differences when comparing stimulation at the wrist and elbow: signal amplitude between the left and right arms in the early stage of mature adulthood under wrist stimulation (p=0.026857). This finding may point to more pronounced age-related changes in the sensory system of younger athletes compared to their older counterparts.

Overall, the results of the Sign test suggest that age-related changes in the sensory system may be more pronounced than those in the motor system. Such insights could prove beneficial in developing targeted training and rehabilitation programs that take into account the specific age-related differences observed in female athletes.

Conclusions

The findings of our study indicate that probably, regular pole training does not lead to significant differences in most parameters of the sensorimotor system's response between the left and right arms. An exception is reaction latency under elbow stimulation, where a statistically significant difference was observed. This suggests potential asymmetries in the functional activity of the arms, possibly due to the specific demands involved in pole acrobatics training.

Regarding the sensory system, statistically significant discrepancies emerged only under wrist stimulation, specifically in signal amplitude between the left and right arms. This could point to more pronounced changes in the sensory system, driven by the particular exercises included in pole acrobatics training.

Thus, our results suggest that regular pole training may affect the sensorimotor system in female athletes by inducing asymmetries in arm function. These findings could be applied to the design of more effective training programs that take such features into account and enhance athletic performance.

DECLARATIONS

Disclosure Statement

The authors declare that there is no conflict of interest that could have influenced the study's results.

Data Transparency

All data generated during the study can be made available upon reasonable request from the corresponding author.

Ethics Statement

No ethical standards were violated in the course of this research. All participants took part voluntarily on a volunteer basis and provided written informed consent.

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Consent for Publication

Both authors confirm their consent to publish this article and guarantee that there are no violations of copyright.

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CLINICAL FEATURES OF FUNCTIONAL GASTROINTESTINAL DISORDERS IN PRETERM INFANTS: AN ANALYTICAL STUDY

Godovanets O.S., Babintseva A.H.

Bukovinian State Medical University, Chernivtsi, Ukraine

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ABSTRACT

Background. Pathology associated with digestive system insufficiency in newborns occurs in 33.8% to 53.45% of cases.

Aim. To conduct a comparative analysis of the clinical manifestations of nutritional deficiency in preterm infants, considering the gestational age and severity of perinatal pathology.

Materials and Methods. Clinical signs of nutritional deficiency in 355 preterm infants with perinatal pathology of varying severity were analyzed. Group I included 54 infants born at 26–31/6 weeks of gestation and with a serious condition at birth; Group II – 149 infants at 32–33/6 weeks of gestation (Subgroup IIA – 67 infants with severe forms of perinatal pathology, Subgroup IIB – 82 infants with moderate pathology); Group III – 102 infants at the gestational age of 34–36/6 weeks (Subgroup IIIA – 41 infants with severe forms of perinatal pathology, Subgroup IIIB – 61 infants with moderate pathology); Group IV – 50 conditionally healthy newborns at the gestational age of 34–36/6 weeks.

Results and Conclusions. Asphyxia, respiratory distress syndrome, primary pulmonary atelectasis, hyaline membrane disease, multiple organ failure syndrome with damage to the central nervous, respiratory, cardiovascular, urinary, and gastrointestinal systems, as well as hemorrhagic, convulsive and anemic syndromes play a crucial role in the severity of the condition in preterm infants. The most frequent clinical markers of food intolerance in perinatal pathology in newborns were: residual volume of more than 50%, regurgitation and/or vomiting, enlarged liver or hepatolienal syndrome; intestinal meteorism, blood in coprofiltrate, acholic stools, jaundice and endotoxemia syndrome. The severity and frequency of food tolerance disorders correlate with the severity of perinatal pathology and the lower gestational age of newborns.

Keywords: *premature infants, digestive system, food tolerance disorders, laboratory diagnostics.*

Introduction

Every year, up to 16% of infants are born prematurely in the world. The consequences of preterm birth, especially at very low gestational age, are impaired postnatal adaptation, as well as the development of functional and chronic pathology in the later years of life. PreTerm Infants (PTI), compared to full-term infants, have a higher risk of physical and neuropsychological developmental disorders, which reduces the quality of life of patients [1–4].

Corresponding Author:
Oleksii Godovanets – MD, PhD, Associate professor, Department of Pediatrics, Neonatology and Perinatology Medicine, Bukovinian State Medical University (Chernivtsi, Ukraine).

✉ Ukraine, 58002, Chernivtsi, Teatralna sq., 2.
E-mail: godovanec.oleksij@bsmu.edu.ua

In the postnatal development of newborns, the full functioning of the GastroIntestinal System (GIS) plays an important role. Pathology associated with insufficiency of the digestive system occurs in 33.8% to 53.45% of cases and is one of the most frequently discussed in modern scientific sources [5]. Due to the Morphological and Functional Immaturity (MFI) of the body of infants at preterm birth, imperfections in the processes of digestion, absorption, and motility of the GastroIntestinal Tract (GIT) are noted, which causes problems in the formation of Enteral Nutrition (EN). Functional deficiency of the GIS is most common in infants of gestational age at birth less than 32 weeks and weighing less than 1500 g. At the same time, newborns have high nutritional needs that are difficult to meet through enteral feeding alone [6–9].

After birth, the PTI organism needs functional and structural maturation of the GIS to establish the processes of digestion and absorption of nutrients. It is important to develop intestinal motility, which includes the coordination of sucking and swallowing, gastroesophageal sphincter tone, as well as adequate gastric emptying, and intestinal peristalsis. In PTI, gastroesophageal reflux, significant gastric residues, and constipation are often observed due to insufficient gastric emptying, and insufficient intestinal motility, which is manifested by abdominal distention and delayed meconium passage [10–12].

Insufficient development of the basic functions of the gastrointestinal tract causes impaired food tolerance in PTI, especially in clinical forms of perinatal pathology, which is an important aspect of medical care in the neonatal intensive care unit – full provision of the newborn's body with basic food ingredients to ensure full functioning. Timely diagnosis and correction of Food Intolerance (FI) in the PTI is an important way to improve survival rates and the health and quality of life of this category of newborns.

The **aim** of the study was to conduct a comparative analysis of the clinical manifestations of nutritional deficiency in preterm infants, taking into account the gestational age and severity of perinatal pathology.

Materials and Methods

The total number of PTIs included in the research program was 355 infants with gestational age at birth of 26–36/6 weeks: Group I consisted of 54 newborns with a gestational age of 26–31/6 weeks who had a serious condition at birth; Group II – 149 newborns with a gestational age of 32–33/6 weeks, of whom: Subgroup IIA – 67 infants with severe forms of perinatal pathology, Subgroup IIB – 82 infants with moderate perinatal pathology; Group III consisted of 102 infants with the gestational age of 34-36/6 weeks, including: Subgroup IIIA – 41 infants with clinical forms of severe perinatal pathology, Subgroup IIIB – 61 infants with moderate perinatal pathology; Group IV included 50 conditionally healthy newborns at a gestational age of 34–36/6 weeks.

The inclusion criteria for the study were: gestational age 26–37 weeks, birth weight <2500 g; the presence of adaptation disorders at birth and clinical signs of perinatal pathology during the neonatal period, manifestations of nutritional deficiencies, and informed consent of the child's parents to participate in the study. The exclusion criteria were: gestational age at birth <29 weeks and ≥37 weeks; weight ≥2500 g; congenital malformations, no food tolerance disorders, and parental consent to the newborn's participation in the clinical trial.

The clinical study was an open-label, single-center, stratified, cohort study. The duration of the newborn observation included the period of stay in the maternity facility. In order to form risk Groups for the predicted development of FI, a comparative analysis of the list of antenatal, perinatal, and postnatal risk factors, as well as pathological conditions of the neonatal period, taking into account the severity of the newborn condition, was carried out in the course of the research. The following were subject to analysis: exchange cards for pregnant women (Form (F)of medical documentation No.113/0), birth histories (F No. 096/0), and newborn development charts (F No.097/0).

The list of diseases of the early neonatal period included clinical diagnoses according to the ICD X revision. The diagnoses were made taking into account the current recommendations of the National Classifier of Ukraine "Classifier of Diseases and Related Health Problems NK 025:2021": Class 16. Certain conditions occurring in the perinatal period (P00–P96).

The diagnoses were verified in accordance with the current clinical guidelines and unified clinical protocols for neonatal care in the areas of neonatology and pediatrics approved by the Ministry of Health of Ukraine in 2015–2024. The correspondence of the degree of maturity of the child to the gestational age at birth was determined by taking into account anthropometric parameters (weight, body length, head circumference, trunk circumference), assessment of morphological and functional characteristics according to the Ballard scale, and using percentile tables [13]. The nature of adaptation was determined taking into account the Apgar score at 1 and 5 minutes of the newborn's life and the results of further dynamic clinical and laboratory observation. The severity of the condition in infants was determined according to a set of clinical signs, as well as using the Score for Neonatal Acute Physiology Perinatal Extension (SNAPPE II) [14; 15]. The diagnosis of multiple organ failure syndrome (MOFS) was made based on the Neonatal Multiple Organ Dysfunction Score (NEOMOD, 2001) [16; 17].

The studies were conducted in compliance with the GCP (1996), the Council of Europe Convention on Human Rights and Biomedicine (1997), the World Medical Association Declara-

tion of Helsinki on the Ethical Principles for Research Involving Human Subjects (1964–2008), and Order of the Ministry of Health of Ukraine No.690 of September 23, 2009 (as amended by Order of the Ministry of Health of Ukraine No.523 of July 12, 2012). Approval of the Commission on Bioethics of Bukovinian State Medical University (Protocol No.2 of February 09, 2015).

Statistical processing of the obtained results was performed on a Pentium MMX CPU personal computer using the Statistica 13 (StatSoft Inc., USA), Excel 2010 (Microsoft, USA), and MedCalc 16.1 (MedCalc Software Ltd., Belgium). After dividing into Groups and comparison Subgroups, descriptive and comparative analysis methods were applied to each of them. Randomization was carried out by centralized computerized Group assignment, taking into account the results of a comprehensive clinical and paraclinical examination of newborns according to the severity of the general condition and gestational age at birth.

The type of distribution was assessed by determining the degree of central tendency between the arithmetic mean, mode, and median, as well as the slope (symmetry) and steepness (kurtosis). In the course of the statistical analysis, the arithmetic Mean of the sample (M), Standard deviation (S), and standard error (m) were determined using the Shapiro-Wilk test (normal distribution of values with a sample size of more than 30, $p>0.05$). The comparison of quantitative indicators in samples with a normal distribution was carried out using the Student's t-test. The significance of differences between relative values was determined using Fisher's angular transformation method «φ». To confirm the significance of differences, the generally accepted probability value (p) was taken into account – $p<0.05$. Statistical differences between the treatment and control Groups are presented with the Bonferroni correction.

Results and Discussion

Comparative characteristics of newborns in the observation Groups by gender ratio were as follows: in Group I – 24 (44.44%) boys and 30 (55.56%) girls; in Group II – 70 (46.98%) boys and 79 (53.02%) girls, respectively; in IIA Subgroup – 39 (58. 21%) and 28 (41.79%); in IIB Subgroup – 31 (37.80%) and 51 (62.20%); in Group III – 36 (35.29%) boys and 66 (64.71%) girls, respectively; in IIIA Subgroup – 22 (53.66%) and 19 (46.34%); in IIIB Subgroup – 14 (22.95%) and 47 (77.05%); in Group IV – 27 (54.00%) boys and 23 (46.00%) girls. There was a tendency for a higher percentage of boys with severe condition at birth, namely: 58.21% in Subgroup IIA and 53.66% in Subgroup IIIA compared to newborns with moderate severity of condition – 37.80% in Subgroup IIB and 22.95% in Subgroup IIIB, respectively, but without significant differences.

Comparative characteristics of anthropometric parameters in newborns of the study groups are presented in *Table*.

Taking into account the Apgar score of newborns, certain features of the respective observation Groups were noted. Thus, the average score in newborns of Group I was [4.20±1.11] points at the 1st minute, [5.52±1.12] points at the 5th minute; in infants of Subgroup IIA – [5.34±1.07] points and [6.56±0.78] points, respectively, Subgroup IIB – [6.17±0.74] and [6.85±0.32] points; in infants of Subgroup IIIA – respectively [5.44± ±1.29] and [6.54±0.71] points, Subgroup IIIB – [6.53±0.70] and [6.68±0.72] points with control indicators in newborns of Group IV, respectively [6.85±0.24] points and [8.32±0.35] points ($p_{I,IIA,IIB,IIIA,IIIB:IV}<0.0001$ at 1 and 5 min; $p_{IIA:IIIA}<0.0001$ at 1 min; $p_{I:IIA,IIIA}<0.0001$ at 5 min). Among all infants, 39 (72.22%) infants of Group I, 46 (68.66%) infants of Subgroup IIA, and 21 (51.22%) infants of Subgroup IIIA required the greatest volume of resuscitation measures to stabilize their condition after birth ($p_{I:IIIA}<0.05$).

Among the 355 newborns included in the study program: 54 (100.00%) infants of Group I; 67 (44.97%) infants of Group II; and 41 (40.20%) infants of Group III (40.20%) had severe forms of perinatal pathology, according to gestational age, $p_{I:II}<0.0001$, OR 55.03%; 95% CI 44.62–62.79; $p_{I:III}<0.0001$, OR 59.8%; 95% CI 48.04–68.79).

It should be noted that most infants in Group I, who had significant severity of the condition at birth, were diagnosed with asphyxia – 32 (59.26%) cases, which was accompanied by Respiratory Distress Syndrome (RDS). A significant number of newborns in Group I had primary pulmonary atelectasis – 50 (92.59%) cases and hyaline membrane disease – 38 (70.37%) cases. In addition, a significant number of newborns in this Group had Multiple Organ Dysfunction Syndrome (MODS), which manifested itself in all 54 (100.00%) cases with Central Nervous System (CNS) and Respiratory System (RS) lesions, in 16 (29.63%) cases – CardioVascular System (CVS); hemorrhagic and convulsive syndrome was noted in 17 (31.48%) cases, 14 (25.93%) infants had Disseminated Intravascular Coagulation (DIC) syndrome, 15 (27.78%) infants had the anemic

Table. Anthropometric parameters in newborns of the observation Groups (n, %)

Indicator	Group I, 26–31/6 weeks (n=54)	Group II, 32–33/6 weeks Subgroup IIA (n=67)	Group II, 32–33/6 weeks Subgroup IIB (n=82)	Group III, 34–36/6 weeks Subgroup IIIA (n=41)	Group III, 34–36/6 weeks Subgroup IIIB (n=61)	Group IV, 34–36/6 weeks (n=50)
Body weight (g)	1314.66± ±176.15$^{*\#\#}$	1776.49± ±241.13^{*+}	1837.91± ±162.91*	2132.99± ±341.03	2145.82± ±334.17	2347.60± ±173.55
Body length (cm)	39.80±2.81*	42.85±1.97*	43.66±1.59*	44.30±2.14*	46.19±7.14	45.88±0.44
Head circumference (cm)	27.66±1.67*	29.80±1.85*	30.22±1.39*	31.79±3.10	31.34±1.48	32.00±1.11
Chest circumference (cm)	25.73±1.98*	27.44±1.91*	27.61±1.62*	28.71±1.65	29.14±1.95	29.85±1.44

Notes: p-values were adjusted using the Bonferroni correction;
* – statistically significant difference compared to the control Group, $p<0.01$;
$^{\#}$ – statistically significant differences between Group I and Subgroup IIA, Group I and Subgroup IIIA, $p<0.017$;
$^{+}$ – statistically significant differences between Subgroup IIA and Subgroup IIIA, $p<0.017$.

syndrome. Signs of food tolerance disorders, taking into account the main objective of the study, were observed in the PTIs of all observation Groups, respectively. Among newborns in Group I, compared with Subgroups IIA and IIIA, there were significantly more infants born prematurely – 19 (35.19%). In newborns of Subgroup IIA, compared with Subgroup IIIA, subependymal hemorrhage of grade I was diagnosed more often – 24 (35.82%) cases; a significantly higher number of infants had CNS lesions in the complex of MODS – 29 (43.36%) cases.

The development of severe forms of perinatal pathology in PTI, the clinical signs of which, among other things, were disorders of the functional state of the GIS, was statistically significantly associated with the following factors: gestational age at birth ($p_{I:IV}<0.0001$, OR 55.03%; 95% CI 41.44–66.34; $p_{IIA:IV}<0.0001$, OR 59.80%; 95% CI 43.20–73.34); low birth weight ($p_{I:IIA}<0.0001$, 461.83±39.25; 95% CI 384.11–539.55; $p_{I:IIIA}<0.0001$, 818.3±53.90; 95% CI 711.30–925.36; $p_{IIA:IIIA}<0.0001$, 356.50±56.114, 95% CI 245.25–467.75).

Taking into account the gestational age at birth, the severe condition of the PTI was determined: RDS against the background of severe asphyxia ($p_{I:IIA}<0.0001$, OR 56.72%; 95% CI 43.09–67.90; $p_{I:IIIA}<0.0001$, OR 48.78%; 95% CI 32.81–63.52); primary pulmonary atelectasis ($p_{I:IIA}<0.0001$, OR 58.21%; 95% CI 39.85–71.61); hyaline membrane disease ($p_{I:IIA}<0.0001$, OR 34.55%; 95% CI 16.74–49.34); MODS in the presence of CNS lesions ($p_{I:IIA}<0.0001$, OR 56.64%; 95% CI 43.01–67.83; $p_{I:IIIA}<0.0001$, OR 85.37%; 95% CI 70.05–93.12; $p_{IIA:IIIA}=0.0021$, OR 28.73%; 95% CI 10.96–42.94); RS ($p_{I:IIA}<0.0001$, OR 71.88%; 58.41–81.23; $p_{I:IIIA}<0.0001$, OR 73.17%; 95% CI 56.67–84.30); CVS ($p_{I:IIA}=0.0044$, OR 20.26%; 95% CI 6.21–34.35); US ($p_{I:IIA}=0.0178$, OR 20.20%; 95% CI 3.51–35.84; $p_{I:IIIA}=0.0084$, OR 25.52%; 95% CI 6.77–41.28); hemorrhagic syndrome ($p_{I:IIA}<0.0001$, OR 28.36%; 95% CI 15.31–41.81; $p_{I:IIIA}=0.0044$, OR 24.16 %; 95% CI 7.93–38.26); anemic syndrome ($p_{I:IIA}=0.0001$, OR 24.66 %; 95% CI 12.14–37.96; $p_{I:IIIA}=0.0122$, OR 20.46 %; 95% CI 4.65–34.42); seizure syndrome ($p_{I:IIA}=0.0518$, OR 15.06 %; 95% CI 0.10–30.05); DIC syndrome ($p_{I:IIIA}=0.0069$, OR 21.05%; 95% CI 6.12–34.53).

A comparison of clinical pathology in newborns with moderate condition severity showed that significantly more infants in Subgroup IIB, compared to Group IIIB, had signs of asphyxia accompanied by moderate and mild respiratory disorders – 11 (13.41%) and 47 (57.31%) cases, respectively, as well as grade I extracardiac heart failure – 20 (24.39%) cases. Adaptation disorders in newborns of the IIIB Subgroup were mainly due to mild respiratory disorders – 16 (26.22%) cases. The diagnoses of MFI and low birth weight were also noteworthy – 4 (6.56%) and 10 (16.39%)

cases, respectively. The risk of developing a ventilator-associated tracheobronchitis at birth in infants of Subgroups IIB and IIIB was 20 (24.39%) and 13 (21.31%) cases.

Among the total number of newborns in Groups I–III, 46 (15.08%) had deterioration during the first week of life, accompanied by persistent metabolic disorders due to hypoxic damage against the background of morphological and functional immaturity. In our opinion, this confirms the fact that a purely clinical assessment of the adaptation of infants at birth using the Apgar score may not be sufficient to predict the risk of deterioration in the postnatal period.

The list of possible clinical and laboratory criteria for disorders of the functional state of the GIS in newborns is actively discussed in modern scientific sources. It is noted that there is currently no generalized list of criteria for FI in newborns, including those with PTI. The recommended list of clinical signs of digestive dysfunction in newborns includes an increase in residual stomach volume, vomiting, abdominal meteorism, and blood in the stool [18]. In our opinion, the formation of disorders of the functional state of the GIS at preterm birth has certain features, taking into account the degree of the body's MFI, given the severity of the course of perinatal pathology and the body's reserve capacity during the formation of short-term and long-term adaptation in the postnatal period of development.

The results of the analysis of published scientific sources indicate some discrepancies in the recommendations for the assessment of signs of FI in newborns, in particular in PTI. For example, the results of a multicenter randomized trial published in 2002 show that the color of gastric residues in preterm infants is not always a confirmation of FI [19]. The guidelines for feeding very low birth weight infants state that the yellow or green color of residual gastric volume alone is not appropriate as a guide for diagnosing FI and that abdominal circumference measurement is not appropriate for diagnosing FI. According to the latest published sources, signs of food intolerance in PTI are manifested by an increase in Total Gastric Volume of more than 50% of the previous feeding volume, accompanied by vomiting and/or meteorism, as well as the detection of blood in the stool [20].

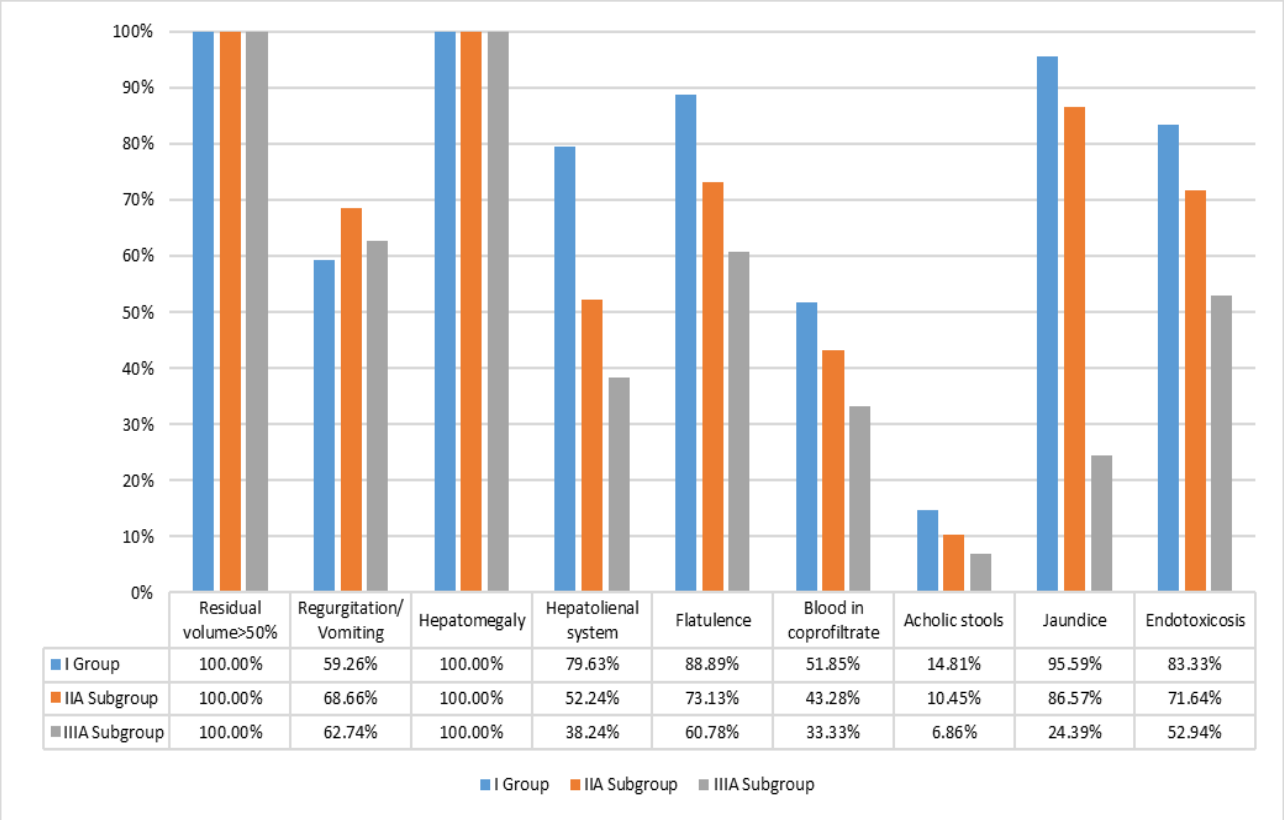
The research paper set the task of clarifying the list of clinical signs of FI in PTI, taking into account the severity of perinatal pathology and gestational age at birth.

Comparative characteristics of the frequency of clinical manifestations of FI in the PTI observation Groups with severe perinatal pathology are shown in *Fig. 1*.

The analysis of the clinical manifestations of FI, which was confirmed by a residual volume of more than 50%, showed the presence of disorders in newborns of all observation Groups, with the percentage of signs having some differences taking into account the gestational age of infants, in particular: regurgitation/vomiting – in Group I 32 (59.26%) cases, in Subgroup IIA – 46 (68.66%) cases, in Subgroup IIIA – 25 (60.98%) cases ($p>0.05$); an increase in liver size more than the physiological norm was noted in infants of all observation Groups – up to 100.00% ($p>0.05$); hepatolienal syndrome – 43 (79.63%) cases in Group I, 35 (52.24%) cases in Subgroup IIA, and 39 (38.24%) cases in Subgroup IIIA ($p_{I:IIA}=0.0018$; OR 27.39%; 95% CI 10.37–41.95; $p_{I:IIIA}<0.0001$; OR 41.39%; 95% CI 21.64–57.19); intestinal meteorism was significantly more common in infants of younger gestational age – 48 (88.89%) cases in Group I, 49 (73.13%) cases in Subgroup IIA and 62 (60.78%) cases in Subgroup IIIA ($p_{I:IIA}=0.0314$; OR 15.76%; 95% CI 1.39–28.83; $p_{I:IIIA}=0.0014$; OR 28.11%; 95% CI 10.72–44.46); blood impurities in coprofiltrate – 28 (51.85%) cases in Group I, 29 (43.28%) cases in Subgroup IIA and 34 (33.33%) cases in Subgroup IIIA ($p>0.05$); acholic stools – 8 (14.81%) cases in Group I, 7 (10.45%) cases in Subgroup IIA and 7 (6.86%) cases in IIIA Subgroup ($p>0.05$); jaundice – 50 (95.59%) cases in Group I, 58 (86.57%) cases in IIA Subgroup, 10 (24.39%) cases in IIIA Subgroup ($p_{I:IIIA}<0.0001$; OR 71.20%; 95% CI 53.68–82.20); endotoxemia syndrome – respectively 45 (83.33%) cases in Group I, 48 (71.64%) cases in Subgroup IIA and 54 (52.94%) cases in Subgroup IIIA ($p_{I:IIIA}=0.0014$; OR 30.39%; 95% CI 11.63–47.10; $\chi^2=10.183$).

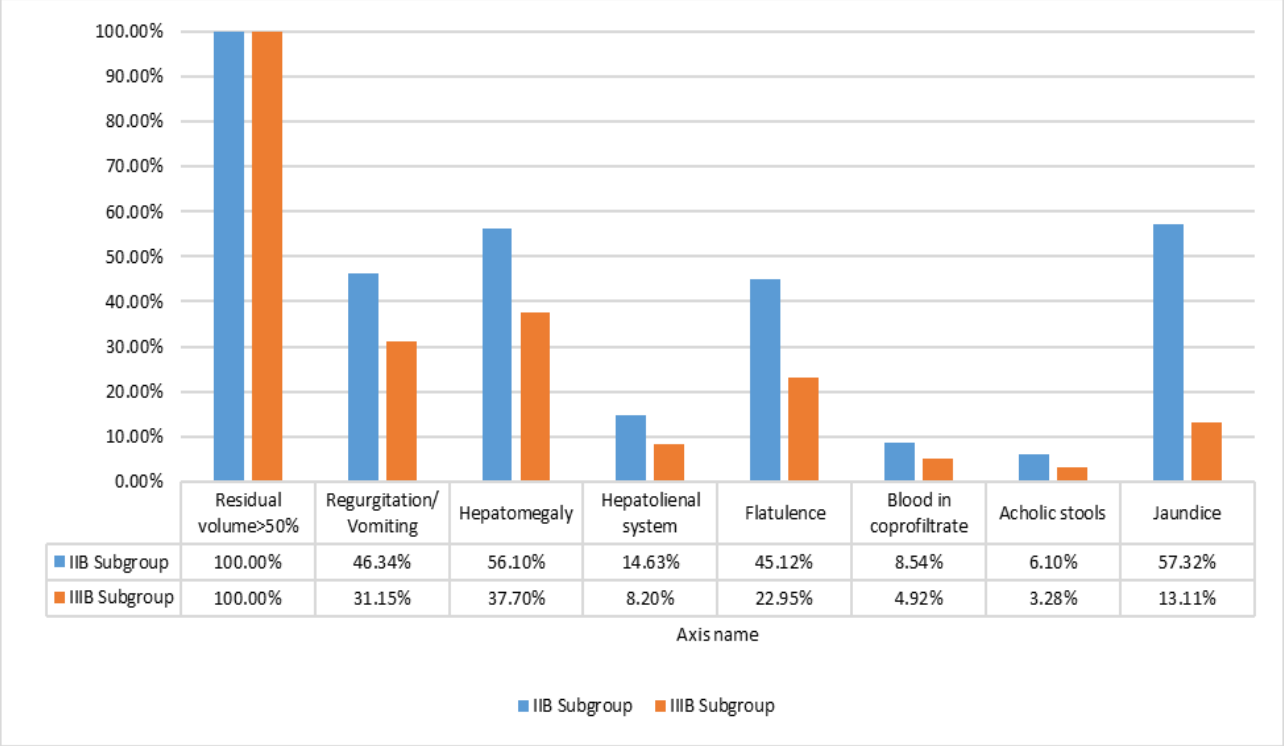
The results of the analysis showed that the incidence of clinical manifestations of FI tended to increase in correlation with a decrease in the gestational age of the PTI according to the entire list of these criteria.

Compared with PTI who had a severe condition due to perinatal pathology, a quantitatively lower percentage of clinical manifestations of FI was observed in newborns with moderate severity of the condition, but there was a tendency for their higher frequency at a lower gestational age of newborns (*Fig. 2*).



	Residual volume>50%	Regurgitation/ Vomiting	Hepatomegaly	Hepatolienal system	Flatulence	Blood in coprofiltrate	Acholic stools	Jaundice	Endotoxicosis
I Group	100.00%	59.26%	100.00%	79.63%	88.89%	51.85%	14.81%	95.59%	83.33%
IIA Subgroup	100.00%	68.66%	100.00%	52.24%	73.13%	43.28%	10.45%	86.57%	71.64%
IIIA Subgroup	100.00%	62.74%	100.00%	38.24%	60.78%	33.33%	6.86%	24.39%	52.94%

Fig.1. Comparative characteristics of clinical manifestations of FI in the PTI observation Groups with severe perinatal pathology.



	Residual volume>50%	Regurgitation/ Vomiting	Hepatomegaly	Hepatolienal system	Flatulence	Blood in coprofiltrate	Acholic stools	Jaundice
IIB Subgroup	100.00%	46.34%	56.10%	14.63%	45.12%	8.54%	6.10%	57.32%
IIIB Subgroup	100.00%	31.15%	37.70%	8.20%	22.95%	4.92%	3.28%	13.11%

Fig. 2. Comparative characteristics of the frequency of clinical manifestations of FI in the PTI observation Groups with moderate perinatal pathology.

Comparison of the results of the analysis of clinical manifestations of FI in newborns of IIB and IIIB Subgroups showed that all infants had a residual volume of more than 50%, but the percentage of other signs still prevailed at a lower gestational age – respectively, in Subgroup IIB compared to Subgroup IIIB. The following was noteworthy: regurgitation/vomiting was observed in infants of Subgroup IIB in 38 (46.34%) cases, in Subgroup IIIB – in 19 (31.15% of cases ($p>0.05$); increase in liver size compared to the physiological norm – 46 (56.10%) and 23 (37.70%) in infants of Subgroup IIB and Subgroup IIIB ($p_{IIB:IIIB}=0.0300$; OR 18.4%; 95% CI 1.86–33.49); hepatolienal syndrome was diagnosed in 12 (14.46%) and 5 (8.20%) cases, respectively, in Subgroup IIB and Subgroup IIIB ($p>0.05$); intestinal meteorism – in 37 (45.12%) and 14 (22.95%) cases in IIB and IIIB Subgroups, respectively ($p_{IIB:IIIB}=0.0064$; OR 22.17%; 95% CI 6.38–36.03); blood impurities in coprofiltrate were detected in 7 (8.54%) and 3 (4.92%) infants of Subgroup IIB and Subgroup IIIB ($p>0.05$); acholic stools were observed in 5 (6.10%) and 2 (3.28%) cases in newborns of Subgroup IIB and Subgroup IIIB, respectively ($p>0.05$); jaundice was detected in 47 (57.32%) and 8 (13.11%) cases in infants of Subgroup IIB and Subgroup IIIB, respectively ($p_{IIB:IIIB}<0.0001$; OR 44.21%; 95% CI 29.09–56.14).

The analysis of statistical data on the frequency of detection of clinical signs of digestive dysfunction in PTI of the corresponding gestational age at birth showed a significantly higher percentage of them in severe perinatal pathology compared to the average severity of the condition. Quantitative characterization of regurgitation/vomiting cases confirmed a significantly higher frequency in infants of Subgroup IIA compared to Subgroup IIB ($p_{IIA:IIB}=0.0065$; OR 22.32%; 95% CI 6.33–36.63), and also, Subgroup IIIA compared to the Subgroup IIIB (pIIIA:IIIB=0.0017; OR 31.59%; 95% CI 11.88–48.20); an increase in liver size compared to the physiological norm was more often detected in severe neonatal condition – respectively, 100.00% of cases in newborns of Subgroup IIA and Subgroup IIIA compared to the detected frequency in Subgroup IIB and Subgroup IIIB ($p_{IIA:IIB}<0.0001$; OR 43.90%; 95% CI 32.32–54.70; $p_{IIIA:IIIB}<0.0001$; OR 62.3%; 95% CI 47.11–73.38); hepatolienal syndrome was also detected in a significantly higher percentage of cases in newborns with severe condition compared to those whose condition was considered as moderate ($p_{IIA:IIB}<0.0001$; OR 37.61%; 95% CI 22.67–50.62; $p_{IIIA:IIIB}=0.0002$; OR 30.04%; 95% CI 13.68–45.99); clinical manifestations of intestinal flatulence were significantly more frequent in infants of Subgroup IIA and Subgroup IIIA compared to Subgroup IIB and Subgroup IIIB ($p_{IIA:IIB}=0.0015$; OR 26.01%; 95% CI 0.08–40.01; $p_{IIIA:IIIB}=0.0001$; OR 37.87%; 95% CI 18.50–53.87); in severe condition, blood impurities in the coprofiltrate were detected relatively more often in newborns ($p_{IIA:IIB}<0.0001$; OR 34.74%; 95% CI 20.96–47.41; $p_{IIIA:IIIB}= 0.0002$; OR 28.41%; 95% CI 13.30–44.05); the frequency of jaundice was higher in PTI with severe forms of perinatal pathology ($p_{IIA:IIB}=0.0001$; OR 29.25%; 95% CI 14.89–41.70).

Conclusion

Analysis of the data from clinical examination of newborns confirms the possibility of using an expanded list of criteria for the diagnosis of food intolerance in newborns in the presence of perinatal pathology, which includes: residual food volume of more than 50%, regurgitation and/or vomiting, increased liver size above the physiological norm or hepatolienal syndrome, intestinal flatulence, blood impurities in coprofiltrate, acholic stools, jaundice and endotoxemia syndrome.

DECLARATIONS:

Prospects for further research.

For a more precise diagnosis of gastrointestinal system dysfunction in preterm infants, an integrated approach is advisable, which allows the use of additional laboratory methods in addition to clinical ones.

Statement of ethics.

The authors have no ethical conflicts to disclose.

Data transparency.

Data can be requested from the authors.

Sources of funding.

There are no external sources of funding.

Consent to publication.

All authors consent to publication.

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EARLY DIAGNOSIS OF MONOGONARTHROSIS (literature review)

Golka G.G., Vesnin V.V., Burlaka V.V., Oliynyk A.O., Fadieiev O.G., Goptsy O.V., Frolova-Romanyuk E.Yu.

Kharkiv National Medical University, Kharkiv, Ukraine

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ABSTRACT

Background. OsteoArthritis of the Knee Joint (OAKJ) is a progressive incurable disease, which in severe cases necessitates total joint arthroplasty.

Aim. To conduct a systematic analysis of the scientific literature on the prospects and possibilities of early diagnosis of monogonarthrosis.

Materials and Methods. A literature search was conducted in the PubMed and Medline databases for the period 2010–2024, using the following keywords: "osteoarthrosis of the knee joint", "monogonarthrosis" (42 sources).

Results. The mainstream of modern literature on the problem of clinical diagnosis of osteoarthritis, including with monoarticular lesions, includes the results of studies of biomarkers of hyaluronic cartilage degradation both in the case of visualization on magnetic resonance imaging scans and according to the data of biochemical and immunological analyses of blood serum. The importance of radiological signs of mainly early stages of osteoarthritis of the knee joint is also separately studied. There are isolated contradictory professional works on the correlation of clinical and radiological manifestations of gonarthrosis. Reports on the results of a comprehensive clinical and radiological examination of patients with monogonarthrosis are almost not presented in the literature.

Conclusions. It was established on the basis of information and analytical studies of modern scientific literature that osteoarthritis of the knee joint is accompanied by persistent pain, significant limitation of lower limb function, decreased working capacity, which often leads to joint replacement. Diagnosis of osteoarthritis in the early stages is difficult due to the lack of pathognomonic clinical, radiological and laboratory indicators, and in the case of monogonarthrosis with synovitis it is complicated by differentiation with specific arthritises of the knee joint. The above data indicate the feasibility of further research to find opportunities for improving methods for early diagnosis of monogonarthrosis.

Keywords: *osteoarthritis of the knee joint, pathogenesis, clinical and laboratory studies*.

Introduction

OsteoArthritis of the Knee Joint (OAKJ) is a progressive incurable disease, which in severe cases necessitates total joint arthroplasty, which requires significant economic costs [1; 2] and medical and social adaptation [3; 4] and has a significant number of postoperative complications and adverse outcomes [5; 6].

OsteoArthritis (OA) of the knee joint is accompanied by persistent pain, significant limitation of lower limb function, decreased performance, which often leads to joint arthroplasty. Diagnosis of the disease in the early stages is complicated by the lack of pathognomonic clinical, radiological and laboratory indicators, and in the case of monogonarthrosis with synovitis it is complicated by differentiation with specific arthritis of the knee joint. Clinical symptoms and structural changes of the knee joint elements in patients with monogonarthrosis are covered in isolated studies, a significant part of which was published more than 10 years ago.

It should be noted that there is still no generally accepted definition of knee osteoarthritis, which leads to certain discrepancies in determining epidemiology indicators, factors of etiology and pathogenesis, and protocols for examination and tre-

Corresponding Author:
Golka Grigoriy G. – MD, DMedSc, Professor, Head of the Department of Traumatology and orthopedics, Kharkiv National Medical University.
✉ Ukraine, 61022, Kharkiv, Nauki ave., 4.
E-mail: hh.holka@knmu.edu.ua

atment of this category of patients. According to clinical guidelines developed by the Associations of Rheumatologists and Orthopedic Traumatologists of Ukraine, osteoarthritis is a metabolically active, dynamic process that involves all tissues of the joint (cartilage, bone, synovial membrane/capsule, ligaments and muscles). The main pathological changes include localized loss of articular (hyaline) cartilage and alteration of the adjacent bone with the formation of new bone (osteophyte) at the edges of the joint [3; 7; 8]. According to the International Statistical Classification of Diseases and Related Health Problems, 10th revision, osteoarthritis is included in sections M15–M19. In this block, the term "osteoarthritis" is used synonymously with the terms "arthrosis" and "osteoarthrosis".

Osteoarthritis is the most common form of joint disease due to increased life expectancy and body mass index [9–11]. Clinical symptoms of osteoarthritis of the hip and knee joints are observed in 242 million people worldwide [10; 12; 13].

In Ukraine, the average long-term prevalence of osteoarthritis was [1836.23±229.19] per 100,000 population, for the period 2014–2017 – [1770.96± ±32.56], respectively, the upward trend continued during 1993–2013. The average long-term incidence rate of deforming arthrosis during 1993–2014 was [266.15±11.73] cases per 100,000 population, for the period 2014-2017 – [229.84± ±5.60] cases per 100,000 population. After 2015, a slight decrease in incidence and prevalence rates was recorded. The prevalence of deforming arthrosis in 2010 exceeded the incidence by 5.66 times, and in 2017 – by 7.80 times, while the gap between the indicators was constantly increasing, there was an accumulation of chronic disorder in the population [3; 8; 14].

The prevalence and incidence ratio in women and men is 1:69 (p<001) and 1:39 (p<0001), respectively [15; 16]. 62% of people with OA are women. Among people younger than 45 years of age, OA is more common in men; over 45 years of age, OA is more common in women [13; 17]. The high prevalence of OA is reflected in enormous social and personal costs. The total economic burden associated with OA in the United States is estimated at $136.8 billion per year. This figure has more than doubled in the last decade. In the long term, the annual economic cost of OA exceeds the consequences of diseases related to smoking, cancer, and diabetes. The direct medical costs of treating patients with knee OA reach $65 billion per year [18]. OA was the second most expensive disease in US hospitals in 2020 [16]. Approximately 1 million knee and hip replacement surgeries are performed annually due to OA [16].

There is now considerable evidence linking knee osteoarthritis to genetic predisposition, obesity, aging [4; 19; 20], mechanical stress [21], and inflammation [22]. However, the pathogenesis and causes of OA are not fully understood.

Diagnosis of knee osteoarthritis in the early stages of the disease presents significant difficulties, which are associated with the absence of typical clinical manifestations, minor radiological signs and uncharacteristic changes in laboratory parameters of biological fluids of the body [22–24]. The diagnosis of the early stages of gonarthrosis is additionally complicated by the lack of correlation between structural changes and their functional consequences, as well as the visualization of the main radiological (including tomographic) signs inherent in knee osteoarthritis in asymptomatic subjects [2; 9; 25; 26].

The clinical diagnosis of knee OA is based on the clinical guidelines of the Ukrainian Association of Rheumatologists and the Ukrainian Association of Orthopedic Traumatologists, as well as the criteria of the American College of Rheumatologists (ACR) and the European League Against Rheumatism (EULAR) [7; 18; 27].

Available literature either discusses differential diagnosis with monoarthritis [9; 22; 28] or provides results of instrumental diagnosis of early stages of knee osteoarthritis [29; 30]. Therefore, the clinical symptoms of monogonarthrosis are almost not presented in the available literature.

In unilateral gonarthrosis in the initial stages, especially in the case of the development of monosynovitis, diagnosis and differential diagnosis are also difficult, due to the variability of the clinical course and the lack of typical data of radiological and laboratory examination [18; 28; 31].

Aim. To conduct a systematic analysis of the scientific literature on the prospects and possibilities of early diagnosis of monogonoarthrosis.

Materials and Methods.

A literature search was conducted in the PubMed and Medline databases for the period 2010–2024, using the following medical subject headings and keywords: "deforming osteoarthritis of the knee joint", "monogonarthrosis". If necessary, in some cases, literature sources that go beyond the search period were used.

The general search revealed 78 sources on diagnostic and treatment methods in the early stages of monogonarthrosis. The primary exclusion con-

cerned literary sources that reflected the diagnosis and treatment of late stages of osteoarthritis of the knee joint (n=22). The secondary exclusion included literary sources that contained only reference information (abstract, figures, references) (n=14). As a result, only relevant full-text articles in professional journals remained (n=42).

Results and Discussion

Osteoarthritis of the knee joint is a chronic progressive pathological process that involves all elements of the joint: articular cartilage, subchondral plate, underlying subchondral bone, synovial membrane, menisci, ligamentous apparatus, periarticular muscles, etc. [19; 23; 32–34]. Osteoarthritis is a multifactorial disease, among the risk factors for its development are age, gender, obesity [2; 26; 35; 36], previous injuries, hereditary predisposition, repeated loads accompanied by cumulative microdamage to the joint tissues (frequent kneeling, prolonged squatting), discongruence of the articular surfaces, joint instability, etc. [4; 23; 30]. An important factor in the pathogenesis of OA is considered to be a decrease in the stabilizing effect of the periarticular muscles due to hypodynamia [30; 34] or sarcopenia [20; 33], which is accompanied by a decrease in the resistance of the knee joint elements to the action of daily loads. However, OA is not a purely mechanical problem. In the pathogenesis and progression of osteoarthritis, especially in the early phase, inflammatory and metabolic processes play a significant role, in which all tissues of the joint are involved. Among the numerous predictors of osteoarthritis, the main independent risk factor is age [4; 29; 35], however, aging and OA are interrelated, not interdependent [33; 35]. The involutive process is accompanied by the cumulative effect of many years of mechanical loads, which leads to "wear and tear" and pathological destruction of articular cartilage [36; 37]. Based on this, some authors consider osteoarthritis as a natural irreversible disease, and not as a degenerative, potentially curable disease. Not only cartilage, but also subchondral bone, menisci, muscles, as well as adipose and synovial tissues play an important role [17; 35; 20].

In the intact joint, hyaline cartilage is an avascular, aneural tissue with chondrocytes as the only cell type in the cartilage tissue [33; 38; 39]. In addition to chondrocytes, articular cartilage is formed by an extracellular matrix.

Since cell division or death is practically absent in adults, chondrocytes of articular cartilage are considered long-lived cells and, therefore, can accumulate age-related changes over time [36; 37]. As a result, aging profoundly alters chondrocyte function, matrix structure, and function. There is increased apoptosis and decreased cell regeneration [38], at the molecular level, the stiffness of the collagen network increases, and glycation increases, which potentiates dysfunction of articular cartilage and, consequently, the joint [11; 39].

OA develops due to the inability of chondrocytes to maintain homeostasis between the synthesis and degradation of extracellular matrix components [4; 5; 34; 35]. Disruption of homeostasis leads to an increase in water content and a decrease in proteoglycans in the extracellular matrix; weakening of the collagen network due to a decrease in the synthesis of type II collagen and an increased breakdown of pre-existing collagen [6; 36]. On the other hand, there is increased apoptosis of chondrocytes. Initially, compensatory mechanisms, such as increased synthesis of matrix molecules and proliferation of chondrocytes in the deeper layers of the cartilage, are able to maintain the integrity of the articular cartilage, but over time, chondrocyte loss and changes in the extracellular matrix prevail, and osteoarthritic changes develop [18; 34]. Early superficial changes in articular cartilage in osteoarthritis manifest as thinning and fibrillation, which spread distally, forming deep cracks with cartilage delamination. Subsequently, the underlying calcified cartilage and subchondral bone are exposed [23; 28; 37], and the calcified cartilage proliferates, which further increases the mechanical load with subsequent production of catabolic factors [28]. In addition, the increased layer of calcified cartilage advances into the underlying articular cartilage. These changes are due to the penetration of vascular channels, sympathetic and sensory nerves from the bone marrow through the subchondral bone and calcified cartilage to the articular cartilage [39].

Subchondral sclerosis develops with an increase in the volume and thickness of the subchondral plate. These changes are accompanied by thinning of the subchondral trabecular bone in the early stage and its sclerosis in the late stage of OA [28].

Altered osteoblast and osteoclast activity leads to bone remodeling with the formation of subchondral cysts and osteophytes [39]. These changes are usually accompanied by erosion and fissures of the overlying cartilage with exposure of the subchondral bone [33; 34]. The appearance of altered bone marrow areas and exposed subchondral bone correlates with clinical symptoms, especially pain [9; 18].

Synovial fluid plays a crucial role in the trophism of avascular articular cartilage as a source of nutrients, as well as a reservoir for its degradation products [24; 28].

Synovitis is an important feature in patients with OA and is associated with both clinical symptoms and structural progression of the disease. Inflammation in OA causes synovial proliferation and infiltration of T and B lymphocytes and mast cells [29], followed by synovial hypertrophy. The latter is defined as synovial thickening ≤4 mm and a depth of effusion ≤4 mm or ≤4 mm in the suprapatellar fossa [24; 38].

Synovial hypertrophy is associated with radiographic and clinical progression of OA with the development of knee pain and dysfunction. Areas of altered synovial membrane are usually associated with sites of articular cartilage degradation [36; 37]. However, in later stages of osteoarthritis, synovitis becomes diffuse [24].

Patients with radiologically confirmed OA almost always have degenerative damage to the meniscus, leading to loss of load-bearing capacity and cushioning in the corresponding (medial or lateral) area of the joint with the development of local instability. This situation can result in static changes in the tibiofemoral joint with pathological changes in the articular cartilage, subchondral bone, and subchondral bone marrow [18; 35; 39].

The cause of joint pain in osteoarthritis is not fully understood. It is recognized that pain has a complex biopsychosocial model; in osteoarthritis, pain reflects a state of altered pain processing, in which every day stimuli are perceived as painful. These changes occur in response to critical interactions with specific joint, bone, and periarticular factors that may vary from person to person. The resulting sensitization of nociceptive pathways at both the peripheral and central levels depends on many independent and unique factors for the individual. These include individual characteristics of the patient (gender, age, previous medical history, (effectiveness in pain perception and management, pain catastrophizing, environmental factors, lifestyle, and social (social support, working conditions) [9; 11; 23; 26].

The relationship between joint pain and the progression of osteoarthritis may be that pain with concomitant aseptic inflammation and decreased joint mobility produces structural disorders in all intra- and periarticular tissues [19], which will lead to increased functional disorders [2; 9; 40] with a corresponding increase in pain intensity and movement limitation and, thus, contributes to the further development of the pathological process.

One of the important clinical manifestations of gonarthrosis is periarticular muscle dysfunction due to reduced strength of the muscles that stabilize the knee joint and altered proprioception indicators, mainly such muscle sensations as the feeling of force and movement of the knee joint [18; 28; 39].

Pain in the affected joint, together with associated functional limitations, is the main cause of disability in patients with gonarthrosis [9; 15] and is the main reason that prompts this category of patients to undergo arthroplasty [41; 42].

The prevalence of clinical symptoms of knee OA is negatively associated with education level [11; 43]. This situation may be explained by the fact that people with a lower level of education are often engaged in heavy physical labor or have little knowledge about the prevention of knee OA [33]. The same authors [33] did not find a statistically significant difference in the prevalence of clinical manifestations of knee OA between rural and urban areas.

Knee OA negatively affects the quality of life and physical function in both sexes, but in women this disease is more pronounced compared to men [15]. In almost 44% of cases, patients with OA experience activity limitations due to pain. By 2040, the number of patients with OA is expected to grow, with an increase in the frequency of observations with activity limitations by [11–14] %. About 30% of patients with knee OA report significant limitation of kneeling and bending; 20% are unable to walk 3 blocks without pain. Activity limitations associated with clinical manifestations of OA can lead to loss of work [11]. The presence of effusion in the suprapatellar bursa increases the risk of arthralgia [28; 38]. At the same time, other studies using the WOMAC scale have shown that in the presence of joint effusion in only 3.6% of cases (when examining 409 participants and 775 knee joints), pain and stiffness in the joint were reported in 31% and 34% of observations, respectively. Almost 42% of the examined had limited movement in the affected joint, and 52% of cases had at least one of the WOMAC indicators [19]. Such data may indicate that one of the reasons for increased joint pain in the presence of effusion may be purely mechanical, due to the activation of proprioceptors of intra-articular tissues that are in a stretched state and subjected to increased pressure by an excessive amount of synovial fluid.

Structural changes in knee joint tissues in osteoarthritis are not visualized by modern radiological methods at all stages of the clinical course. The initial changes that define the early stage of OA are characterized by a long period of molecular changes in extracellular matrix macromolecules, which are detected by biochemical analyses of biological fluids of the body [23; 24; 27; 28]. The stage of molecular changes is followed by changes in the articular tissue. Early damage to the articular tissue, detected by sensitive imaging methods such as magnetic resonance imaging [29], is also considered to be early stages of OA. Radiographic diagnostics is informative, usually when arthralgia occurs with the development of structural damage in the subchondral plate and underlying subchondral bone. In the terminal stages, with the development of deformation of the joint elements, the diagnosis of osteoarthritis is usually beyond doubt.

OA is a disease that affects joint tissues, and therefore the search for biomarkers of degenerative and inflammatory processes characteristic of osteoarthritis has focused on biopolymer molecules associated mainly with cartilage tissue, bone metabolism and inflammation. These biomarkers are soluble in serum, synovial fluid and urine.

C-reactive protein, type 2 collagen and myeloperoxidase correlate with the severity of erosive OA. In addition, hyaluronic acid is considered a marker of synovitis [17]. Some authors [1] considered the concentration of C-reactive protein and oligomeric cartilage matrix protein as biomarkers of the development of knee OA.

C-Reactive Protein (CRP) is a central component of the innate immune inflammatory response; by binding to the cell surface of dead or dying cells and some bacteria, it leads to activation of the complement system. The synthesis of CRP is mediated by factors secreted by macrophages and adipocytes. CRP also contributes to the stimulation of pro-inflammatory cytokines, which enhances the inflammatory response [26]. Several studies have also attempted to establish a relationship between serum CRP levels and osteoarthritis [23]. A recent meta-analysis of 32 studies found statistically significant differences in serum CRP levels between patients with osteoarthritis and healthy controls. The study also found that CRP was significantly associated with pain and decreased physical function, but not with radiographic OA [28]. In studies that adjusted for body weight, CRP has been shown to be independently associated with osteoarthritis, whereas others have found no such association.

Hunter T.M. et al. [18] reported that serum C-reactive protein and Erythrocyte Sedimentation Rate (ESR) in patients with knee OA significantly correlated with clinical and radiographic features of the disease. ESR was significantly higher in patients with arthralgia and/or patellar bulging compared with patients without these symptoms. High-sensitivity CRP levels were significantly higher in patients with pain, swelling, and patellar bulging compared with patients without swelling, pain, or patellar bulging. ESR and CRP levels were not significantly different in patients without flexion contracture (>5º) and reduced flexion (<120º).

Osteoarthritis with an inflammatory component is a debilitating and very common disease, but it often occurs subclinically. There is increasing evidence that inflammatory and destructive synovial reactions play an important role in OA. In addition, the role of inflammation in OA has been recognized through the association of joint effusion with joint pain [9]. It is still unclear to what extent inflammation is the initiator or the result of the destructive process of the joint [33]. Of particular interest is the emerging evidence that the extent to which immune and wound-healing responses can be activated partly controls an individual's susceptibility to chronic diseases, including OA. Despite the global burden of OA, diagnostic tests and treatments at molecular or early subclinical stages are still not available for clinical use.

Inflammatory and metabolic processes, which involve all tissues of the joint, play a significant role in the pathogenesis and progression of osteoarthritis, especially in the early phase. Macrostructural changes occur in the form of early superficial changes in the articular cartilage, namely thinning and fibrillation, which spread distally, forming deep cracks with cartilage delamination. Subsequently, the underlying calcified cartilage and subchondral bone are exposed [22; 36; 39], subchondral sclerosis develops with an increase in the volume and thickness of the subchondral plate. These changes are accompanied by thinning of the subchondral trabecular bone in the early stage and its sclerosis in the late stage of OA [39].

Subchondral bone marrow changes occur in the form of microtrauma of bone tissue with localized fibrosis, fat necrosis, and local increased bone remodeling with a predominance of bone re-

sorption, leading to microfractures of trabecular bone [20]. These changes are usually accompanied by erosion and fissures of the overlying cartilage with exposure of subchondral bone [34]. The appearance of altered bone marrow areas and exposed subchondral bone correlates with clinical symptoms, especially pain [9; 18]. Most people with knee OA suffer from pain, joint stiffness, and limitations in daily activities. Orthopedic examination may reveal clinical signs such as joint crepitus, smoothing of the contours, or, less commonly, swelling of the affected joint, deformity, or a slight increase in joint temperature. In addition, this category of patients often has impaired indicators such as lower limb muscle strength and knee proprioceptive accuracy, which are considered important factors for knee joint stabilization [9; 19; 31].

Thus, the mainstream of modern literature on the problem of clinical diagnosis of osteoarthritis, including with monoarticular lesions, includes the results of studies of biomarkers of hyaluronic cartilage degradation both in the case of visualization on magnetic resonance imaging scans [28] and according to biochemical and immunological analyses of blood serum [24; 26]. The importance of radiographic signs of mainly early stages of knee osteoarthritis is also studied separately [22; 28]. There are isolated contradictory professional works on the correlation of clinical and radiographic manifestations of gonarthrosis [9]. Reports on the results of a comprehensive clinical and radiological examination of patients with monogonarthrosis are almost absent in the literature.

Conclusions

1. It was established on the basis of information and analytical studies of modern scientific literature that osteoarthritis of the knee joint is accompanied by persistent pain, significant limitation of lower limb function, decreased working capacity, which often leads to joint replacement.

2. Diagnosis of OA in the early stages is difficult due to the lack of pathognomonic clinical, radiological and laboratory indicators, and in the case of monogonarthrosis with synovitis it is complicated by differentiation with specific arthritises of the knee joint. The above data indicate the feasibility of further research to find opportunities for improving methods for early diagnosis of monogonarthrosis.

DECLARATIONS:

Disclosure Statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Statement of Ethics

The authors have no ethical conflicts to disclosure.

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THE SYSTEM OF RISK FACTORS FOR DISEASES IN VALEOLOGICAL DISCIPLINES

Shevchenko A.S.[1–3], Shevchenko V.V.[3, 4], Pomogaybo K.G.[1], Danylchenko S.I.[5], Brown G.W.[6], Shumskyi O.L.[7], Bilyi Ye.Ye.[1], Zhoga R.A.[8], Yushko V.I.[9]

[1]Kharkiv National Medical University, Kharkiv, Ukraine
[2]Kharkiv Regional Institute of Public Health Services, Kharkiv, Ukraine
[3]V.N. Karazin Kharkiv National University, Kharkiv, Ukraine
[4]National Technical University "Kharkiv Polytechnic Institute", Kharkiv, Ukraine
[5]Kherson State University, Kherson, Ukraine
[6]International Public Health Institute, Berlin, Germany
[7]Simon Kuznets Kharkiv National University of Economics, Kharkiv, Ukraine
[8]Kharkiv Humanitarian-Pedagogical Academy, Kharkiv, Ukraine
[9]Kharkiv Regional Bar Council, Kharkiv, Ukraine

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ABSTRACT

Background. With a view of primary prevention of diseases common in the world, medical workers and educators can effectively work together within teaching valeological disciplines at higher education institutions. Medical information should be adapted for non-medical students using the methods of scaling, aggregation, balancing and system analysis. Their application requires studying the content of main topics of valeological disciplines, determining the boundaries of didactic adaptation and testing in different higher education establishments. Adaptation of medical information on risk factors for understanding by non-medical students has not been studied enough.

Aim. To study the characteristics and interrelationships of risk factors of socially significant diseases for the didactic adaptation of the content of valeological disciplines.

Materials and Methods. The bibliosemantic method, comparative method, and system analysis method were used for the study. The analysis takes into account the experience of primary prevention of diseases and teaching valeological disciplines in higher education institutions in Ukraine and Germany.

Results and Conclusions. The system of risk factors for diseases that are responsible for a significant number of deaths in most countries of the world is the subject of study of modern valeological disciplines. Medical research allows us to divide risk factors into controllable, conditionally controllable and uncontrollable. The impact of the first two groups of risk factors on health can be eliminated or significantly weakened by forming non-medical students' valeological competence and adherence to a healthy lifestyle throughout life. The programs for primary prevention of socially significant diseases should include recommendations for quitting smoking, alcohol abuse, drug use, overeating, overfatigue, hypodynamia, or, conversely, extreme sports, and unprotected sex. Didactic adaptation of complex medical information is needed for valeological education of non-medical students. Its algorithms are analyzed in this article.

Keywords: *primary prophylaxis, preventable disease, controllable risk factors, healthy lifestyle, valeological competence, didactic adaptation.*

Corresponding Author:
Shevchenko Alexander S. – MD, MM,E&P, Director of the Kharkiv Regional Institute of Public Health Services.
✉ Ukraine, 61057, Kharkiv, Rymarska str., 8.
E-mail: as.shevchenko@knmu.edu.ua

Introduction

In 2024, the main causes of death worldwide were chronic diseases, infections and external factors [1–3]. [16–18]% of all deaths were due to Ischaemic Heart Disease (IHD), [11–12]% to stroke, [6–7]% to Chronic Obstructive Pulmonary Di-

sease (COPD; it should be distinguished from deaths caused by COronaVIrus Disease 2019, COVID-19); [5–6]% to lower respiratory tract infections (pneumonia, COVID-19, influenza); 13% to lung, liver, stomach and breast cancer; [3–4]% to type 2 diabetes; 3% to dementia (including Alzheimer's disease); [2–3]% to car and other accidents; [1.5–2]% – Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS); 1.5% – neonatal pathologies that cause perinatal mortality. External causes account for 8% of global mortality (injuries, accidents, violence). The listed diseases and life-threatening conditions have common risk factors, the connection of which, is well known to the medical community, but is not sufficiently covered in the programs of many modern valeological disciplines for non-medical students [4–6]. For example, the main risk factors for death from vascular crises are arterial hypertension, atherosclerosis, smoking, obesity and stress; COPD – smoking and air pollution; lung cancer – smoking, radon and smog; type 2 diabetes mellitus – obesity and a sedentary lifestyle. Of the listed risk factors, at least smoking is a completely controllable factor, and quitting smoking is not as difficult as quitting other addictive psychoactive substances.

The study of risk factors for diseases that cause death allows us to determine the list of issues that need to be studied with non-medical students within a limited time and depending on their level of training (knowledge of anatomy, human physiology, hygiene and the basics of a healthy lifestyle) [7–11]. Risk factors in educational materials can be described for non-medical students in a simplified way, but within the framework of evidence-based medicine [5; 7; 12]. Such balancing and scaling should allow us to increase the preventive impact of valeological disciplines taught in higher education institutions of Ukraine on the fulfillment of the requirements of national educational standards, and will also improve preparation for the formation of models of safe behavior and a healthy lifestyle among graduates of higher education institutions for their education throughout life [13–15].

We did not find any studies devoted to the didactic adaptation of information about risk factors for socially significant diseases for their understanding by non-medical students of higher education institutions in Ukraine. This gap in the literature highlights the need for tailored educational approaches, which determined the aim of our study.

The **aim** of the study was to study the characteristics and interrelationships of risk factors for socially significant diseases for the didactic adaptation of the content of valeological disciplines.

Materials and Methods

The bibliosemantic method, comparative method, and system analysis method were used in the study. In our analysis we took into account the experience of primary disease prevention and teaching of valeological disciplines "Health Pedagogy" and "Fundamentals of Medical Knowledge and Health Preservation" in higher education establishments of Ukraine and Germany. In particular, in Ukraine, teaching took place 1) in such higher education institutions as Ukrainian Engineering Pedagogics Academy (V.N. Karazin Kharkiv National University), National Technical University "Kharkiv Polytechnic Institute", Simon Kuznets Kharkiv National University of Economics; 2) in classroom and distance learning modes during 2004–2024; 3) for full-time, part-time (evening), and distance learning students; 4) with teaching of disciplines in full volume and individual lectures at the request of the higher education institution. Understanding of risk factors and their interrelationships by non-medical students of higher education institutions was taken into account according to the feedback principle when they performed creative and control tasks [16; 17].

The study was approved by the Ethics Committee of the International Institute of Public Health (protocol No.23 of December 24, 2024).

Results and Discussion

The valeological programs "Health Pedagogy" and "Fundamentals of Medical Knowledge and Health-Saving" were created in compliance with a number of principles [14; 18–23]:

1) evidence-based medicine (in particular, facts about diseases and risk factors are given only from peer-reviewed scientific publications; all controversial, debatable in the scientific community, the points are indicated when citing each fact) [24; 25];

2) first of all, students are offered to study the diseases that are responsible for the largest number of deaths [26; 27];

3) information obtained about the health of students and their relatives during the educational process is kept confidential by teachers, and is provided for scientific analysis in a generalized form [28–31];

4) the purpose of teaching subjects is to form valeological competence in students, which the authors of the subjects consider to be the ability to

lead a healthy lifestyle, practice safe behavior models, and provide emergency care in critical conditions [32–36].

The analysis of risk factors for socially significant diseases included their significance for the disease development (causes the disease in the first place or enhances the effect of other decisive risk factors), preventability (the ability to take certain actions to prevent the *negative realization* of the factor or, conversely, to abandon certain actions). In fact, the realization of the risk means the transition from the potential probability of getting sick to the actual development of the disease. The consequences of negative realization are complications, deterioration in the quality of life, disability or even death. Examples of negative realization are: the influence of smoking on the development of lung cancer, COPD); the influence of an unhealthy diet on the development of obesity, type 2 diabetes [37]; the influence of physical inactivity on the development of cardiovascular diseases [38]; the influence of genetic predisposition on Alzheimer's disease, the development of atherosclerosis, hypertension, diabetes mellitus [39; 40].

The risk management system included prevention (e.g., vaccination, healthy eating, physical activity), early diagnosis of diseases (regular medical examinations, tests), their treatment and correction of functional disorders (medication, rehabilitation). Trends in the prevalence of socially significant diseases in the world and the WHO European region, in different populations and countries depending on income levels of the population were studied [9; 39; 41].

We also took into account, firstly, social factors of disease development, associated with low incomes of the population, low accessibility to prevention and treatment, long-standing unresolved issues in the organization of health care, widespread chemical addictions (primarily smoking and alcohol abuse), low adherence of the population to a healthy lifestyle, and population aging, which are inherent in the population of Ukraine, especially since the beginning of the full-scale war. Thus, it is known that the number of strokes is significantly higher and survival after vascular crises is lower in countries with low incomes of the population due to insufficient prevention [42; 43]; that population aging increases the number of dementias in the population, in particular because of Alzheimer's disease [40; 44]; that the high number of car accidents and deaths in these accidents is caused by the poor quality of roads [45; 46]; that perinatal diseases and prematurity are largely associated with insufficient medical care [47; 48]. Secondly, we took into account regional features of disease prevalence. Thus, Europe and North America are characterized by high rates of IHD, cancer and dementia; Asia and Africa are characterized by high mortality due to infections (malaria, tuberculosis), road accidents and severe perinatal conditions; Latin America – due to diabetes and violence (homicide) [26; 49]. Thirdly, we took into account the main trends in morbidity in 2024: an increase in the number of deaths from chronic diseases (+12% since 2010) due to the population aging; because of COVID-19, which remains in the TOP-5 of deaths in countries with low vaccination rates; due to antibiotic resistance, which causes approximately 1.3 million deaths annually and is expected to increase [50; 51]. Fourth, we focused on the main preventive areas recommended by the WHO: reducing salt intake (<5 g/day) and constant blood pressure monitoring – for the prevention of cardiovascular diseases; screening examinations (colposcopy, mammography, colonoscopy) and smoking cessation – for the reduction of cancer mortality; reducing sugar and trans fat intake – for the prevention of diabetes mortality [52–54].

This approach is consistent with the guidelines for assessing the impact of risk factors on global health and disease indicators, the Global Health Estimates 2024 (WHO) and the Global Burden of Disease Study 2024 (IHME) [55; 56], which are key documents for analyzing global health trends and are used to shape health policies. Our approach to risk factor analysis is based on a comprehensive methodology that integrates quantitative and qualitative indicators. We pay particular attention to the interactions between different levels of health determination – from individual behavioral factors to macrosocial conditions. An important aspect is the dynamic nature of these interactions, especially in the context of modern global challenges. In particular, we observe how socioeconomic crises amplify the impact of traditional risk factors, creating a "double burden" effect. This is especially noticeable in populations that simultaneously face the consequences of aging and deteriorating access to health care. The current approaches to prevention that we review increasingly shift the emphasis from individual responsibility to systemic solutions. This includes: 1) creating environments that promote healthy lifestyle choices; 2) developing a "preventive environment" in communities; 3) integrating preventive approaches into all policy decisions. At the

level of social medicine, real-time monitoring of the effectiveness of interventions is of particular importance, which allows for prompt adjustment of strategies. We see prospects in combining traditional epidemiological approaches with modern methods of data analysis, which is especially relevant in conditions of limited resources [57].

In the course of teaching valeological disciplines, we pay special attention to the formation of practical skills in disease prevention, which is based on modern scientific approaches. Our method involves explaining the connection between lifestyle and health, how specific everyday decisions (from eating habits to sleep patterns) affect the likelihood of developing diseases in 10–20 years. Special emphasis is placed on the fact that [75–85]% of premature mortality from non-communicable diseases can be prevented through behavioral changes [58–61]. In practical classes, we model real-life situations where students learn to make informed decisions about their health. For example, we analyze typical dietary mistakes that lead to obesity, or analyze how regular preventive examinations can detect diseases at an early stage [22; 23; 62]. An important element is working with motivation [63; 64], which determines personal motives for leading a healthy lifestyle. We emphasize that prevention is not a limitation, but an investment in one's own future, which allows maintaining quality of life in adulthood and old age. We teach to use modern technologies, such as mobile applications for monitoring physical activity or nutrition, to show how digital tools can help in prevention. But at the same time, we note the need for critical evaluation of the results. In addition, we teach students how to become agents of change in their families and communities, transferring knowledge about prevention to loved ones [65].

The topics of the curricula of the disciplines "Health Pedagogy" and "Fundamentals of Medical Knowledge and Health-Saving" are generally presented by the following questions: personal hygiene; household and medical protection against infectious diseases (anti-epidemic regime and vaccination); rational interaction with medical workers and pharmacists; self-examination skills, determining restrictions and regime according to the state of one's own health; ability to use medicines from the home first aid kit; optimal work and rest regime, sleep; rational regime of physical activity; rational nutrition; optimization of everyday life ecology; choice of work according to the state of one's health; safe traffic behavior; psychological hygiene and conflict resolution; protection from violence, bullying; emergency care, self-help; absence of particularly dangerous harmful habits (tobacco smoking, use of narcotic and toxic psychoactive substances, alcohol abuse); responsible sexual behavior; willingness to donate. With an emphasis on the need for timely medical examinations and visits to the doctor, training is provided in self-diagnosis of individual conditions, physical and psychological: for example, determining the level of blood pressure, weight, height, body temperature, muscle strength and endurance, emotions, stress level, cognitive abilities (memory, intelligence), levels of empathy, fatigue, determining signs of burnout; searching for skin and breast neoplasms; detecting signs of stroke, etc.

To develop a self-diagnostic toolkit, a research group of doctors and teachers carefully studied the issues of cardiovascular diseases, crises (myocardial infarction, cerebral strokes) related to their prevention [66–76]. The result of that study was a series of publications that reflect the directions of prevention of these diseases related to valeological education, as well as the development of the "Test for the detection of arterial hypertension by blood pressure indicators and risk factors of hypertension by genetic factors, lifestyle and nutrition", which was included in the program of the discipline "Health Pedagogy". The predictive validity of the questionnaire was determined by experts. In addition, a validity check in the course of longitudinal studies with factor and correlation analysis is planned and is being carried out.

Besides, keeping on doing the study of the effects of tobacco smoking, which was started by our group more than 20 years ago [77; 78], was also close in its theme. Smoking remains one of the main preventable risk factors for the development of Cardiovascular Diseases (CVD), as well as for the vast majority of other diseases considered in the program of valeological disciplines. In recent years, the negative effects of smoking on the background of the smoker's genetic characteristics have been added to the discussion [79; 80]. Prevention of the negative effects of smoking at the individual, group and population levels in the educational programs of valeological disciplines is considered in accordance with the WHO global strategy and the framework convention [78; 81] and the concept of the state policy of Ukraine on reducing the harm from tobacco products [82].

The negative impact of smoking is considered together with other risk factors, which is presented in *Figure 1*.

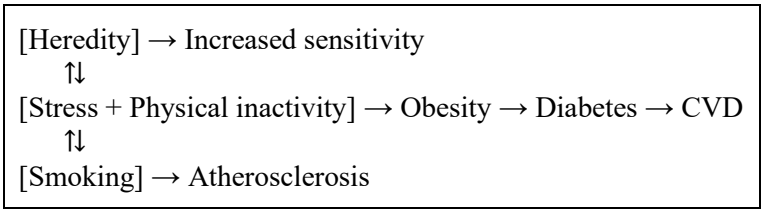


Fig. 1. Visualization of the relationships between risk factors for cardiovascular disease (CVD).

The relationships between risk factors for cardiovascular disease are complex and multifaceted. Hereditary factors play a key role in determining individual susceptibility to the development of metabolic disorders. Studies have shown that certain genetic variants can increase the risk of obesity and insulin resistance [83]. These hereditary characteristics often interact with external factors, such as chronic stress and low physical activity, resulting in a cumulative effect. Chronic stress activates the hypothalamic-pituitary-adrenal axis, which contributes to increased cortisol levels and the accumulation of visceral fat [84]. At the same time, insufficient physical activity contributes to reduced energy expenditure and the development of metabolic syndrome.

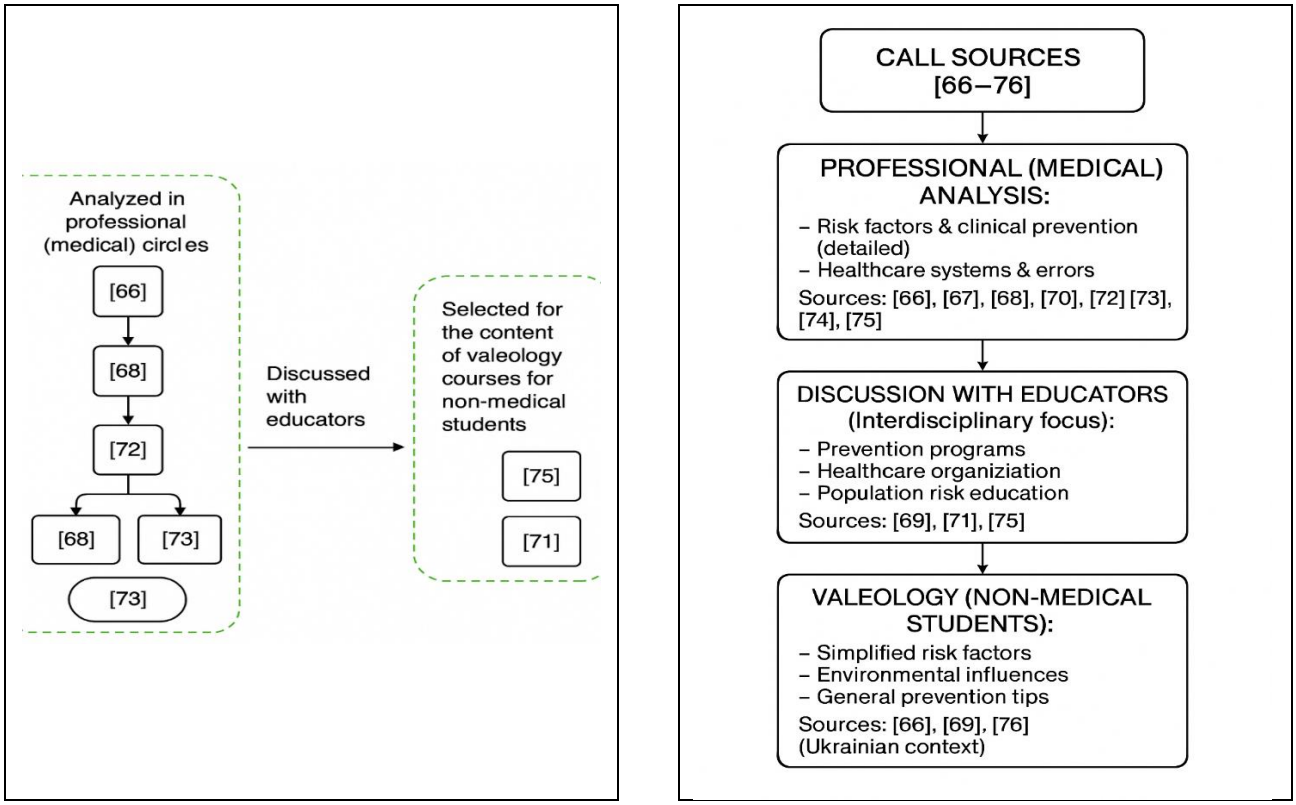
Obesity, which develops under the influence of these factors, is a major driver of insulin resistance and type 2 diabetes. Excess adipose tissue, especially visceral, releases proinflammatory cytokines and free fatty acids that disrupt insulin signaling [85]. Diabetes, in turn, significantly increases the risk of cardiovascular complications through several mechanisms, including endothelial dysfunction, increased oxidative stress, and activation of inflammatory processes [86].

Smoking is an independent risk factor that interacts with other elements of this pathological chain. Tobacco smoke contains numerous toxic substances that damage the vascular endothelium, activate inflammation and accelerate the development of atherosclerosis [87]. The interaction of smoking with other risk factors is particularly dangerous. For example, in patients with diabetes, smoking significantly increases the risk of cardiovascular complications [88]. At the same time, obesity can increase the negative impact of smoking on the body, creating a vicious circle.

It is important to note that genetic predisposition may modulate the effects of all of these factors. Some genetic variants increase stress sensitivity, while others increase the likelihood of developing nicotine dependence or metabolic disorders at the same level of physical activity [89]. This complex network of interactions explains why the same external factors can lead to different clinical outcomes in different individuals.

The methods of *balancing*, *aggregation* and *scaling* developed for the didactic adaptation of complex medical information in the context of generalization by the method of *systems analysis* [4–6] allowed us to study various aspects of the negative implementation of CVD risk factors during 2020–2023, develop an algorithm for didactic adaptation (*Fig. 2* and *3*), and introduce new data on CVD prevention in the educational process of students of engineering and engineering-pedagogical profiles. At the first stage, information on various CVD risk factors was discussed in a professional environment in the form of speeches at scientific and practical conferences, publication of abstracts of speeches [66–76], and with subsequent discussion of the results together in groups with medical workers (scientists) and teachers (*Fig. 2*).

The sequence of using sources and stages of didactic adaptation and validation of data included the following stages: 1) discussion in professional medical circles, 2) in joint groups of medical workers and teachers, 3) in pedagogical circles. Observation of the process of sequential didactic adaptation of data made it clear that professional medical circles were focused on clinical studies of risk factors and on criticism of the organization of the healthcare system [67; 68; 72]. When discussing information at the second stage, with teachers, the scope of the problem review became expanded, but the detailing of risk factors was smaller, which was a manifestation of the simultaneous work of scaling and balancing methods. At this stage, curricula were developed for non-medical students [4; 22; 23], which included characteristics of risk groups with an emphasis on individual publications [69; 71], on a competency-based approach to education [95; 96], namely, the rules for the formation of valeological competence [6; 13; 14; 16; 19; 21; 62; 97–99], some related competencies (primarily environmental) [100; 101]



a b

Fig. 2. Primary algorithm for studying risk factors for cardiovascular diseases for the purpose of their further didactic adaptation for valeological education.

a – taking into account the sequence of use of the main sources and the stages of didactic adaptation and validation of data;

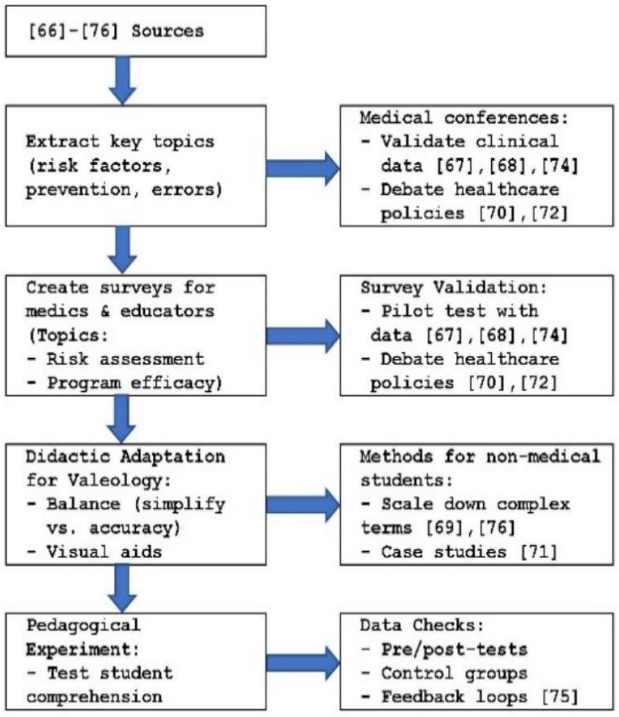
b – taking into account the sequence of use of all sources and with a detailed discussion of the topic.

and additional competencies (e.g., resilient) [102; 103]. At this stage, positive results of interdisciplinary cooperation were obtained. When teaching valeological disciplines at the third stage, simplified, student-friendly content was used (e.g., environmental risks [76], basic prevention of CVD [66]). The creation of this publication implements the principle of feedback necessary for basic algorithms of system analysis.

Further detail of the algorithm is presented in *Fig. 3*. The scheme depicts the distribution of scientific sources by areas of their use depending on the target audience and depth of analysis. The focus is on materials devoted to risk factors for cardiovascular and cerebrovascular diseases, assessment of the effectiveness of preventive programs, the role of medical personnel, and the impact of environmental factors on health. When discussing in medical circles, where publications are analyzed [66–75], the focus is on facts that are important for clinical practice, planning treatment strategies, developing national prevention programs, and improving the management of health care systems. The source materials are combined into a common analytical block that provides a scientific basis for making decisions in the field of health care.

In the second stage, during interdisciplinary interaction and discussion of research results with educators, more attention was paid to sources [71; 76] that allow adapting data from the field of medicine to the field of education, in particular for raising public awareness of risk factors, prevention and environmental safety. These publications can serve as a basis for discussing strategies for medical education, informing the population and developing communication policies in the field of public health.

At the third stage, when using materials in curricula for non-medical students within the framework of valeological disciplines, the emphasis is not on in-depth clinical analysis, but on an acces-



#	Content Focus
66	Cardiovascular risk factors, monitoring medical staff actions
67	Stroke risk factors (clinical focus)
68	Ischemic stroke risks and interconnections
69	Stroke prevention programs (adaptable for educators)
70	Cardiovascular disaster risks, healthcare monitoring
71	Healthcare organization to reduce CVD mortality (policy focus)
72	Errors in national prevention programs (critical analysis)
73	Methods to assess individual/ population CVD risks
74	Stroke risk factors via regional registries (data-driven)
75	Impact of healthcare financing/ staffing on stroke care (Ukraine-specific)
76	Environmental CVD risks (simplified for non-medical audiences)

Fig. 3. Algorithm for analysis and adaptation of medical sources for different target audiences.

Notes: CVD – cardiovascular diseases.
Additional comments on the algorithm:
Input sources [66–76].
Key topics extraction (risk factors, prevention).
Conference validation (clinical data [67; 68; 74]).
Survey development (for physicians [66; 73]).
Didactic adaptation (balance of accuracy and simplicity [69; 76]).
Pedagogical experiment (testing effectiveness [75]).

sible presentation of basic concepts, a simplified understanding of CVD risk factors, in particular myocardial infarction and stroke, the importance of the organization of healthcare system in Ukraine and the impact of environment on health. Sources [66; 67; 71; 76] are the basis for developing the content of relevant educational modules aimed at forming a healthy lifestyle and responsible attitude to their own health among students. The scheme demonstrates the relationships between these levels of application of scientific data, emphasizing how the same studies can have different levels of processing and presentation depending on the target audience.

The presented algorithm demonstrates the full cycle of work with medical sources: from initial analysis through professional validation to the creation of educational materials for non-medical audiences. Key stages include scientific verification, content adaptation, and assessment of learning effectiveness. Types of activities for conducting didactic adaptation are listed in *Table 1*.

Algorithms for didactic adaptation show how to integrate sources for a full cycle of research (from analysis to practical implementation). Sources [67; 68; 74] contain detailed analyses of stroke risk factors, including data from regional registries and clinical trials. This information is critical for discussion at medical conferences, as it allows to verify the relevance of recommendations for prevention and treatment. For example, studies in [74] show how statistical data can be used to predict risks, which is important for planning national health programs.

Table 1. Actions for didactic adaptation of complex medical information

Type of activity	Comments
Conferences	Sources [67; 68; 74] contain data on the validation of clinical guidelines, while [70; 72] are suitable for discussions on health policy.
Poll	Based on [66; 73], questions for doctors are developed, and [69; 71] help create questionnaires for teachers.
Adaptation	Materials [69] (prophylaxis) and [76] (ecology) are simplified through cases and visualization, while maintaining scientific accuracy [68].
Experiment	Data from [75] are used to evaluate the effectiveness of training, for example, through pre-tests and feedback.

For surveys of physicians and educators, key sources are [66] and [73], where methods for assessing individual and population risks of cardiovascular diseases are discussed. These materials will help to create valid questionnaires, for example, on the effectiveness of preventive measures or errors in their implementation [72]. Pilot testing of surveys among physicians will allow to clarify the formulation and eliminate ambiguity.

Materials [69; 76] are suitable for didactic adaptation of complex medical concepts. [69] describes stroke prevention programs that can be simplified through case studies or visualization, and [76] emphasizes environmental factors, which is convenient for teaching non-medical students. It is important to balance scientific accuracy [68] with accessibility of information (e.g., comparison with everyday phenomena).

At the pedagogical experiment phase, data from [75] (on the impact of funding on the quality of health care) will help assess whether the adapted materials are clear to students. The assessment can include pre- and post-tests, as well as group discussions to identify weak points and improve the program. The source [71] is also useful because it offers structured approaches to organizing prevention that can be simulated in educational scenarios.

When forming modern valeological curricula, special attention is required to the constant updating of global statistical data on the main risk factors of socially significant diseases. For example, to update data on risk factors for CVD, we conducted an analysis of statistical sources [90–94] on the prevalence of obesity in the countries of the WHO European Region in terms of the percentage of the population that is overweight and obese (we identified trends, ranking of countries in the list, and dynamics of the indicator). The result is shown in *Table 2*.

Table 2. Dynamics of the prevalence of overweight and obesity among the adult population of the WHO European Region (2019&2023) with their ranking.

Country	2019		2023	
	Rank	%	Rank	%
Albania	20	62.3	20	65.2
Austria	30	54.2	30	56.4
Belgium	24	59.1	25	61.3
Bosnia & Herzegovina	15	64.7	15	67.5
Bulgaria	18	63.9	18	66.7
Croatia	17	64.2	17	67.0
Cyprus	26	58.4	26	60.8
Czech Republic	3	68.0	3	70.4
Denmark	29	54.6	29	56.6
Estonia	22	61.2	22	63.6
Finland	21	62.5	21	64.9
France	27	56.8	27	58.8
Germany	23	59.7	24	62.1
Greece	2	68.3	2	70.7
Hungary	10	65.9	10	68.7
Iceland	25	58.9	23	61.3
Ireland	19	60.1	19	62.5
Italy	28	58.5	28	60.9
Latvia	16	63.4	16	65.8
Lithuania	14	62.7	14	65.1
Malta	8	66.2	8	69.0
Netherlands	31	53.1	31	55.1
Norway	22	57.3	25	59.3
Poland	12	64.5	12	67.3
Portugal	13	59.4	13	61.8
Romania	11	63.1	11	65.9
Slovakia	9	66.4	9	69.2
Slovenia	19	61.9	19	64.3
Spain	7	61.6	7	64.0
Sweden	32	52.3	32	54.3
Switzerland	33	51.8	33	53.8
Turkey	6	66.5	6	69.3
Ukraine	5	67.1	5	69.9
United Kingdom	4	63.7	4	66.5

As shown in *Table 2*, almost all countries in the WHO European Region demonstrated an increase in overweight and obesity rates among adults between 2019 and 2023. The average increase was approximately [2–3]%, indicating a steady downward trend in the region. The highest rates in 2023 were recorded in the Czech Republic, Greece, Malta, Turkey and Ukraine, where more than 69.0% of adult population was overweight or obese. Ukraine ranks fifth in this ranking with a rate of 69.9%, which is a very high level.

Compared to 2019, when this indicator was 67.1% in Ukraine, there is an increase of 2.8%. Only four countries bypass Ukraine in this indicator: Greece, the Czech Republic, Malta and Turkey. The lowest rates of overweight and obesity are recorded in Switzerland, Sweden and the Netherlands, where they do not exceed 55.0%. These countries, despite a slight increase in indicators over the past five years, continue to demonstrate the best results in the region.

Country rankings remain relatively stable throughout the observation period. Countries with high rates such as the Czech Republic and Greece maintain their leading positions, while Switzerland and Sweden consistently rank at the bottom of the rankings. It is worth noting that Eastern European countries, including Ukraine, show higher rates than Northern and Western European countries. This difference may be due to differences in dietary habits, levels of physical activity, and the availability of effective prevention programs.

The situation in Ukraine requires serious attention, as the high level of overweight and obesity is a significant risk factor for the public health. The experience of countries with the lowest rates, such as Switzerland or Sweden, where effective prevention programs are implemented, can be useful for developing a national strategy to combat this phenomenon. The constant increase in rates in most countries indicates that the problem of obesity remains relevant for the entire European region.

Hypodynamia as a risk factor for the development of cardiovascular diseases and obesity is defined as a stereotype of the movement of people without disabilities, which limits or completely deprives of the opportunity to move and perform physical exercises. It is about the habit of moving little, lifestyle, work.

Thus, CVDs are influenced by a variety of risk factors that are closely related to one another. It is important for non-medical students to understand these relationships in order to effectively prevent the disease. The main uncontrollable risk factors that we cannot affect are age (the risk increases after 45 years in men and 55 years in women), gender (men have a higher risk at a younger age), heredity (the presence of CVDs in close relatives), and ethnicity. Studies show that heredity can increase the risk of developing hypertension by [30–50]% [104].

Controllable and ***conditionally controllable*** risk factors are much more important for prevention. Some researchers consider smoking [105], obesity [106] and physical inactivity [107] to be conditionally controllable risk factors because quitting smoking is difficult due to chemical dependence, obesity may be associated with endocrine disorders rather than overeating, and physical inactivity with forced isolation during the COVID-19 pandemic and war. But we consider these three factors to be controllable. Yes, quitting smoking is not as difficult due to addiction as quitting alcohol abuse and drug use [108], overeating is the main cause of most cases of obesity [109], and during the pandemic and war, it is possible to perform a set of physical exercises with sufficient load at home [110].

Conditionally controllable risk factors for the development of CVD at the group and population levels include stress [111], especially acute in war conditions, insufficient sleep [112] associated with war or work schedules (for example, with daily shifts of doctors, rescuers, power engineers, etc.), insufficient medical literacy associated with low accessibility of valeological education for non-medical students of Ukraine. That is, when determining the degree of risk factors controllability, we suggest taking into account not only the ability to eliminate the factor effect through personal efforts (for example, keeping to a balanced diet, avoiding overeating and quitting smoking), but also the socio-economic circumstances of the post-pandemic and wartime. Confirmation of the controllability of risk factors is the availability of valeological tools for correcting their impact on health [113; 114].

Thus, the study by Anderson L. et al. (2016) [114], which is considered the "gold standard" of evidence-based medicine in the field of cardiac rehabilitation, published in the Cochrane Database, is based on a meta-analysis of 63 scientific papers with the participation of 14,486 patients with chronic coronary heart disease. Most of these studies compared usual care with physical rehabilitation programs. The average age of the participants was [55–75] years. In 85% of cases, the stu-

dies had a control group, where patients received only standard care without physical exercise. Most often (72% of studies) used aerobic training (walking, exercise bikes), and in 28% combined aerobic and strength exercises. Scientists found that physical rehabilitation reduces the risk of death by 26% (relative risk 0.74). The number of hospital admissions was reduced by 18%. The patients' quality of life, as measured by the SF-36, improved by an average of 5.8 points. The greatest effect was observed in patients after a heart attack, whose risk of death was reduced by 31%. Women benefited more from workout than men (reduction in mortality was 29% versus 22%). The evidence of influence on mortality is considered high-quality (GRADE A), but the data on life quality are of moderate quality, as different studies used different assessment methods. The best results were obtained with 8–12 weeks of physical exercise, with training 3 times a week. This study shows that even in the presence of cardiovascular disease, physical activity remains an important controllable factor that can significantly improve health. These findings may be useful for the development of heart disease prevention programs in both medical and educational settings.

The impact of controlled and conditionally controlled risk factors on health can be eliminated or significantly weakened by forming non-medical students's valeological competence and commitment to a healthy lifestyle throughout life. Programs for primary prevention of socially significant diseases should include attitudes towards quitting smoking, alcohol abuse, drug use, overeating, overfatigue, leading a sedentary lifestyle or, conversely, engaging in extreme sports, and practicing unprotected sex.

To improve the curricula of valeological disciplines, legal issues and the work of legal experts were used. The legal aspects of the prevention of socially significant diseases in higher education institutions are based on the ability to influence controllable risk factors through regulatory acts and educational programs. According to the Order of the Ministry of Health of Ukraine No.417 of 2018, educational institutions are obliged to implement preventive measures, in particular to combat physical inactivity, unhealthy diet and smoking. For example, a study by Anderson L. et al. (2016) proves that regular physical activity reduces the risk of cardiovascular complications by 26%, which confirms the need to include physical education in educational programs. At the same time, the Law of Ukraine "On Protection of Health from the Harmful Effects of Tobacco" prohibits smoking in university premises, which helps to control this risk factor. For non-medical students, such activities are especially important, since their career includes low physical activity, and valeological education can compensate for this impact.

Given the complex effect of several important risk factors on the development of diseases, which are considered in the curricula of valeological disciplines, at the stage of the pedagogical experiment we used integral risk assessment models. We also noticed that determining the level of risk of one's own diseases increases motivation for valeological education [64], so we involved students in such assessments of their own health. Simple models of risk assessment and prevention are offered to non-medical students. For example, a simplified formula for the integral risk of cardiovascular diseases, proposed by the International Institute of Public Health for valeological education programs:

$$R = \frac{\mathrm{Sm}+\mathrm{PA}_{30}+\mathrm{JF}_2}{3} \times \frac{\mathrm{St}}{10} \qquad (1),$$

where Sm – smoking (1 – yes, 0 – no);
PA_{30} – daily physical activity less than 30 minutes per day;
JF_2 – junk food more than twice a day;
St – stress level (scale 1–10 units).

A high risk requiring correction (R>1.5) during the 2019–2024 years of teaching the valeological discipline "Health Pedagogy" was detected in approximately 3 out of 4 non-medical students, which indicates the feasibility of conducting primary prevention of CVD in institutions of higher non-medical education [115].

To prevent CVD, as a result of didactic information, we can offer students correctly simplified explanations of risk factors and simple advice: sufficient rest, rational nutrition (for example, "health plates", on which 50% are vegetables, 25% are cereals, and the protein content in products should be at least 25%; limiting salt to 5 g per day, avoiding overeating), rational physical activity (not sports, but physical education, 7–8 thousand steps per day to reduce the risk of developing diseases and vascular crises by 20%), stress management (breathing and relaxing exercises, rational time management, avoiding "toxic" people and situations, transforming negative emotions into neutral and positive ones), taking into account heredity (reasonable vigilance with blood pressure

control) and the use of practical valeological tools (risk calculators, mobile applications for tracking physical activity, etc.).

Conclusions

The examples of didactic adaptation of complex medical information on risk factors of socially significant diseases for teaching valeological disciplines to non-medical students indicate the feasibility of using the developed methods of balancing, scaling and aggregation in combination with the method of systems analysis. Didactic adaptation is carried out in three stages, in the first of which the developers of the curriculum describe the risk factors of socially significant diseases according to the rules of medical science and discuss them in the scientific environment. In the second stage, a joint scientific discussion of the material of the educational discipline takes place by doctors and teachers. In the third, testing is carried out in the student environment when teaching valeological disciplines.

Risk factors for cardiovascular diseases are heredity, stress, physical inactivity, obesity and smoking. We propose to consider the first two uncontrollable in war conditions, the other three controllable. An additional non-specific uncontrollable risk factor is the low level of valeological education. The latter problem can be solved by teaching valeological disciplines to non-medical students, with didactic adaptation of medical information.

Prospects for further research

We are planning to continue research into socially significant risk factors, in particular cardiovascular diseases, in order to reduce the number of uncontrollable risk factors at the group and population levels by transferring them to the group of conditionally controllable ones.

DECLARATIONS:

Disclosure Statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Statement of Ethics

The authors have no ethical conflicts to disclosure.

Data Transparency

The data can be requested from the authors.

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Consent for publication

All authors give their consent to publication.

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NURSING SUPPORT OF MILITARY SERVICE MEMBERS WITH A MILD DEGREE OF INTELLECTUAL DISORDERS WITH GASTROINTESTINAL DISEASES IN THE PROCESS OF MEDICAL REHABILITATION

Sushchenko V.O.[1], Smirnova V.I.[1], Sushchenko E.M.[2]

[1]Kharkiv National Medical University, Kharkiv, Ukraine
[2]H.S. Skovoroda Kharkiv National Pedagogical University Kharkiv, Ukraine

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ABSTRACT

Background. Throughout the time of martial law in Ukraine, the number of military service members with mild degrees of intellectual impairment has increased, which requires significant attention to nursing support during the period of diagnostic, medical, therapeutic, and rehabilitation medical practice. The importance of nursing support for military personnel with mild intellectual disorders during exacerbation of gastrointestinal diseases in the process of medical rehabilitation should be better investigated, which is due to the increase in the number of military personnel with this nosology and the need to select methodological recommendations for improving nursing support for patients in the process of medical rehabilitation. The relevance of this study will be maintained during warfare and in the first years after the war. It will also help medical professionals better understand the specifics of supporting patients with intellectual and cognitive developmental disorders.

Aim. Analysis the degree of quality of nursing support for military personnel with mild intellectual impairment with gastrointestinal diseases during medical rehabilitation.

Materials & Methods. Bibliosemantic methods and system analysis were used. PubMed, Google Scholar sources, orders of the Ministry of Health of Ukraine were analyzed. The article is written in the form of a short scientific report.

Results & Conclusions. Nursing support for military personnel with intellectual disabilities cannot be implemented qualitatively and effectively without prior training of specialists. Nurses often cannot choose the right approach to these patients due to a lack of relevant experience and understanding of the needs of people with intellectual disorders. Our conclusion proposed possible solutions to this problem through various and specific ways to improve the skills of medical professionals.

Keywords: *military medicine, cognitive developmental disorders, warfare regions, advanced training, behavioral disorders.*

Nursing support reflects a system of comprehensive measures taken by a nurse to provide care and support for a patient during rehabilitation and treatment. Varava O.B., Kit O.M., et al. emphasize that in communication between medical personnel and the patient, a nurse plays an important role, which requires the nurse to master the skills of nursing specialists in high-quality, accessible, and effective support for this category of patients, by the degree of their intellectual disabilities and psychological state [1; 2].

It should be noted that the social role of the nurse is underestimated, which necessitates a change in the direction of rethinking her professional potential and professional training [1; 3; 4]. As a part of the disclosure of this issue, we analyzed the importance of nursing support for military personnel with mild intellectual disorders and gastrointestinal diseases in medical rehabilitation, the percentage of which has been increasing recently. The result is presented in the form of a short scientific report.

Corresponding Author:
Sushchenko Viktoriia O. – Postgraduate student, Department of Internal Medicine Propedeutics, Nursing and Bioethics, Kharkiv National Medical University, Ukraine.
✉ Ukraine, 61022, Kharkiv, Nauki ave., 4.
E-mail: vikastudyknmu@gmail.com

According to Article 19 of the Military Medical Commission as amended by Order No.262 dated April 27, 2024 [5], a mild degree of intellectual impairment is no longer considered a recognition of military unsuitability, which leads to increasing the number of men and women with this nosology in the ranks of military personnel defending our state. Consequently, medical employees are faced with the problem of an accurate medical and psychological approach to military personnel with intellectual disorders during the treatment of acquired concomitant injuries and diseases that were received at the time of military service.

In the work of departments specializing in the diagnosis and treatment of gastrointestinal diseases, nursing care for patients consists of providing psycho-emotional support to the patient, collecting personal information to fill out relevant documentation, collecting existing complaints, and processing them to make a diagnosis. Kit O.M. et al. [2] state that preparation for most diagnostic operations, such as endoscopic examination, includes a moral component that is part of nursing support. Transduodenal lavage, duodenal sounding, colonoscopy, and biopsy require the nurse to inform the patient of the specifics of the examination and possible side effects and explain the step-by-step process of the upcoming examination. The presence of mild intellectual disabilities in the history of military service members creates special conditions for medical personnel for social interaction with patients, which is complicated by the possible presence of psychogenic disorders in the patient due to combat injuries received through warfare [6–8].

For a practical, understandable, and qualitative explanation of some elements of the examination and provision of moral and psychological support in communication with military personnel with intellectual disabilities, a nursing specialist must understand the specifics of volitional and cognitive processes associated with this nosology, taking into account the possible regression of these areas of development under the influence of traumatic experiences and stressful situations. Nursing support should be integrated through an individual approach aimed at simplifying the explanation of technical words, making them more accessible to people with intellectual disabilities [6; 9]. In addition, when explaining the anatomical features of the body parts and organs being examined, the medical worker should pay attention to the patient's limited level of perception of information and visual-active thinking, which completely replaces the formative visual-figurative. It should be noted that a specialist can help the patient better understand by using illustrative visual materials when explaining medical words and limiting the use of scientific and technical words [10; 11]. Synev V. M. [12] noted that the lack of motivation and volitional participation leads to the fact that most actions are performed not according to the verbal instructions of doctors and nurses but exclusively by imitating similar actions. A nurse should provide positive support for the actions of military personnel with mild intellectual disabilities in the context of providing emotional support and reducing the impact of stress factors, which may include staying in medical institutions and complaints about illness and well-being [13]. The main difficulty of this approach is the lack of awareness of medical workers about the peculiarities of the psycho-emotional and volitional state of people with intellectual disabilities, which often leads to the wrong approach, negative emotional state of the patient, isolation, and refusal to cooperate with doctors and nurses.

Without establishing high-quality two-way contact with the patient, the nurse will not be able to ensure a safe medical rehabilitation process. All things considered, we reflect on the necessity of paying attention to important aspects of social services for nurses to provide nursing support better, the implementation of which in the future will contribute to increasing the awareness of nurses for interaction with patients:

1. Additional courses should be created to increase cooperation with psychologists for nurses.
2. Special consultation sessions with specialists in the field of defectology and psychiatry can have a positive impact on deepening the knowledge of medical professionals regarding the special needs of people with intellectual disorders.
3. Conducting training by psychologists and psychotherapists to increase awareness of the professional qualities of a nurse for the further provision of high-quality nursing support.

Conclusions

It can be seen that the analysis of this problem allows us to point out the need for a new approach to improving nursing support. The lack of knowledge among nurses whose work is related to gastrointestinal diseases regarding the care of military patients with mild intellectual disabilities is a primary factor in the emerging difficulties of care in the military.

Effective medical rehabilitation cannot be safely ensured without establishing high-quality two-way communication between the nurse and the patient. Given this, it is essential for nurses to focus on key aspects of social services to enhance their ability to provide proper nursing care. Implementing these measures will improve nurses' awareness and skills in patient interaction. This includes developing additional training courses in collaboration with psychologists, organizing specialized consultations with experts in defectology and psychiatry better to understand the needs of patients with intellectual disabilities, and conducting psychological and psychotherapeutic training sessions to strengthen nurses' professional competencies for delivering high-quality care.

DECLARATIONS:

Disclosure Statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

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All authors give their consent to publication.

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FEATURES OF PSYCHOLOGICAL SUPPORT FOR NURSES IN CHILDREN'S HOSPITALS UNDER MARTIAL LAW

Tovstohon K.V., Yeryomenko G.V.

Kharkiv National Medical University, Kharkiv, Ukraine

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ABSTRACT

Background. Martial law presents significant challenges for nurses working with children. Children's hospitals are becoming institutions that provide not only medical care but also comprehensive medical and social support for both children and their families.

Aim. To analyse the provision of psychological support in the professional activities of nurses in the paediatric unit.

Materials and Methods. A survey on the psychological aspects of nurses' work was conducted in April 2024 among the parents of 20 children from the Orthopedics and Traumatology Department of the Municipal Non-Profit Enterprise "Chernihiv Regional Children's Hospital" of Chernihiv Regional Council. An anonymous questionnaire of our own design was used to evaluate the work of a nurse. Respondents signed an informed consent to participate in the study.

Results. Positive communication was noted by 90% of respondents, indicating the nurses' professionalism, empathy, and willingness to create favorable conditions for children's treatment. In addition, the respondents reported a high level of nurses' adaptation to the extreme conditions of martial law, as well as their ability to ensure effective interaction with patients and their families. Data analysis regarding nurses' ability to create a friendly atmosphere for children during hospital interactions showed consistently positive feedback from parents. The individual needs of children were rated positively in 85% of responses. However, 5% of respondents answered negatively, indicating that some parents believed their child's needs and interests were not adequately considered by the nurses.

Conclusions. The need to work under crisis conditions may affect the effectiveness of nurses' performance. The development of specialized psychological support programs can assist nurses in adapting to the changing realities of wartime, foster their emotional resilience, contribute to the creation of an emotionally safe environment for patients, and support parents during the challenging period of their children's treatment.

Keywords: *nursing, adaptation, patient care.*

Introduction

Martial law presents significant challenges to the healthcare system, particularly for health professionals working with children [1; 2]. Pediatric hospitals serve not only as centers for medical care but also as institutions providing comprehensive support to children and their families, who often experience severe stress due to military operations. In such conditions, nurses play a crucial role not only as medical professionals but also as psychological supporters, educators, and social communicators [3; 4].

The war significantly alters the format and nature of nurses' work, as they are required to function not only as mid-level professionals but also to assume additional responsibilities. They become not merely executors of medical procedures but also intermediaries between children, their families, and other healthcare providers [5; 6]. In critical hospital settings, psychological support for children is crucial, as children represent the most vulnerable population during times of war. They often fail to comprehend the full extent of the events occurring around them, which can lead to heightened fear, anxiety, and depression. These emotional responses, in turn, may affect their

Corresponding Author:
Yeryomenko Galyna V. – Doctor of Medical Sciences, Professor of the Department of Propedeutics of Internal Medicine, Nursing and Bioethics of the Kharkiv National Medical University, Ukraine.
✉ Ukraine, 61022, Kharkiv, Nauki ave., 4, KhNMU.
E-mail: galyna0512@ukr.net

physical condition and the overall effectiveness of treatment [7].

Nurses working in pediatric hospitals must possess not only professional medical skills but also knowledge of crisis psychology, and effective communication with traumatized children and their families [8–10]. Creating a supportive psychological environment is crucial, as it helps reduce stress and accelerates the rehabilitation process in children [11]. Research indicates that high-quality psychological and pedagogical support during treatment significantly reduces the risk of post-traumatic stress disorder in children [12; 13].

Aim. To analyse the provision of psychological support in the professional activities of nurses in the paediatric unit.

Materials & Methods

In April 2024, eight children with traumatic injuries (40%), four with congenital anomalies and malformations (20%), two with osteochondropathy (10%), four with scoliosis (20%), and two with hip dysplasia (10%) were treated in the Orthopedics and Traumatology Department of the Municipal Non-Profit Enterprise "Chernihiv Regional Children's Hospital" under the Chernihiv Regional Council. The parents of children with these conditions participated in our anonymous survey titled "Psychological Aspects in the Work of a Children's Hospital Nurse under Martial Law". The respondents signed an informed consent to participate in the scientific study.

Results and Discussion

In response to the question, "Are you satisfied with communication with nurses at the children's regional hospital under martial law?" 90% of respondents answered positively. This suggests a high level of professionalism among the nursing staff, their ability to adapt to the extreme conditions of martial law, and their capacity to maintain effective interaction with patients and their families. One respondent (5%) gave a negative response, indicating dissatisfaction with communication. Possible reasons for this may include personal conflict, lack of attention, or insufficiently clear explanations, particularly in the stressful context of wartime.

In response to the question, "How would you rate the level of care and support your children received from nurses during their hospital stay?" 19 out of 20 parents surveyed (95%) stated that the level of care and support provided was high. This reflects the professionalism of the nurses, their empathy, and their commitment to creating favorable conditions for children’s treatment. One respondent (5%) rated the level of care as average, which may suggest occasional shortcomings in the work of the medical staff, such as a lack of individualized approach, insufficient attention, or limited resources in certain situations.

In response to the question, "Do you think that nurses are able to communicate effectively with children and their parents during hospital visits in wartime?" 18 out of 20 parents surveyed (90%) believed that nurses were able to do so. This suggests a high level of communication skills and the ability of medical staff to establish trusting relationships even under the stressful conditions of martial law. At the same time, two respondents (10%) indicated that they found it difficult to answer. This may reflect limited interaction with nurses, an ambiguous experience, or the absence of a clearly positive or negative impression.

In response to the question, "Have you been provided with information on how to help your child psychologically adapt to martial law?" 18 out of 20 parents (90%) stated that they had received all the necessary information. This reflects the high level of nurses’ competence in providing psychological support to children and parents, as well as their professional approach to facilitating children's adaptation under challenging conditions. Two respondents (10%) indicated that the information was provided only partially. This may suggest a lack of detail in the recommendations, limited time for comprehensive communication, or unclear explanations in some cases.

In response to the question, "Were you provided with recommendations on stress management and psychological support for you and your child during your hospital stay?", 18 out of 19 parents surveyed (95%) reported that they had received comprehensive recommendations. This reflects the professional approach of nurses in providing psychological support to families under challenging hospital conditions. One respondent (5%) indicated that the information was provided only partially, which may suggest insufficient detail in the recommendations, limited time for communication, or difficulties in understanding the guidance.

In response to the question, "Do you think that nurses interact appropriately with children, creating a friendly atmosphere?" all 20 parents surveyed (100%) gave a positive answer. The data analysis revealed unanimous parental approval of nurses' ability to foster a friendly and supportive environment for children during hospital interactions. This reflects the exceptional professiona-

lism, empathy, and high standard of communication demonstrated by the nursing staff.

In response to the question, "Do nurses take into account the individual needs and interests of children during treatment?" the majority of parents (85%) stated that the medical staff, particularly nurses, paid attention to the individual needs of children when providing care. However, 5% of respondents answered negatively, indicating that some parents did not believe their child's individual needs and interests were adequately considered. Additionally, 10% reported that these needs were only partially taken into account, suggesting certain shortcomings or challenges in addressing individualized care during treatment.

In response to the question, "How do you assess the level of psychological support you and your child received from nurses during inpatient treatment?", 17 out of 20 respondents (85%) stated that nurses fully considered their children's individual needs and interests. This reflects the high level of staff competence in applying an individualized approach, which likely has a positive impact on the child's emotional state and treatment outcomes. Two parents (10%) reported that individual needs were only partially considered, which may suggest instances where nurses lacked the time or resources to fully address specific requests or did not pay sufficient attention to minor details. One respondent (5%) indicated that individual needs were not taken into account. Although isolated, such responses are noteworthy, as they may point to systemic issues such as insufficient staff training in pediatric care or organizational shortcomings in the treatment process.

In response to the question, "How do you assess the psychological approach of nurses towards your child during treatment?" 85% of surveyed parents expressed satisfaction with the way nurses interacted with their children and provided psychological support. This suggests that most parents are content with the communication, emotional support, and educational efforts offered by the medical staff. It may be assumed that nurses effectively tailor their approach to the child's age and psychological needs, thereby helping children better understand the treatment process and cope with stress.

Fifteen percent of surveyed parents assessed the psychological approach as average. This may suggest that, for some families, certain aspects of care could be improved or given greater attention by the medical staff – such as insufficient focus on individual needs, communication challenges, or, in some cases, limited psychological training. According to the survey, 90% of parents are satisfied with communication with nurses, indicating a high level of interaction and trust. Ninety-five percent of respondents rated the level of care for children as high, highlighting the professionalism and attentiveness of the nurses. Eighty percent of parents believe that nurses create a friendly atmosphere for children, which positively impacts the patients' emotional well-being. However, 20% of respondents reported a lack of information regarding children's psychological adaptation in the hospital, suggesting the need for additional training for nurses in psychological support methods and working with children under stressful conditions.

In wartime, nurses play an important psychological and pedagogical role that extends beyond medical care to include education and support. They instruct parents on how to properly care for their children during treatment, providing information on preventing complications and managing wound care. They also explain the specifics of the child's condition and treatment, helping to alleviate fear and anxiety. Nurses organize educational sessions for children in long-term hospital care to support their development and minimize the effects of isolation. Additionally, they assist children in developing self-care skills, which are essential for their rehabilitation and adaptation to everyday life following discharge.

These aspects highlight the important role of nurses in both medical and pedagogical support for children, a role that becomes even more significant in the context of martial law.

Based on the results of studying the role of the nurse in care and psychological support, we formulated recommendations for treatment and care organizers.

1. The primary role of nurses in children's hospitals during martial law is not only to provide medical treatment to children but also to offer psychological support to both the children and their families. This includes creating an emotionally safe environment for patients, as well as assisting parents during the challenging period of their children's treatment.

2. The main challenges faced by nurses include high levels of stress and psychological burnout, a lack of resources, and the need to work in crisis conditions, such as the constant threat of insecurity, shelling, evacuation, and interruptions in the supply of energy and medicine. These factors significantly affect the effectiveness of healthcare professionals.

3. It is essential to enhance the training system for nurses in the psychological aspects of their work, particularly in methods of mental support, the development of emotional resilience, and adaptation to changing conditions. This will improve their effectiveness and ensure the delivery of high-quality medical care in challenging wartime conditions.

Conclusions

Under martial law, nurses in pediatric hospitals play a multifaceted role, not only delivering medical care but also providing essential psychological and educational support to children and their families. Survey results revealed that [90–100] % of parents appreciated nurses' communication, empathy, and ability to create a supportive environment, although up to 20% noted gaps in psychological information or individualized care. This highlights both the strengths and the areas needing improvement in nurse training, especially concerning crisis communication and trauma-informed care. The findings confirm that nurses are key figures in maintaining the emotional stability of pediatric patients, which directly influences treatment outcomes.

DECLARATIONS:

Disclosure Statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Statement of Ethics

The authors have no ethical conflicts to disclosure.

Data Transparency

The data can be requested from the authors.

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ENGLISH-MEDIUM INSTRUCTION IN EUROPEAN MEDICAL SCHOOLS: AVAILABILITY AND DISTRIBUTION

Korneyko I., Petrova O., Krainenko O., Ovsiannikova H.

Kharkiv National Medical University, Kharkiv, Ukraine

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ABSTRACT

Background. English-Medium Instruction (EMI) is a popular trend in modern higher education. Statistical data indicate a constant increase in the number of English-Taught Programmes (ETP) and courses, and Europe is the world leader in EMI implementation. Programmes in Medicine and Health Sciences are not included in the group of main ETPs in the world, European indicators of their number are lower than global, but they also demonstrate an increase in the number. Since these programmes were not described in detail, the **aim** of our work was to study the availability, distribution, and features of ETPs in Medicine and Health Sciences in Europe.

Materials and Methods. Information from the websites of medical schools of the European Union/European Economic Area was studied using systematic analysis, comparative and bibliosemantic methods. The analysis covered 577 ETPs (160 higher education institutions from 26 countries where English has the status of a foreign language).

Results. EMI in Medicine and Health Sciences has been implemented in two forms: single medium and partial (bilingual). The leader in the total number of completely ETPs is the Netherlands. The most common are Master programmes. Single-cycle programmes in medicine, dentistry and pharmacology are available in the Baltic countries, Central East Europe, South East Europe, South West Europe. Bachelor programmes in English are the smallest in number and are offered in selected countries. Bilingual programmes were found in Spain, Austria, Luxembourg, and Sweden.

Conclusions. Teaching Medicine and Health Sciences in the medium of English is a common practice in the EU/EEA, but the choice of the type of teaching (single medium or bilingual) and the education level depend on the language policy of the country, the target group of students, and the internationalization strategy of a particular higher education institution.

Keywords: *English language, medium of instruction, English taught programme, higher education, medical higher education institution, Europe.*

Introduction

According to the most recent data, English is spoken by approximately 1.5 billion people worldwide [1]. 18.8% of the world's population speaking English make it the most-spoken language [2]. Moreover, the non-native speakers of English (1.1 billion) outnumber its native speakers (390 million) [1]. Besides, English remains the most popular language to study worldwide: in 2023, it was the number 1 language to study in 122 countries [3].

Corresponding Author:
Korneyko Iryna V. – Candidate of Sciences (Linguistics), Professor and Chair, Department of Foreign Languages, Kharkiv National Medical University.
✉ Ukraine, 61022, Kharkiv, Nauki ave., 4.
E-mail: iv.korneiko@knmu.edu.ua

At present, a domain where English is not used can hardly be found; it has become a global *lingua franca* in politics, diplomacy, economy, trade, traffic, logistics, media, entertainment, and academia, "a 'natural', spontaneously arisen domain where the choice of language has taken shape in something like an evolutionary process" [4, p.6]. Nowadays, English is the language of various academic events, research publications, and the medium of instruction in Higher Education Institutions (HEI) worldwide. The 2023 Duolingo Language Report states that "a large percentage of English learners in India (40%), Vietnam (50%), and China (54%) all cite education as the primary motivation for their language study" [3].

English-Medium Instruction (EMI) has experienced a significant rise in popularity in recent years, with more universities and schools world-

wide adopting it as a mode of instruction [5]. The report, *Mapping English-taught Programmes in Europe (2024)*, has demonstrated that owing to 43% on-campus and 58% online English-Taught Programmes (ETP) outside the US, Canada, UK, Australia, Europe has become a major supplier in the EMI market [6, p. 31]. The leaders, Ireland, Germany, and the Netherlands, offer over 2,000 on-campus ETPs each, while France, Italy, and Spain – more than 1,000 each [6].

The global list of the programmes in the highest demand shows that preferences differ from country to country. According to the report, the bulk of on-campus ETPs in non-English-speaking countries is made up by Business & Management, Engineering & Technology, Social Sciences, and Natural Sciences ("main disciplines"), while Medicine & Health are attributed to the group of so-called "staple disciplines", forming a part of nearly every country's on-campus ETP offer, but less common than programmes of the main group [6, p. 25] with the lowest share (5%) in the EHEA countries when compared to MENA (12%), East Asia (9%) and Sub-Saharan Africa (14%) or 8% in the world [6, p. 24], though the growth of +15% in the EHEA region has also been noted [6, p. 15].

Thus, statistics suggest availability and even growth in the number of English- medium programmes in Medicine and Health Sciences in Europe; however, they have not been described in detail. With this in mind, we **aimed** to assess the availability, distribution, and characteristic features of ETPs in Medicine and Health Sciences in Europe.

Materials and Methods

The investigation was conducted using system analysis, comparative and bibliosemantic methods. The medical HEIs of EU/EEA and Switzerland were chosen. The list of European medical schools was taken from the World Directory of Medical Schools (https://search.wdoms.org/) and was supplemented by the Internet search with the help of Google search engine using key words *English-medium instruction, medicine, Europe, study medicine in English in [country]*. Only the official sites of HEIs were selected for analysis. The sites of agencies were not considered due to possible bias. Ireland and Malta were excluded from the study as English is the only language of higher education in these countries. The medical schools were also excluded from the study in cases if: 1) the school did not have an English website on the day of the study; 2) the site was not accessible on the day of the study; 3) only the homepage was in English, but the details of the courses were described in the national language. The search was conducted in January 2025.

Our study involved 160 HEIs from 26 countries with a total number of 577 ETPs. The countries were grouped similarly to Watcher B. & Maiworm F. [7]: Baltic, Nordic, Central East Europe, Central West Europe, South East Europe, South West Europe.

We sought the answers to the following questions:

• Are ETPs in Medicine and Health Sciences available at the HEI of EU/EEA?

• What level programmes are they?

• Are there any specific features in the programmes' design?

• Are there medical schools that teach separate courses in English?

Results and Discussion

Within a short period contemporary higher education has adopted a new worldwide strategy, English-medium instruction. Several phenomena in social and political life are responsible for this; among them are the internationalization of higher education, the Bologna declaration, the formation of the European Higher Education Area, neoliberal trends in social life, and the role of English as a *lingua academica* [8, p. 2], an increasingly globalized higher education sector, student mobility, and integration initiatives such as the Erasmus programme.

The implementation of EMI programs is considered to be motivated by various reasons. From the policy makers' perspective, some of them may include: improving the learning of English, providing a common language of instruction in countries with multilingual populations, promoting economic competitiveness through developing an English-proficient workforce, producing graduates with global literacy skills, enabling institutions to attract international students, raising university rankings, increasing the prestige of an institution, promoting the competitiveness of universities, facilitating regional and international communication, developing students' intercultural communication skills [9].

It is considered that in Europe, the Netherlands pioneered EMI at the tertiary level of education in the early 1990s, introducing a programme specialized in international management [10]. In 2014, Wachter B. & Maiworm F. [7] published the data that demonstrated approximately tenfold growth in English-taught degree programmes in Europe between 2001 and 2014; such dramatic increase

allowed E. Macaro to call EMI an "unstoppable train" [11]. The 2024 research, conducted by the British Council and Studyportals Analytics and Consulting Team, has identified about 41,000 on-campus English-taught programmes offered by countries other than the UK, the US, Canada, and Australia. This makes 22.3% of total global ETPs [6, p. 5] and demonstrates increase by 48% since 2019 [6, p. 10]. Half of them are located in the European Higher Education Area (EHEA) [6, p.13].

English-medium instruction is defined as "the use of English language to teach academic subjects in countries or jurisdictions where the first language of the majority of the population is not English" [12, p. 2]. The countries under this study are those where English does not play any official role, is learned at schools as a foreign language, and is used for international communication, but despite its status in the EU/EEA countries, the English proficiency level there is relatively high. According to the EF English Proficiency Index, these countries occupy the leading positions in the world. Eight countries included in our study are ranked as *very high proficiency*, 15 – *high proficiency*, and only 3 – *moderate* [13, p. 4]. The countries of the Nordic group (except Finland) are characterized by very high English proficiency, while all the countries with the lowest scores (moderate proficiency) belong to South West Europe. Latvia was not included in the 2024 report, though in 2022, its rating was *high proficiency*.

EF EPI is compiled using the data of an online standardized, objectively scored test. The 2024 report is based on the test results of 2023 (2.1m adults in 116 countries and regions with a minimum of 400 test takers). The authors state that "EF EPI 2024 scores have been found to correlate strongly with TOEFL iBT 2022 scores (r=0.76) and IELTS Academic Test 2022 scores (r=0.58). These correlations show that, while these tests have different designs and test taker profiles, they reveal similar trends in national English proficiency" [13, p. 24]. It should be mentioned that EF EPI has been suffering criticism as "the data that EF uses are not representative of the population and suffer from self-selection bias" [14, p. 28], which was deemed fair by EF [13, p.24]. More objective analysis employing a different study design and large-scale testing will require serious monetary investment, therefore, it is unlikely to be undertaken. Nevertheless, despite the criticism, there is no other source of information rating English proficiency, and EF EPI is frequently cited in academic works.

Over the period of the investigation, we found ETPs in Medicine and Health Sciences at undergraduate and graduate levels in Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Italy, Latvia, Lithuania, Luxembourg, the Netherlands Norway, Poland, Portugal, Romania, Slovakia, Spain, Sweden, and Switzerland. Slovenia and Iceland did not offer ETP in Medicine and Health, while in Liechtenstein Private University in the Principality of Liechtenstein offered only doctoral programmes.

Irrespective of the medium of instruction, the programmes leading to a degree in Medicine and Health Sciences are taught in two different ways: either as a long cycle (in other words, single or integrated cycle), which combines Bachelor and Master programmes in one (total >360 ECTS for medicine and >300 ECTS for dentistry) or as two separate short cycles – Bachelor and Master (240 ECTS and 120 ECTS, respectively). The long-cycle programs are medicine, dentistry, and pharmacy; this mode of instruction is practiced in Bulgaria, Cyprus, Croatia, Czech Republic, Estonia, Greece, Hungary, Italy, Latvia, Lithuania, Poland, Romania, Slovakia, Spain, and Sweden.

We managed to identify 577 ETPs; of them, Master programmes account for almost two-thirds, about a quarter are single-cycle programmes, and Bachelor programmes constitute a minority. *Figure 1* demonstrates the proportion of the ETPs in EU/EEA countries.

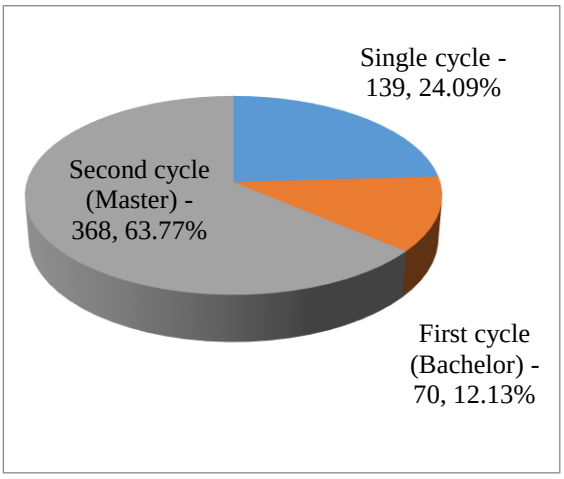

Fig.1. Undergraduate and graduate ETP in Medicine and Health in EU/EEA.

The region leading in the total number of the programmes is Central West Europe (160 ETPs); second in the total number of ETPs is Central East

Europe (111), followed by the Nordic region (99). Of the countries, the leaders are the Netherlands (95), Poland (64), Italy (41) and Sweden (41).

It should be noted that there are considerable regional differences in the levels of ETPs. *Figure 2* shows the distribution of the programmes by regions.

The most significant number of Master programmes was identified in Central West Europe. Following it is the Nordic region; South West Europe follows in the third place. South East Europe and Central East Europe lag behind with 26 institutions offering 22 Master programmes and 32 institutions offering 24 programmes, respectively. The leading position among Master programmes providers is held by the Netherlands, offering 84 programmes, followed by Sweden (37 programmes), Germany (34), and Denmark (34). These programmes are offered in a wide variety, for instance, Leiden University announced 22 programmes, namely *Biomedical Sciences, Bio-Pharmaceutical Sciences and Business Studies, Bio-Pharmaceutical Sciences and Education, Bio-Pharmaceutical Sciences and Industrial Pharmacy, Child and Adolescent Psychology, Clinical and Health Psychology, Clinical Psychology, Cognitive Neuroscience, Developmental Psychology, Economic and Consumer Psychology, Health and Medical Psychology, Health, Ageing and Society, Imaging and Intervention, Population Health Management, Sensing and Stimulation, Molecular Genetics and Biotechnology, Occupational Health Psychology, Population Health Management, Psychology, Research in Bio-Pharmaceutical Sciences, Technical Medicine, Transfusion Medicine and Cellular and Tissue Therapies*. The programmes are often multidisciplinary, innovative, involve high technology, and are fre-

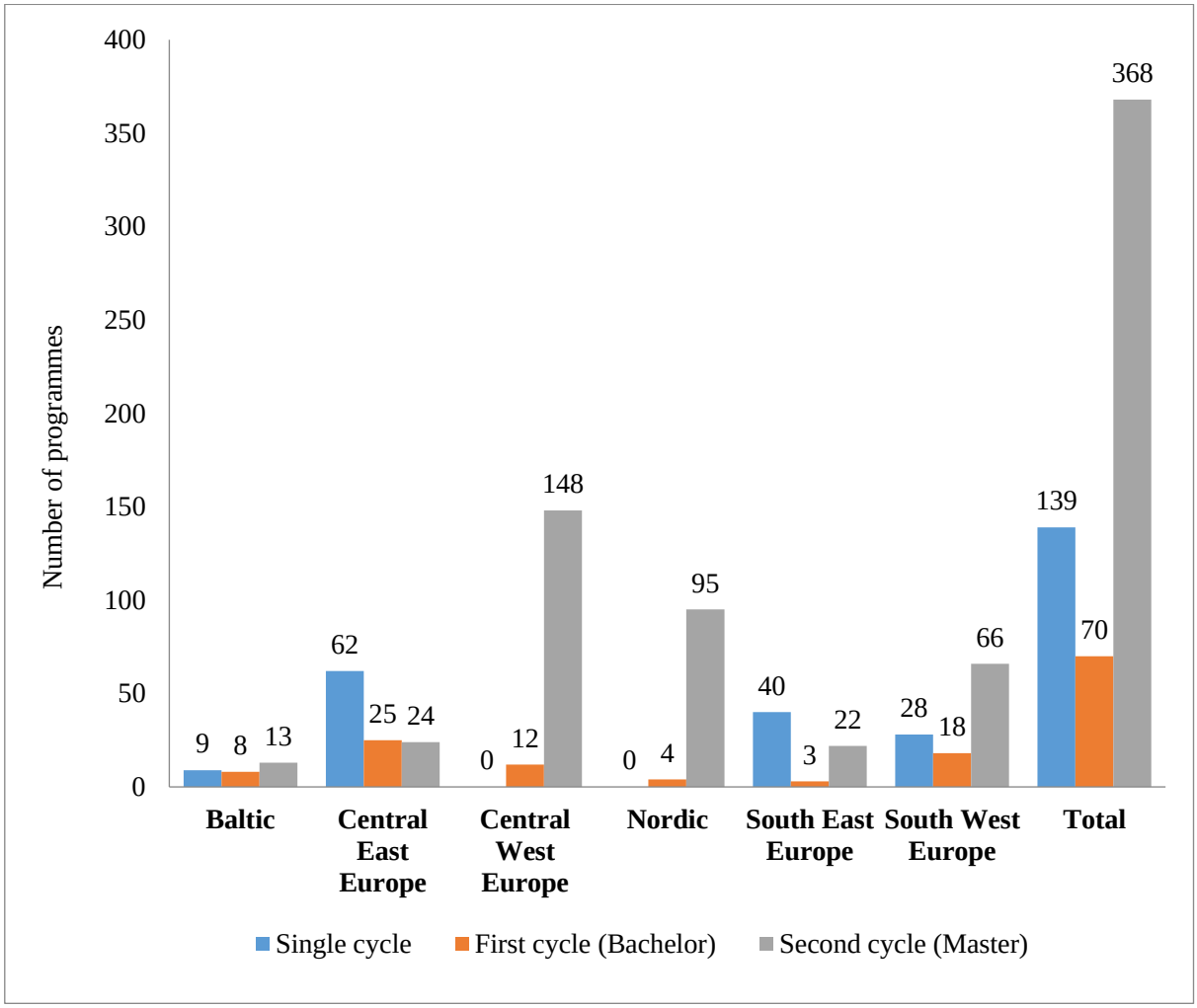

Fig. 2. Distribution of single-cycle, Bachelor, and Master programmes by regions.

quently research-oriented. For example, the Master programme *Biofabrication* at the University of Utrecht deals with 3D printing with a biomedical approach to prepare designed tissue constructs. It covers 3D bioprinting, biomaterials, 3D cell culturing, computer models and imaging. The programme *Bioinformatics and Biocomplexity* teaches how to apply biology, computer sciences, data sciences, and computational and mathematical modelling to understanding complex biological systems. *Cancer, Stem Cells and Developmental Biology* covers post-genomic research, including single cell and next generation sequencing, proteomics, metabolomics, and advanced microscopy techniques. *Figure 3* shows the proportion of Master programmes in EU/EEA countries.

In contrast, Master programmes taught in Baltic countries, Central East Europe, and South East Europe are traditional study areas oriented to clinical work. For example, the leader in the group, Poland, with its 16 medical schools, offers English-taught Master programmes in *Nursing, Midwifery (Obstetrics), Medical Biotechnology, Public Health, Dietetics, Cosmetology, and Clinical Psychology*.

English-taught Master programs were not identified in three countries: Romania (Central East Europe), Croatia, and Slovakia (South East Europe).

Bachelor-level ETPs (*Figure* 4) are not numerous and are mainly taught in Central East Europe. South West Europe follows it, while the policy of

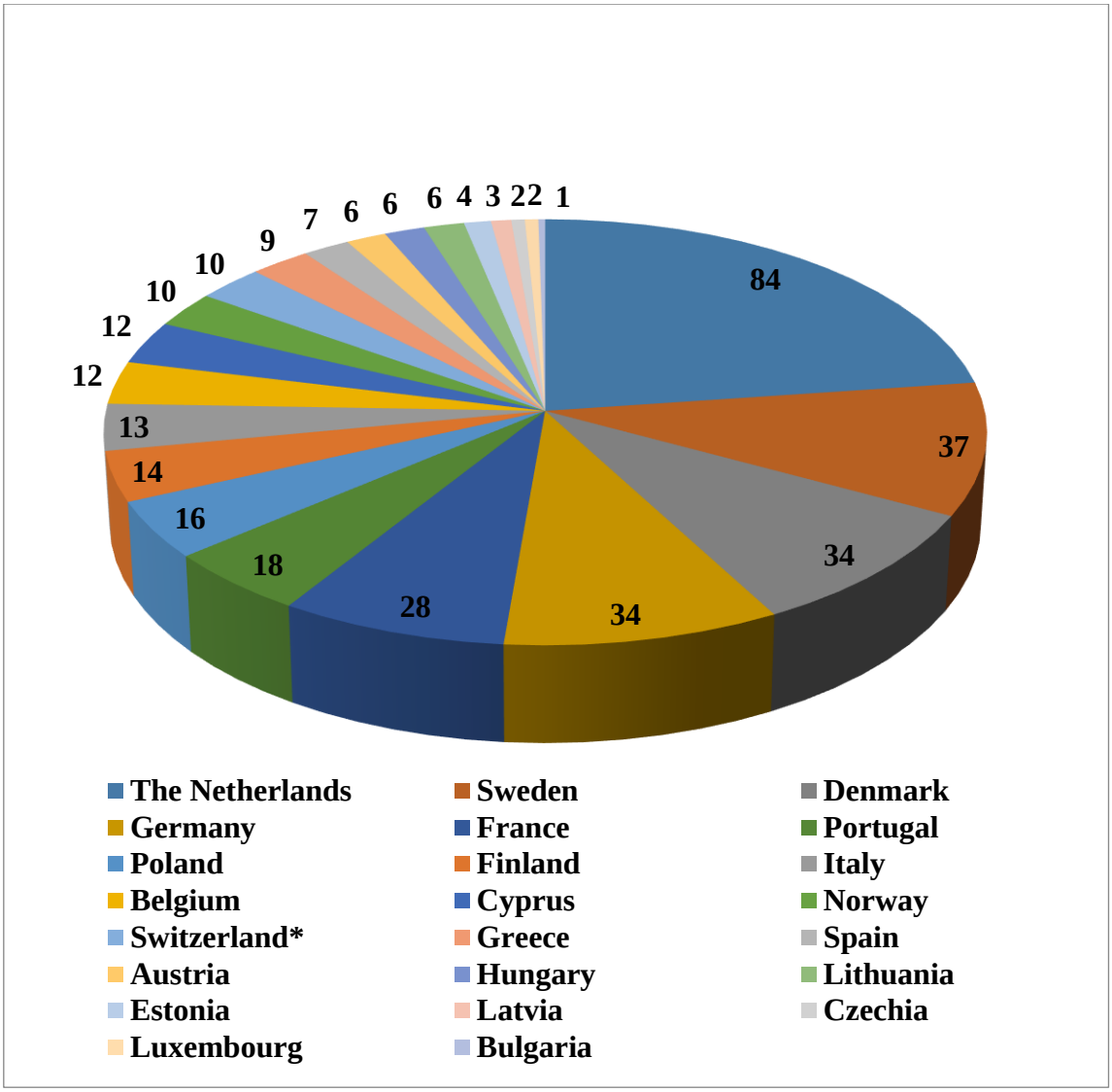

Fig. 3. Master programmes by countries.

Note: * – Master program in medicine is taught in English.

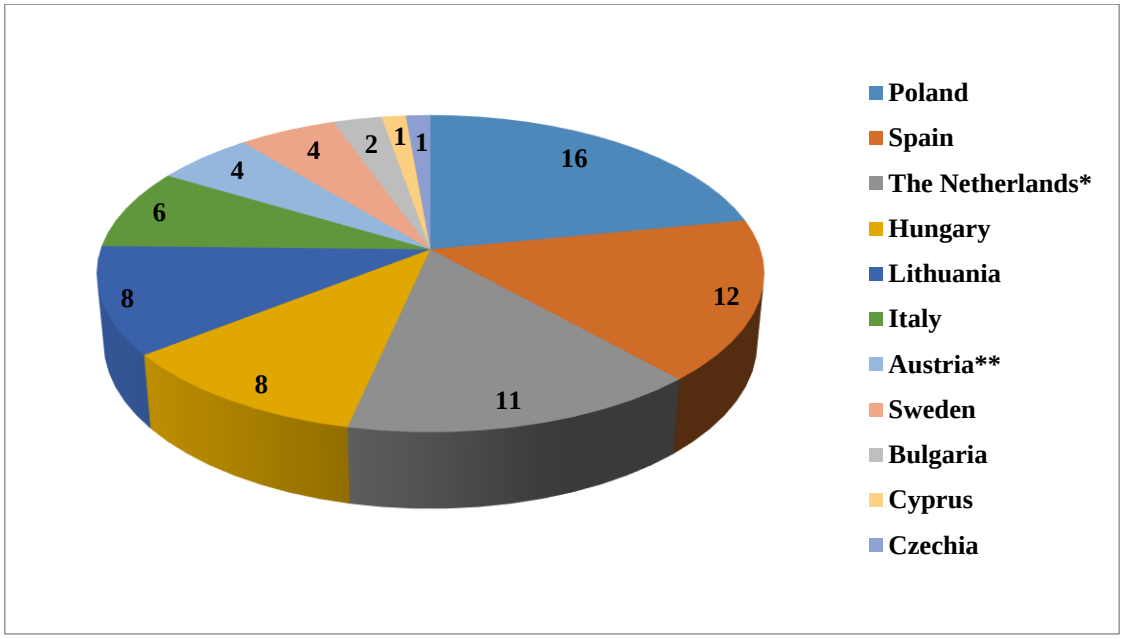

Fig. 4. Bachelor programmes by countries.

Notes: * of them, 1 Bachelor ETP in medicine is offered;
** of them, 3 Bachelor ETPs in medicine are offered.

some Nordic universities is to teach Bachelor programmes only in the national language. Similarly, the Studyportals and the British Council have noticed the low share of Bachelor in relation to Master studies among the total number of ETPs in the EHEA region [6].

One hundred and thirty-eight single-cycle ETPs (medicine, dental medicine, pharmacy) are offered in only four regions: Baltic, Central East Europe, South East Europe, and South West Europe. The leader is Central East Europe (62 programmes), followed by South East Europe (40) and South West Europe (28). Baltic countries offer nine single-cycle programmes. It is worth noting that in the Baltic region, Central East Europe, South East Europe, single-cycle programmes are offered in every country by the majority of (if not all) medical schools. The leaders among the countries are Poland (32), Italy (22), Romania (15), Hungary (12), Czech Republic (11). The distribution of the single-cycle ETPs is demonstrated in *Figure 5*.

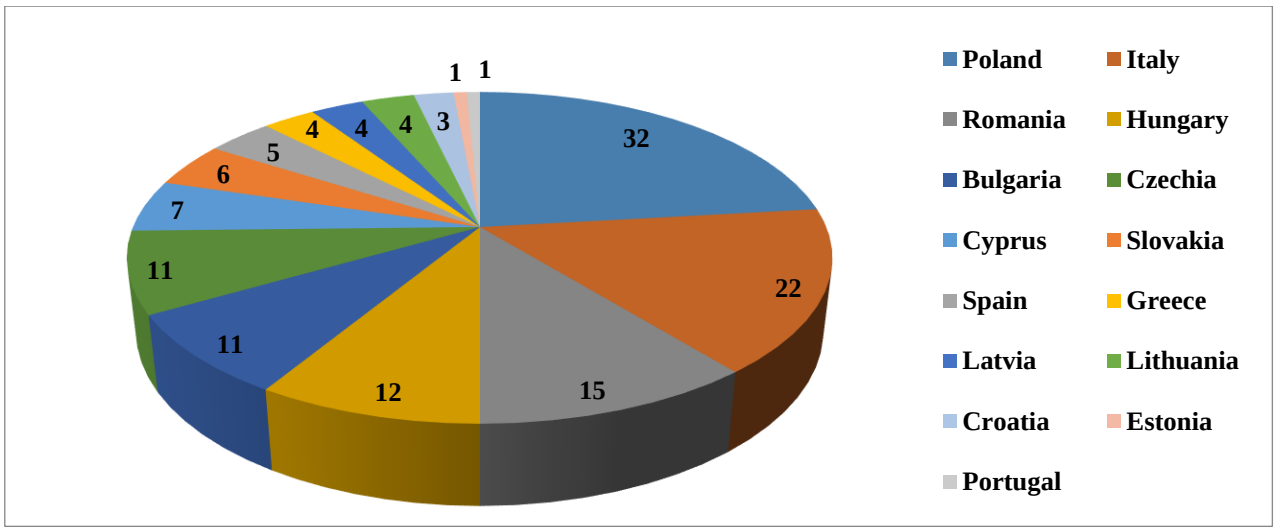

Fig. 5. Single-cycle programmes by countries.

The programmes leading to the degree in medicine can be found in Estonia, Latvia, Lithuania, Czech Republic, Hungary, Poland, Slovakia, Bulgaria, Cyprus, Greece, Croatia, Romania, Italy, Portugal, dentistry (dental medicine) – in Latvia, Lithuania, Bulgaria, Croatia, Cyprus, Czech Republic, Hungary, Italy, Poland, Romania, Slovakia, Spain, pharmacy – Estonia, Romania, Bulgaria, Cyprus, Czech Republic, Hungary, Poland, physiotherapy – Poland (interestingly that physiotherapy, usually taught in two cycles, is offered as a single-degree programme only by Polish HEIs). The leader in providing single-cycle programmes is Poland (32 programmes); Italy follows with 22 programmes, Romania (15 programmes) and Hungary (12 programmes) share the third place.

Of the countries teaching Medicine, Dentistry, and Pharmacy as two separate cycles, first-degree ETPs in medicine are offered by 3 universities in the Netherlands (Rijksuniversiteit Groningen, Maastricht University, European Medical School Oldenburg-Groningen) and one school in Austria (Karl Landsteiner Privatuniversität für Gesundheitswissenschaften). In addition, Utrecht University offers a three-year Bachelor programme in Pharmaceutical Sciences while the respective Master programmes are taught in the National languages. Given this fact, the offer of the Faculty of Biomedical Sciences of Università della Svizzera Italiana (Switzerland) looks contrasting. This school provides an EMI 6-semester Master of Medicine Programme for undergraduate students, mainly from the partner universities. The Bachelor study is provided in German but the language of tuition for the Master of Medicine is English. This observation is consistent with the language policy in the country: Durham M. (2016) claimed that English had acquired the status of a "de facto" additional language of Switzerland [15, p. 107]. More recent work argues that "in spite of the fact that English has no official status in Switzerland, English has, over the past few decades, been increasingly used as a vehicle for communication across language regions and in many professional domains within Switzerland, replacing national languages" [16].

Our observation revealed significant differences between countries within individual regions.

In the Baltic region, Lithuania offers more than half of ETPs (18 of 30). Bachelor ETPs were not found in Latvia and Estonia.

Poland (64 programmes) is leading in Central East Europe, followed by Hungary, although 26 programmes in Hungary are taught by four medical schools, while in Poland – by 16. Slovakia offers only single-cycle programmes.

In Central West Europe, Bachelor programmes were found in Austria and the Netherlands, while the rest offer only Master programmes. The Netherlands holds a leading position, and Germany is another country with a large number of ETPs.

In South East Europe, Cyprus and Romania demonstrate a large number of ETPs. Croatia offers only single-cycle programmes. Slovenia does not offer any ETP in Medicine and Health Sciences.

In South West Europe, considerable differences can be seen between the countries in the number and types of the programmes. Single-cycle programmes in medicine and dentistry are actively offered by Italian universities (both public and private), making the country one of the leaders in EU/EEA, despite the fact that the English proficiency level in the country is not high. Analysing the slow increase in EMI offer in Italy, Amanda C. Murphy and Beatrice Zuaro [17] assumed that a possible reason is the overall moderate English language proficiency in Italy. However, the number of single-cycle ETPs in the country, contrasting with other regions of Old Europe, does not support this assumption. In our view, English proficiency in the country is hardly of paramount importance for EMI implementation. It is just one (and not the most essential) aspect of socializing in the country for an English-speaking person (in the case of international students who do not know the language of the country), as well as an issue of academic and non-academic staff preparedness. Overall, the question whether the level of English is associated with English proficiency level in the country requires more accurate analysis.

In the Nordic region, all countries offer Master programmes, while Bachelor programmes are taught only in Sweden.

Overall, the situation demonstrated by our study is consistent with the literature data concerning selected countries. Medicine and Dentistry have been described as popular study areas in Poland (ranking first and sixth, respectively, among 15 according to the number of students enrolled) [18, p. 273]. It is reported that in Spain, business studies, economics, and engineering are more likely to be taught in English. In contrast, other areas of study, such as physical education, health sciences, history, or art are usually less internationally driven [19]. In Belgium, most English-taught Master-level programmes are in Applied Economics, Commercial Sciences and Business Administra-

tion, and Applied Sciences [20, p. 45]. The most popular ETPs in Austria are business administration, STEM, tourism, sports [21, p. 295].

According to the Studyportals and the British Council, EU/EEA countries are the leaders by the number of ETPs in the EHEA region: 13 of top 15 destinations by the supply of on-campus programmes [6, p. 16], but the positions of some countries in our rating are strikingly different from theirs. Thus, Poland, occupying the second position in our investigation, is the 10th in the 2024 report, Sweden – 3 in our study vs. 8 in the report, and Hungary – 8 vs. 15, in contrast to Germany (6th position in our study vs. 2 in the report). Denmark and Cyprus are 5th and 10th, respectively, in our study, but dropped out from the top 15 in the 2024 report. The 5 leaders among the providers of single-cycle ETPs (Poland, Italy, Czech, Hungary, except for Romania), appear in this list of top 15, where their positions are 10, 6, 13, and 15, respectively [6, p.16]. This inconsistency of our data with the general rating of destinations can be explained by the fact that the EU/EEA countries give different emphasis to ETPs in Medicine and Health Sciences in pursuing university internationalization. Besides, medicine and dentistry have higher than other professions requirements for language proficiency, which can also restrain the adoption of ETPs.

The term English-medium instruction is used to designate a wide range of English usage to teach content subjects. The detailed taxonomy of EMI forms proposed by Richards J.C. and Pun J. distinguishes ten models; one of them, the *EMI curriculum model*, is based on the mode of English use in the educational process and includes *single medium EMI* (all content subjects are taught in English), *dual medium/partial* (some subjects taught in English and others in another language), *parallel* (some subjects taught both in English and another language), *transitional* (some subjects are initially taught in another language and later taught in English), *collaborative* (the content teacher and the English teacher collaborate in teaching content classes), *interdisciplinary* (teachers of different disciplines share the teaching), *sheltered* (content teacher teaches a content course specially designed for L2 students), *adjunct* (a content and language course are linked with the same content base and co-ordinated assignments), *bridging* (a preparatory or bridging course prepares students to EMI) [9, p. 7].

In addition to entirely English-taught programmes (single medium EMI), we found medical schools offering bilingual and trilingual (national + English) programmes. For instance, Paracelsus Medizinische Privatuniversität (Austria) offers selected courses taught in English as well as clinical rotations, internships, and a four-month research trimester abroad at partner universities. To be enrolled in a Bachelor programme "a sufficient level of English" is required. Therefore, the entrance test includes questions (multiple choice and filling gaps) to evaluate English comprehension at the B2+ level. In addition, to complete the Bachelor program and earn the Bachelor of Science in Medicine, students must pass an external exam: the USMLE Step 1. Admission to the Master program (also German-taught) in Human Medicine requires successful completion of the USMLE Step 1.

Programmes taught in three or two languages are available at the University of Luxembourg. Though the main languages of instruction are German and French, English is used to teach some courses. The study programme *Bachelor in Medicine* includes courses taught in German and English (Biochemistry-Pathobiochemistry), French and English (Physics 1, Introduction to Public Health, Quantitative Biomedicine, Microbiology 1, Sensory system), French, German and English (Cross-disciplinary cardio-respiratory teaching). The recommended literature includes English-language textbooks. English at the B2 level confirmed by passing exams (TOEFL, IELTS, Cambridge) is required to be enrolled, and exemptions are made for the students who have completed secondary education in Luxembourg. The Bachelor programmes taught in three languages (one of them is English) are Psychiatric Nurse, Medical Technical Assistant in Surgery, Nurse in Anaesthesia and Reanimation, Paediatric Nurse, Nurse in General Care, and Midwifery; Life Sciences–Biomedicine is taught in French and English.

More examples of bilingual programmes can be found in Spain. English-taught courses are available at the Faculty of Medicine, the University of Cantabria; the Faculty of Medicine, the University of Barcelona; the Faculty of Medicine, the University of Vic. The example of the University of Vic is rather illustrative. All programmes in Medicine and Health offered by this university contain English-taught courses. The programme in Dentistry includes the following courses taught in English: *Communication and Psychology* (10 ECTS, basic training), *Technology and Digital Tools* (10 ECTS, compulsory), all optionals each 5 ECTS: *Academic Papers, Advanced Biostatistics, Advanced Community Dentistry, Aesthetic*

Dentistry, Global Health, Human Nutrition and Healthy Living, Leadership and Professionalism, Current Health System, Update on Dental Materials. Optional courses of the programme in medicine are English-taught: *Biomedical Research, Clinical Sexology, Health Management, Integrated Palliative Care, Leadership and Professionalism, Multidisciplinary Teams for Patient Safety and Quality, Occupational Health, Physical Activity, Sport and Health, Current Healthcare System, Mindfulness and Health, ICT in Health, Global Health, Climate Change and Health, Art and Medicine*; the programme in nursing includes 6 ECTS in English: compulsory *Scientific Method in Nursing Sciences* and optional *Nutrition and Cooperation in Nutrition Crisis Situations*; the programme in occupational therapy – 6 ECTS: *E-Health* and *Artistic Activity as Therapy* (both optional); physiotherapy – 6 ECTS: *e-Health*, *Nutrition and Physiotherapy* (both optional); biomedicine – 72 ECTS: *Integrated Project I – VI* (compulsory), *Molecular Genetics* (basic training), *Omics Technologies* (compulsory), *Clinical Genomics* compulsory, *Cancer Biology* (compulsory), *Bioscience and Business* (optional), *Emerging and Re-emerging Infections (*optional), *Systems Medicine* (optional). Our attention was attracted by the course *Integrated Project*, which ends each semester from the first to the third year and is aimed at consolidating at a practical level of the knowledge that students have acquired during the semester. As the course is taught in English, the students gain the skills of scientific communication in English, both in oral and written form.

According to Gustafsson M. & Valcke J. [22, p. 224], at Karolinska Institutet, the largest medical school in Sweden, "all undergraduate and postgraduate degrees must have at least 7.5 credits taught through English". We could not find the details of the English-taught courses on the website, but to enter medicine or dentistry, English proficiency equivalent to 6.5 in IELTS or 90 in TOEFL (B2) is required.

Programmes run in Polish, with selected courses carried out in English as the language of instruction were mentioned by Cierpich A. & Sieradzka-Baziur B. (2020) [23], but we could not identify them among programmes in medicine and health sciences. Perhaps more information could be obtained by surveying the universities' officials dealing with English-taught programmes.

We believe that the potential of partial EMI is underrated, especially when the course is planned for L1 students. It can motivate them to improve their English language skills, allows them to get the latest professional information, and will prepare them to participate in academic mobility. It can be adopted as parallel EMI when the same course is offered both in L1 and English. It is worth noting that partial EMI has long been successfully practiced by Ukrainian secondary schools with in-depth study of foreign languages.

Describing the steady growth of English-medium instruction of Medicine and Health Sciences in Europe it would be unfair not to mention that EMI implementation has not been uneventful. It is reported that in France, "teaching, exams, dissertations, and theses must be in French, in public and private schools and universities alike" [24, p. 36] with the exception of teaching foreign languages, special education (i.e., international schools) and visiting professors. In Flanders (the region of Belgium), the law states that languages other than Dutch may be used on condition that they provide an "added value" and that there is an equivalent programme in Dutch [19, p. 43]. Legal proceedings concerning EMI implementation in Italy [25] and the Netherlands [26] are also well-known. Anti-EMI movement often takes place under the flag of organizations concerned with national language and cultural heritage.

Together with the expansion of ETPs in Europe, the recent report on ETPs [6] shows significant cuts in Spain, Sweden, Denmark, and Finland. The measures to limit the number of the programmes taught in English only (such as modifying programmes to be taught entirely in Dutch, adding a Dutch-language option, and employing a quota for English admissions) were announced in the Netherlands. The measures are planned to be introduced in the 2025–2026 academic year [27]. The share of the programmes in Medicine and Health Sciences is not known, but given that these programmes are language-sensitive, this trend may affect them.

Conclusion

Our findings suggest that teaching Medicine and Health Sciences in English is a common practice in European countries. However, the types of EMI (single medium or bilingual) as well as the level of education (undergraduate or graduate) are implemented selectively, which might be related to several reasons, such as the language policy in the country, target groups of students and their incentives, peculiarities of the HEI internationalization policy. Among single medium ETPs, Master programmes are more common; with some exemp-

tions, they can be found in every country that has implemented EMI in Medicine and Health Sciences and is the only type of ETP in many countries. Programmes leading to the degree in medicine, dentistry, and pharmacy are offered by the medical schools in the Baltic region, Central East Europe, South East Europe, and South West Europe. Implementing ETPs is not directly associated with the level of language proficiency in the country; however, this issue requires a more accurate investigation within the group of countries.

Because of the role EMI plays in higher education internationalization, students' mobility, university competitiveness, and rating, investigation of the global experience of EMI implementation should be taken into account when developing ETPs in a particular university.

The use of the information from the university site is a limitation of the study, as it chiefly reflects the declared policy of the HEI. More information about the actual state of affairs, achievements, and challenges can be obtained using surveys and interviews.

DECLARATIONS:

Disclosure Statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Statement of Ethics

The authors have no ethical conflicts to disclosure.

Data Transparency

The data can be requested from the authors.

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Consent for publication

All authors give their consent to publication.

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FEATURES OF EMOTIONAL BURNOUT SYNDROME IN MEDICAL COLLEGE TEACHERS

Kulyk A., Bezditko T.

Kharkiv National Medical University, Kharkiv, Ukraine

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ABSTRACT

Background. Due to the high emotional intensity of the teacher's professional activity, responsibility and complexity of the of teaching work, the risk of developing emotional burnout syndrome increases.

Aim. To investigate the characteristics of emotional burnout syndrome in medical college teachers.

Material & Methods. This work was carried out using the sociological method (according to Maslach Burnout Inventory by Maslach C. & Jackson S., 1986) at Bohodukhiv Medical Vocational College, a municipal health care institution of Kharkiv Regional Council. The survey involved 38 teachers, including 6 men and 32 women. The age of the teachers ranged from 30 to 62 years, and their teaching experience ranged from 3 to 35 years.

Results. According to the "emotional exhaustion" scale, 15 (39.4%) of the respondents had the first degree of emotional burnout, 13 (34.2%) had the second degree, and 4 (10.5%) had the third degree. According to the scale of "alienation", 14 (36.8%) of the respondents showed the first degree of emotional burnout, and 10 (26.3%) – the second degree. According to the scale of "devaluation of own achievements", 7 (18.4%) of the respondents had the first degree of emotional burnout, 8 (21.1%) – the second degree, and 4 (10.5%) – the third degree. It should be noted that the teaching experience of all 4 (100.0%) respondents with the third degree of emotional burnout was over 20 years.

Conclusions. Emotional burnout poses a threat to both personal and professional development, as well as mental and somatic health. Teaching experience is directly proportional to the increase in the degree of emotional burnout. The prevention of emotional burnout symptoms should be comprehensive, psychological, and organizational, aimed at correcting mental health disorders and, if necessary, improving the psychological climate in the team, optimizing the teacher's work.

Keywords: *emotional exhaustion, alienation, devaluation of personal achievements*.

Introduction

Teaching activity is constantly accompanied by a large number of stress factors that cause high emotional stress. In particular, it is the need for frequent and intensive contacts, high dynamism, lack of time, work overload, complexity of pedagogical situations, social evaluation, etc. Due to the high emotional intensity of the teacher's professional activity, responsibility and complexity of the teacher's professional work, the risk of developing emotional burnout syndrome increases [1].

The study of the problem of emotional burnout originated in foreign psychology at the end of the XX century. The term "emotional burnout" appeared in 1974, when psychiatrist Herbert Freudenberg noticed exhaustion in psychiatric hospital volunteers [2]. Nowadays, many scientists are actively studying this problem [3; 4].

Symptoms of burnout indicate the characteristic signs of prolonged stress and mental overload that accompany professional activities, the main content of which is interpersonal interaction. The development of burnout syndrome has a staged

Corresponding Author:
Kulyk Anastasiia – 2nd year master's student, Department of Internal Medicine Propedeutics, Nursing and Bioethics, Kharkiv National Medical University, Ukraine.

✉ Ukraine, 61022, Kharkiv, Nauky ave., 4.
E-mail: anastasiakulik575@gmail.com

nature, during which there is a change in attitude towards professional activity to indifference and even negative, disruption of contacts with people, and suppression of humane forms of behavior. All researchers, without exception, point out that burnout poses a threat to both personal and professional development, as well as to a person's mental and somatic health.

Maslach C. (1998) conditionally divides the symptoms of emotional burnout into physical (fatigue, feeling of exhaustion, asthenia, frequent headaches, gastrointestinal disorders, overweight or underweight, shortness of breath, insomnia), behavioral and psychological (work becomes more and more difficult, and the ability to perform it becomes less and less, feelings of unconscious anxiety, decreased enthusiasm, feelings of resentment, frustration, uncertainty, guilt, easily triggered anger, irritability, rigidity, general negative attitude towards life prospects, alcohol abuse, etc. [5].

According to [6], the professional burnout of a higher education teacher can be caused by objective and subjective factors. Researchers [7–9] refer to subjective factors as insufficient motivation or formation of a value-based attitude to professional activity; some personal characteristics: anxiety, introversion, perfectionism, workaholism, presentism, etc.

Objective factors include socio-economic transformations in Ukraine that affect the material stability of society members, psychological state and professional well-being; the risk of losing a job due to lack of funds associated with low (absent) funding and insufficient enrolment of applicants during the admission campaign; failure to provide an employee with a full-time job if he or she wants to work fully and efficiently; overloading a teacher with work tasks in the absence of encouragement and appropriate remuneration, etc.

Based on the model of the American researchers Maslach C. and Goldberg J., "burnout" is interpreted as a syndrome of emotional exhaustion, alienation and devaluation of personal achievements. Emotional exhaustion is seen as the main component of "professional burnout" and is characterized by a low emotional background, indifference or emotional overload. Alienation manifests itself in deformation of relationships with other people. In some cases, this may be an increase in dependence on other people, in others – an increase in negativism, cynicism and feelings towards recipients: patients, clients, subordinates, etc. The devaluation of personal achievements is either a tendency to negatively assess oneself, one's professional achievements and successes, negativism about one's professional dignity and capabilities, or the leveling of personal dignity, limiting one's capabilities, responsibilities towards others [5].

Aim of study was to investigate the peculiarities of the course of emotional burnout syndrome in medical college teachers.

Material and Methods

This work was carried out using the sociological method (according to Maslach Burnout Inventory by Maslach C. & Jackson S., 1986) on the basis of the Municipal Health Care Institution "Bohodukhiv Medical Professional College" of Kharkiv Regional Council. The survey involved 38 teachers, including 6 men and 32 women. The age of the teachers ranged from 30 to 62 years, and their teaching experience was from 3 to 35 years. All survey participants signed an informed consent for participation in scientific research. Statistical processing of the data was carried out using Excel 2019 (Microsoft, USA).

Results

The age of the teachers ranged from 30 to 62 years, the teaching experience – from 3 to 35 years (*Table 1*).

Table 1 shows that the largest number of teachers was aged 30–50 years – 24 (63.2%), of which 18 had more than 10 years of experience, i.e. were specialists of a high level of teaching skills. Distribution of respondents by level of emotional burnout and key components Maslach Burnout Inventory is given in *Table 2*.

In the group of surveyed teachers, 18 (47.4%) had a pronounced first degree of general emotional burnout, which was manifested by rare and short-lived symptoms (fatigue, feeling of exhaustion, decreased enthusiasm, irritability, general negative attitude to life prospects). They were alleviated by the ability to take care of oneself and relaxation (rest and holidays). It should be noted that out of 18 teachers, 13 (72.2%) had more than 10 years of experience, and 5 (27.8%) had over 20 years of experience.

In 10 (26.3%) of the teachers, there were pronounced symptoms of the second degree of general emotional burnout (asthenia, frequent headaches, gastrointestinal disorders, insomnia, feelings of resentment, feelings of disappointment, uncertainty, guilt, rigidity). At this stage, the signs of burnout are more regular, last longer and are more severe. Strategies that were previously suitable for relieving symptoms (rest and holidays) become ineffective. Teachers may continue to feel tired

Table 1. Age and length of service of teachers of Bohodukhiv Medical Professional College

Age	n (%)	Work experience		
		1–10 years	10–20 years	>20 years
25–30 years	6 (15.8%)	4	2	-
30–45 years	15 (39.5%)	5	6	4
40–50 years	9 (23.7%)	1	2	6
more than 50 years	8 (21.1%)	–	–	8

Table 2. The severity of emotional burnout syndrome among teachers of "Bohodukhiv Medical Professional College

Components of emotional burnout syndrome	Levels of emotional burnout		
	first degree	second degree	third degree
General emotional burnout	18 (47.4%)	10 (26.3%)	-
Emotional exhaustion	15 (39.5%)	13 (34.2%)	4 (10.5%)
Alienation	14 (36.8%)	10 (26.3%)	-
Devaluation of personal achievements	7 (18.4%)	8 (21.1%)	4 (10.5%)

after a night's sleep, after a weekend's rest. More and more effort is required to "get back to normal" and take care of oneself. It is worth noting that the teaching experience of all 10 (100%) respondents with the second degree of general emotional burnout was over 20 years.

Next, the emotional burnout syndrome is analyzed in terms of individual scales. According to the "emotional exhaustion" scale, 15 (39.4%) of the respondents had the first degree of emotional burnout, 13 (34.2%) had the second degree, and 4 (10.5%) had the third degree. According to the scale of "alienation", 14 (36.8%) of the respondents showed the first degree of emotional burnout, and 10 (26.3%) – the second degree. According to the scale of "devaluation of own achievements", 7 (18.4%) of the respondents had the first degree of emotional burnout, 8 (21.1%) – the second degree, and 4 (10.5%) – the third degree.

It should be noted that the teaching experience of all 4 (100%) respondents with the third degree of emotional burnout was over 20 years.

The obtained results indicate that the problem of emotional burnout is really relevant for medical college teachers.

Discussion

The findings of this study highlight significant parallels between emotional burnout in medical college teachers and other high-stress healthcare professions. Among the surveyed teachers, nearly half (47.4%) exhibited first degree of burnout, characterized by intermittent symptoms such as fatigue and irritability, while 26.3% reported second degree of emotional burnout, marked by chronic exhaustion and somatic complaints. Notably, all respondents with third degree of burnout – a severe condition involving emotional detachment – had over 20 years of teaching experience. This aligns with research by Galaiya R. et al. (2020), which found that senior surgeons with extensive career tenure were disproportionately affected by burnout due to prolonged exposure to high-stress environments [7]. The consistency in these trends underscores the role of occupational longevity as a critical risk factor across medical education and clinical practice.

Further comparisons reveal similarities in emotional exhaustion between educators and critical care nurses. In this study, 39.5% of teachers reported moderate emotional exhaustion, a figure comparable to rates observed among ICU nurses facing relentless workplace demands [9]. Both professions involve sustained emotional labor, whether through patient care or student engagement, suggesting that burnout mechanisms transcend specific job functions. However, while nurses often benefit from targeted resilience interventions – such as the positive emotion skills program tested by Cheung E.O. et al. (2020) [8] – medical educators rarely receive comparable support. This disparity points to an unmet need for institutional burnout prevention strategies in academic settings.

The depersonalization component of burnout, referred to as "alienation" in this study, affected 36.8% of teachers with first degree, with a subset progressing to second degree. This mirrors fin-

dings in surgical teams, where cynicism and emotional detachment were linked to reduced job satisfaction [7]. Strikingly, the most severe cases of burnout in both groups correlated with decades of service, implying that early intervention is essential to mitigate long-term consequences. Cochran K.L. et al. (2020) emphasized organizational-level changes – such as workload redistribution and mental health resources – as effective measures for healthcare workers [5]. Applying these approaches to medical education could similarly alleviate burnout among faculty, particularly those with extensive tenure.

Finally, the devaluation of personal achievements, reported by 18.4% of teachers with first degree and 21.1% with second degree of emotional burnout, reflects a broader pattern observed in caregiving professions. When educators or clinicians perceive their efforts as futile, motivation declines, exacerbating burnout. The results of this study reinforce the need for systemic reforms, including mentorship programs and recognition initiatives, to sustain professional fulfillment. The parallels between medical teachers and frontline healthcare workers underscore burnout as a universal occupational hazard, demanding tailored yet cohesive solutions across disciplines.

Conclusions

Emotional burnout poses a threat to both personal and professional development, as well as mental and somatic health. Recommendations for the prevention and overcoming of teachers' emotional burnout syndrome include optimization of work and rest regimes, healthy lifestyle, proper nutrition, mastering self-regulation skills, professional and personal development and self-improvement.

Teaching experience is directly proportional to the increase in the degree of emotional burnout.

Thus, the prevention of emotional burnout symptoms should be comprehensive, psychological, and organizational, aimed at correcting mental health disorders and, if necessary, improving the psychological climate in the team, optimizing the teacher's work.

DECLARATIONS:

Disclosure Statement

The authors have no potential conflicts of interest to disclosure, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Statement of Ethics

The authors have no ethical conflicts to disclosure.

Data Transparency

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