

IMMUNOHEMATOLOGICAL INDICES AS MARKERS OF INFLAMMATION, CELLULAR AND NONSPECIFIC IMMUNOLOGICAL DEFENSE IN CHILDREN WITH ACUTE OTITIS MEDIA

O. P. Sakovets, L. P. Sydorchuk, T. V. Kazanceva, O. A. Petrynych, M. M. Semianiv, Y. V. Repchuk, K. O. Voroniuk

Bukovinian State Medical University, Chernivtsi, Ukraine

Acute otitis media (AOM) ranks among the most common childhood illnesses worldwide, impacting millions of children annually and representing a considerable public health concern. Although the fundamental immunological pathways involved in AOM are relatively well understood, the role of non-specific immune responses in the disease's pathogenesis remains underexplored.

Objective – to evaluate immune-hematological indices as integral indicators of cellular and general immunological reactivity and nonspecific anti-infective protection in children with AOM depending on the ear discharge (catarrhal vs purulent).

Material and methods. Prospective cohort study included 95 children diagnosed with AOM, aged between 7 and 18 years: 34.74% (n=33) were girls and 65.26% (n=62) were boys. The study was carried out in accordance with the principles of Good Clinical Practice, Good Laboratory Practice, and established ethical standards for biomedical research involving human subjects. Participants were categorized based on the type of mucosal inflammation: catarrhal in 52.63% (n=50) and purulent in 47.37% (n=45) of cases. The control group consisted of 50 generally healthy children: 20 girls (40.0%) and 30 boys (60.0%). Cellular and general immunological reactivity and resistance, neutrophil reactive response were assessed on the basis of a complete blood cell count with subsequent calculation of the integral indices. Statistical analysis was conducted using Statistica 7.0 (StatSoft Inc, USA) software and Excel® 2016™. The differences between groups for independent samples were verified using the unpaired Student's t-test (if the data distribution were close to normal according to the Kolmogorov-Smirnov tests and the Shapiro-Wilk W-test), or the Wilcoxon-Mann-Whitney U-test (for an uneven data distribution). Differences were considered significant at P values <0.05.

Results. Immuno-haematological indices certify two conditional clinical and laboratory variants of the AOM course in the examined children. The first variant (purulent AOM) is characterized by moderate neutrophilosis (+II), pronounced hyporegenerative nuclear shift due to rod-shaped neutrophils, eosinophilic granulocytes and a significant increase in intoxication indices. Such blood changes indicate the predominance of the bacterial component (purulent process in the middle ear), pronounced severity of inflammation against the background of increased cellular and immune reactivity, corresponding activation of resistance and sensitization of the organism with a predominance of immediate-type hypersensitivity. In these children, a specific humoral immune response begins to form. The second variant of the AOM course (catarrhal) is characterized by relative and absolute rod-shaped neutrophilosis (less pronounced than in the purulent AOM), higher lymphocytosis and monocytosis, with an increase in nonspecific and immune resistance indices, which prove sensitization of the organism with the development of delayed-type hypersensitivity, against the background of moderately pronounced intoxication. The revealed pattern indicates the predominance of lymphocytic activation with the development of specific cellular defence.

Conclusions. AOM in children is characterized by laboratory manifestations of endotoxemia (more severe in purulent AOM) caused by endointoxication at the level of peripheral blood and exointoxication of infectious origin.

Key words:

Acute Otitis Media; inflammation; catarrhal and purulent Otitis; children; cellular and nonspecific immunological defense; nonspecific and immune resistance.

Clinical and experimental pathology 2025. Vol.24, №2 (92). С. 27-35.

DOI 10.24061/1727-4338.XXIV.2.92.2025.05

E-mail: oleksii.sakovets@gmail.com

ІМУНО-ГЕМАТОЛОГІЧНІ ІНДЕКСИ ЯК МАРКЕРИ ЗАПАЛЕННЯ, КЛІТИННОГО І НЕСПЕЦИФІЧНОГО ІМУНОЛОГІЧНОГО ЗАХИСТУ У ДІТЕЙ ІЗ ГОСТРИМ СЕРЕДНІМ ОТИТОМ

О. П. Саковець, Л. П. Сидорчук, Т. В. Казанцева, О. А. Петринич, М. М. Сем'янів, Ю. В. Репчук, К. О. Воронык

Буковинський державний медичний університет, м. Чернівці, Україна

Гострий середній отит (ГСО) займає передові позиції серед найбільш розповсюджених захворювань дитячого віку, щорічно вражаючи мільйони дітей та створюючи значну проблему для громадського здоров'я. Незважаючи на те, що фундаментальні імунологічні шляхи, що беруть участь у розвитку ГСО, відносно добре вивчені, роль неспецифічних імуних реакцій у патогенезі захворювання залишається досліджена недостатньо.

Ключові слова:

катаральний та гнійний гострий середній отит, діти, клітинний та неспецифічний імунологічний захист, неспецифічна та імунна резистентність.

Клінічна та експериментальна патологія 2025. Т.24, №2 (92). С. 27-35.

Метароботи – оцінити імуногематологічні індекси як інтегральні показники клітинної, загальної імунологічної реактивності та неспецифічного протиінфекційного захисту у дітей із ГСО залежно від характеру виділень із вуха (катаральні чи гнійні).

Матеріали та методи. Проспективним когортним дослідженням охоплено 95 дітей із діагнозом ГСО віком від 7 до 18 років: 34,74% ($n=33$) – дівчатка та 65,26% ($n=62$) – хлопчики. Дослідження проводили відповідно до принципів належної клінічної та лабораторної практики і встановлених етичних стандартів для біомедичних досліджень за участі людей. Учасників класифікували за типом запалення слизової оболонки середнього вуха: катаральне у 52,63% ($n=50$) та гнійне у 47,37% ($n=45$) випадків. Контрольну групу становили 50 практично здорових дітей: 20 дівчаток (40,0%) та 30 хлопчиків (60,0%). Клітинну та загальну імунологічну реактивність і резистентність, реактивну відповідь нейтрофілів оцінювали на основі загального аналізу крові з подальшим розрахунком інтегральних індексів. Статистичний аналіз проводили з використанням програмного забезпечення Statistica 7.0 (StatSoft Inc, США) та Excel® 2016™. Відмінності між групами для незалежних вибірок перевіряли за допомогою непарного t -критерію Стюдента (якщо розподіл даних був близьким до нормального згідно з тестами Колмогорова-Смірнова та W -критерієм Шапіро-Вілکا) або U -критерія Вілкоксона-Манна-Вітні (для нерівномірного розподілу даних). Відмінності вважали достовірними при значеннях $P < 0,05$.

Результати. Імуногематологічні показники засвідчують два умовні клініко-лабораторні варіанти перебігу ГСО в обстежених дітей. Перший варіант (гнійний ГСО) характеризується помірним нейтрофіліозом (+II), вираженим гіпорегенеративним ядерним зсувом за рахунок паличкоядерних нейтрофілів, еозинофільних гранулоцитів та значним підвищенням показників інтоксикації. Такі зміни крові засвідчують про переважання бактеріального компонента (гнійний середній отит), виражену тяжкість запалення на тлі підвищеної клітинної та імунної реактивності, відповідну активацію резистентності та сенсibiliзацію організму з переважанням гіперчутливості негайного типу. У цих дітей починає формуватися гуморальна специфічна імунна відповідь. Другий варіант перебігу ГСО (катаральний) характеризується відносним та абсолютним паличкоядерним нейтрофіліозом (менш вираженим, ніж при гнійному ГСО), вищим лімфоцитозом та моноцитозом, зі збільшенням показників імунної та неспецифічної резистентності, що засвідчує про сенсibiliзацію організму з розвитком гіперчутливості уповільненого типу на тлі помірно вираженої інтоксикації. Виявлена закономірність вказує на переважання лімфоцитарної активації з розвитком специфічного клітинного захисту.

Висновки. Гострий середній отит у дітей характеризується лабораторними проявами ендотоксикозу (більш тяжчого за гнійного варіанту), спричиненого ендоінтоксикацією на рівні периферичної крові та екзоінтоксикацією інфекційного походження.

Introduction

Acute otitis media (AOM) is one of the most prevalent infectious conditions in paediatric populations globally, with millions of new cases reported each year [1, 2]. This high incidence positions AOM as a significant concern for public health systems, particularly due to its association with antimicrobial resistance and recurrent morbidity in early childhood. Acute otitis media involves inflammation of the mucosal lining throughout the middle ear cavity, including the lining of the tympanic cavity and the tympanic membrane [3]. While core immunological mechanisms underlying the onset of AOM have been extensively characterized, the contribution of non-specific immune factors, including innate and inflammatory responses, remains insufficiently studied and is often underestimated in both clinical and research settings. Greater attention to these mechanisms may improve early diagnostic markers and therapeutic strategies.

Among possible early diagnostic markers, the various hematologic indices, such as absolute counts of neutrophils, lymphocytes, monocytes, and platelets, along with derived indices like the neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), and platelet-to-lymphocyte ratio (PLR), have been suggested as useful

tools for diagnosing infections, providing early warning of disease progression, and stratifying patient risk [4]. The NLR is a fundamental inflammatory marker derived from the complete blood count (CBC), with a typical range of 0.78 to 3.58 [5]. Elevated NLR values have been identified as a useful indicator in various otolaryngological conditions, including otitis media with effusion [6], virus induced facial palsy [7], and as a positive prognostic factor in idiopathic sudden sensorineural hearing loss [8].

NLR has proven to be a valuable indicator for both diagnosing and gauging the severity of community acquired pneumonia and bacteremia [9, 10]. Similarly, MLR and PLR have been validated as surrogate biomarkers for identifying influenza virus infection in patients with respiratory tract illnesses [11], rheumatoid arthritis [12]. However, there remains a paucity of research evaluating the diagnostic utility of these hematologic indices specifically in otitis media in children [13].

Therefore, this study aimed to examine the absolute and relative number of the main populations of immunocompetent cells of a complete blood cell count (CBC) (neutrophils, lymphocytes, monocytes, platelets, etc, with following calculation of immuno-hematological

indices and ratio NLR, MLR, PLR, etc) in children with AOM to determine their diagnostic value and explore their relationship with disease severity.

The aim of the study

To evaluate immune-hematological indices as integral indicators of cellular and general immunological reactivity and nonspecific anti-infective protection in children with AOM depending on the ear discharge (catarrhal vs purulent).

Research material and methods

Clinical data for the study were collected at the Municipal Non-profit Enterprise «Multidisciplinary Hospital of Intensive Care» in Kitsman between 2023 and 2024. The prospective study enrolled 100 children diagnosed with acute otitis media (AOM). After screening, 95 participants aged 7 to 18 years met the inclusion criteria. Informed consent was obtained from their parents or legal guardians. Each participant underwent a comprehensive evaluation, including medical history, clinical examination, laboratory testing, and instrumental diagnostics.

The research adhered to ethical standards outlined in the Council of Europe Convention on Human Rights and Biomedicine, the principles of Good Clinical Practice (GCP, 1996), and the Declaration of Helsinki by the World Medical Association. The study protocol received approval from the Biomedical Ethics Commission of Bukovinian State Medical University (BSMU).

Diagnosis and assessment of AOM severity were conducted according to the National Unified Clinical Protocol for Acute Otitis Media, authorized by the Ministry of Health of Ukraine (Order № 688, April 9, 2021), alongside relevant national clinical guidelines

(2021) [14, 15] and international standards [1, 3, 16]. When indicated, additional radiographic imaging – including X-rays of the mastoid bones, paranasal sinuses, and chest – was performed in two standard projections.

The children were categorized by age into two groups: 7-11 years ($n = 81$) and 12-18 years ($n = 14$). Based on the severity of AOM, 43 cases (45.26%) were classified as severe, while 52 (54.74%) were non-severe. In terms of the inflammatory type of the mucous membranes and ear discharge, 50 children (52.63%) had catarrhal inflammation and 45 (47.37%) had purulent forms. When classified by tympanic membrane condition, 77 patients (81.05%), presented with a pre-perforative stage, and 18 (18.95%) had a perforative stage.

Among the study group, 33 participants (34.74%) were girls and 62 (65.26%) were boys. The control group consisted of 50 clinically healthy children with a similar age and sex distribution (20 girls and 30 boys), who had no signs of inflammatory diseases at the time of the study or during the previous six months. No statistically significant differences in age were found between the study and control groups.

Cellular reactivity and resistance, neutrophil (NEU) reactive response and general immunological reactivity of children with AOM were assessed on the basis of a complete blood cell count (CBC) – the absolute and relative number of the main populations of immunocompetent cells (ICC) with subsequent calculation of the integral indices given in Table 1. Extended CBC was performed on the CELL-DYN 3700 SL hematological analyzer (manufacturer – «Abbott Laboratories», USA). The evaluation of the immunohematological indices for other diseases was analyzed in our former publications [17-19].

Table 1

Immuno-hematological indices [13, 20, 21]

Indices of inflammation, cellular reactivity and cellular resistance		
1	Lleukocytes Intoxication Index (LII) after Kalf-Kalif	$(2 \text{ RNEU} + \text{SNEU}) / (\text{LYM} + \text{Mono}) \times (\text{EOS}+1)$
2	LII after R. A. Reys	$(\text{RNEU}+\text{SNEU}) / \text{Mono}+\text{LYM}+\text{EOS}$
3	Intoxication Index	$(\text{LII} \times \text{Leu} \times \text{ESR}) / 100$
4	Index of Endotoxiosis degree (Neutrophil shift index)	$\text{RNEU} / \text{SNEU}$
5	Cellular reactivity index	$(\text{WBC} / (\text{LII} \times \text{age-year})) \times 100$
6	Cellular resistance index	$\text{WBC} / \text{LII Kalf-Kalif}$
7	Nonspecific resistance index (Harkavi)	LYM / SNEU
Reactive response of Neutrophils		
1	Lymphocyte-to-granulocytic index	$\text{LYM} \times 10 / \text{EOS} + \text{NEU}$
2	Neutrophil-to-lymphocyte ratio (NLR)	NEU / LYM
3	Leukocyte shift index	$(\text{BASO}+\text{EOS}+\text{NEU}) / (\text{Mono}+\text{LYM})$
4	Neutrophil-to-monocyte ratio (NMR)	NEU / Mono
5	Leukocyte-ESR ratio	$(\text{WBC} \times \text{ESR}) / 100$
6	Nonspecific reactivity index	$(\text{LYM} \times 100) / \text{SNEU}$
General immunological reactivity		
8	Immune reactivity index	$(\text{LYM} + \text{EOS}) / \text{Mono}$
9	Immune resistance index	$\text{LYM} / (\text{Age-year} \times \text{LII Kalf-Kalif})$
10	Index of immunological reactivity growth	$\text{Immune reactivity index} / \text{Immune resistance index}$
11	Allergy index	$(\text{LYM} + (\text{EOS}+1) \times 10) / (\text{NEU} + \text{Mono} + \text{BASO})$
12	Lymphocyte index	LYM / NEU
13	Lymphocyte-to-monocyte ratio (LMR)	LYM / Mono
14	Lymphocytes-to-eosinophils ratio	LYM / EOS
15	Agranulocytes-to-ESR ratio	$(\text{LYM} + \text{Mono}) / \text{ESR}$

Notes: LII-Leukocytes Intoxication Index; NEU – neutrophil; BASO – basophil; RNEU – rod-shaped neutrophil; SNEU – segmented neutrophil; LYM – lymphocyte; Mono – monocyte; EOS – eosinophil; WBC (leukocytes) – white blood cell; ESR – erythrocyte sedimentation rate; NLR – Neutrophil-to-lymphocyte ratio; NMR – Neutrophil-to-monocyte ratio; LMR – Lymphocyte-to-monocyte ratio

Statistical analysis was conducted using Statistica 7.0 (StatSoft Inc, USA) software and Excel® 2016™. The differences between groups for independent samples were verified using the unpaired Student's t-test (if the data distribution were close to normal according to the Kolmogorov-Smirnov tests and the Shapiro-Wilk W-test), or the Wilcoxon-Mann-Whitney U-test (for an uneven data distribution). Differences were considered significant at P values <0.05.

Results and Discussion

The course of AOM is generally accompanied by leukocytosis, higher in the purulent process (Table 2). In children with purulent AOM hemoglobin level was lower than in the catarrhal process 14.68% (p=0.046). Relative granulocytopenia due to neutropenia (mature forms – segmented neutrophils – SNEU) was found in children with

serous AOM – 8.36% (p=0.042) and 16.59% (p=0.009), respectively, with compensatory rod-nuclear neutrophilosis (RNEU), both relative and absolute – 2.1 and 3.14 times (p<0.001). Relative neutropenia due to SNEU was also found in purulent AOM – 11.77% (p = 0.016). The RNEU level (relative and absolute) in children with purulent AOM exceeded that in catarrhal otitis – 55.36% (p=0.003) and 70.45% (p=0.006). The lymphocytes level in children with catarrhal AOM exceeded the reference values – 23.87% (p=0.017) and 76.16% (p=0.004). The relative content of monocytes was, on the contrary, lower than in the control group: in serous AOM – 17.76% (p=0.024), in purulent – 50.09% (p=0.001), respectively. ESR in children with AOM exceeded that in the control group: in serous AOM – 2.21 times (p<0.001), somewhat more in purulent AOM – 3.04 times (p<0.001), with a significant difference between the groups with AOM – 37.11% (p<0.001).

Table 2

Laboratory findings based on complete blood cell count in children with acute otitis media depending on the ear discharge

Laboratory findings		Control, n=50	Catarrhal AOM, n=50	Purulent AOM, n=45
Erythrocytes, $\times 10^{12}/L$		4.25 $\pm$ 0.15	4.36 $\pm$ 0.20	4.29 $\pm$ 0.16
Hemoglobin, g/L		128.94 $\pm$ 5.42	139.50 $\pm$ 6.07	119.02 $\pm$ 6.10 $p_1=0.046$
WBC (leukocytes), $\times 10^9/L$		5.80 $\pm$ 0.14	8.50 $\pm$ 0.65 p<0.001	9.20 $\pm$ 0.56 p<0.001
Granulocytes	%	66.35 $\pm$ 0.53	60.80 $\pm$ 3.40 p=0.042	66.77 $\pm$ 3.61
	$\times 10^9/L$	3.85 $\pm$ 0.17	5.17 $\pm$ 0.27 p=0.001	6.14 $\pm$ 0.38 p<0.001; $p_1=0.021$
NEU	%	64.71 $\pm$ 0.88	57.11 $\pm$ 2.65 p=0.004	63.03 $\pm$ 3.03
	$\times 10^9/L$	3.75 $\pm$ 0.26	4.85 $\pm$ 0.22 p<0.001	5.80 $\pm$ 0.41 p=0.002
RNEU	%	2.50 $\pm$ 0.18	5.22 $\pm$ 0.58 p<0.001	8.11 $\pm$ 0.30 p<0.001; $p_1=0.003$
	$\times 10^9/L$	0.14 $\pm$ 0.06	0.44 $\pm$ 0.08 p<0.001	0.75 $\pm$ 0.09 p<0.001; $p_1=0.006$
SNEU	%	62.21 $\pm$ 1.05	51.89 $\pm$ 4.23 p=0.009	54.89 $\pm$ 3.15 p=0.016
	$\times 10^9/L$	3.62 $\pm$ 0.34	4.41 $\pm$ 0.45	5.05 $\pm$ 0.36 p=0.003
EOS, %		1.60 $\pm$ 0.10	1.94 $\pm$ 0.15	3.44 $\pm$ 0.30 $p, p_1<0.001$
Agranulocytes	%	34.09 $\pm$ 0.21	39.20 $\pm$ 2.52 p=0.023	33.23 $\pm$ 1.75 $p_1=0.027$
	$\times 10^9/L$	2.0 $\pm$ 0.16	3.33 $\pm$ 0.18 p=0.001	3.06 $\pm$ 0.23 p=0.004
LYM	%	28.74 $\pm$ 0.20	35.60 $\pm$ 2.57 p=0.017	30.33 $\pm$ 1.52 $p_1=0.045$
	$\times 10^9/L$	1.68 $\pm$ 0.15	3.03 $\pm$ 0.35 p=0.004	2.79 $\pm$ 0.41 p=0.009
Mono	%	5.35 $\pm$ 0.18	4.40 $\pm$ 0.44 p=0.024	2.67 $\pm$ 0.53 p=0.001; $p_1=0.007$
	$\times 10^9/L$	0.31 $\pm$ 0.03	0.37 $\pm$ 0.04	0.23 $\pm$ 0.03 p=0.031; $p_1=0.003$
ESR, mm/h		5.78 $\pm$ 0.12	12.80 $\pm$ 0.27 p<0.001	17.55 $\pm$ 0.39 $p, p_1<0.001$

Notes: AOM – acute otitis media; NEU – neutrophil; BASO – basophil; RNEU – rod-shaped neutrophil; SNEU – segmented neutrophil; LYM – lymphocyte; Mono – monocyte; EOS – eosinophil; WBC (leukocytes) – white blood cell; ESR – erythrocyte sedimentation rate; P – significance of differences with control group; p_1 – significance of differences with group of children with Catarrhal AOM

Leukocyte intoxication indices (LII) after Kalf-Kalif and R. A. Reys (Table 3), as well as the intoxication index and the nuclear index of the Endotoxiosis degree are high in both study groups and indicate an active inflammatory process, but at the same time these indexes are significantly higher in children with purulent course of AOM, than in catarrhal – 34.61% (p=0.048) and 22.92% (p=0.025) and 2 times (p<0.001) and 14.29% (p=0.05), respectively. The cellular reactivity index increased in both groups, more in purulent AOM, but not significantly. While cellular resistance prevailed in children with purulent AOM course over that with catarrhal – 27.96% (p<0.001). And the adaptive stress index of (ASI) after L. H. Harkavi (nonspecific reactivity index, resistance coefficient, Harkavi stress index), on the contrary, was higher in patients with serous AOM – 24.14% (p=0.049).

The reactive response of NEU, as a marker of nonspecific anti-infective protection, in patients with

purulent AOM is lower (due to a lower lymphocytic-granulocytic index and index of nonspecific reactivity) than in the catarrhal process – 22.51% (p=0.012) and 20.33% (p=0.006), against the background of a higher neutrophil-lymphocyte ratio – 23.20% (p=0.042), the shift index of leukocytes and neutrophils – 22.09% (p=0.012) and 14.29% (p=0.05), the ratio of neutrophils to monocytes and leukocytes to ESR – 35.98% (p=0.002) and 26.02% (p=0.01), respectively (Table 3).

The general immunological reactivity (Table 3) increases more strongly in children with purulent AOM (after immune reactivity indices) than with catarrhal AOM – 26.97% (p=0.009) and 29.96% (p=0.03), respectively. The lymphocytes to monocytes ratio reflects the activity of the humoral (effectors) and cellular (affectors) links of the immune system and prevails in children with purulent AOM – 36.46% (p=0.03) and indicates the dominance of the effector / humoral immune response activity.

Table 3

Cellular and general immunological reactivity and resistance, reactive response of neutrophils in children with acute otitis media depending on the ear discharge

N	Immuno-hematological indices, unit	Catarrhal AOM, n=50	Purulent AOM, n=45
Indices of inflammation, cellular reactivity and cellular resistance			
1	Leukocytes Intoxication Index (LII) after Kalf-Kalif	0.52±0.06	0.70±0.09 p=0.048
2	LII after R. A. Reys	1.44±0.14	1.77±0.09 p=0.025
3	Intoxication Index	0.71±0.07	1.42±0.10 p<0.001
4	Index of Endotoxycosis degree (Neutrophil shift index)	0.14±0.01	0.16±0.01 p=0.05
5	Cellular reactivity index	139.80±8.55	150.94±12.54
6	Cellular resistance index	18.31±0.45	23.43±0.70 p<0.001
7	Nonspecific resistance index (Harkavi)	0.72±0.07	0.58±0.05 p=0.049
Reactive response of Neutrophils			
1	Lymphocyte-to-granulocytic index	6.13±0.52	4.75±0.28 p=0.012
2	Neutrophil-to-lymphocyte ratio (NLR)	1.81±0.12	2.23±0.19 p=0.042
3	Leukocyte shift index	1.72±0.10	2.10±0.13 p=0.012
4	NEU shift index, yo	0.14±0.01	0.16±0.01 p=0.05
5	Neutrophil-to-monocyte ratio (NMR)	17.98±0.81	24.45±1.33 p=0.002
6	Leukocyte-ESR ratio	1.23±0.09	1.55±0.10 p=0.01
7	Nonspecific reactivity index	73.18±5.26	58.30±2.40 p=0.006
General immunological reactivity			
8	Immune reactivity index	11.31±0.58	14.76±1.16 p=0.009
9	Immune resistance index	6.23±0.21	5.38±0.29 p=0.021
10	Index of immunological reactivity growth	2.27±0.22	2.95±0.26 p=0.03
11	Allergy index	1.34±0.07	1.17±0.06 p=0.034
12	Lymphocyte index	0.64±0.06	0.45±0.06 p=0.048
13	Lymphocyte-to-monocyte ratio (LMR)	10.01±0.64	13.66±1.80 p=0.03
14	Lymphocytes-to-eosinophils ratio	25.60±2.45	17.28±1.71 p=0.004
15	Agranulocytes-to-ESR ratio	4.80±0.53	3.25±0.39 p=0.011

Notes: AOM – acute otitis media; LII-Leukocytes Intoxication Index; NEU – neutrophil; BASO – basophil; RNEU – rod-shaped neutrophil; SNEU – segmented neutrophil; LYM – lymphocyte; Mono – monocyte; EOS – eosinophil; WBC (leukocytes) – white blood cell; ESR – erythrocyte sedimentation rate; NLR – Neutrophil-to-lymphocyte ratio; NMR – Neutrophil-to-monocyte ratio; LMR – Lymphocyte-to-monocyte ratio; p – significance of differences with group of children with Catarrhal AOM

In children with catarrhal AOM, the activity of nonspecific anti-infective defence factors increases, which generally forms an increased resistance of the body (after elevating the immune resistance index – 15.80% (p=0.021)). At the same time, the allergisation index increased – 14.53% (p=0.034), as well as the lymphocytes-to-eosinophils ratio – 48.15% (p=0.004). That indirectly indicates the predominance of immediate-type hypersensitivity processes with the additional allergic mechanisms of the immune response formation and sensitization of children with catarrhal AOM. Lymphocytes-to-monocytes ratio decrease 26.72% (p=0.03), lymphocyte index increase 42.22% (p=0.048) as well as agranulocytes-to-ESR ratio 37.14% (p=0.011) indicates the predominance of macrophage system activity and cellular immune response stimulation.

CBC is a rapid, straightforward, and cost-effective test routinely performed in clinical practice. It delivers comprehensive data on blood components – white blood cells, neutrophils, lymphocytes, monocytes, and platelets – as well as calculated indices like the NLR, MLR and PLR. In recent years, these hematologic parameters have gained prominence as potential tools for diagnosing conditions, offering early warning signs, and stratifying patient risk in a variety of infections (e.g., sepsis, bacteremia, urinary tract infections) and noninfectious diseases (e.g., liver cirrhosis, coronary artery disease, solid tumors, chronic pancreatitis, nasal polyposis) [4, 23-26].

Numerous studies have shown that during severe infections or systemic inflammatory responses, the NLR rises in parallel with worsening clinical status and

outcomes [9, 10]. Moreover, NLR has been recognized as a fundamental marker in ENT practice, having applications in conditions such as otitis media, facial paralysis, idiopathic sudden sensorineural hearing loss, and head and neck malignancies [5-8, 28]. Few investigations to date have evaluated the NLR in individuals with otitis media [13], therefore, it needs further research.

Thus, the diagnostic value of hematologic markers for different infection-related diseases, like AOM, deserves more studies.

Conclusions

Immuno-haematological indices certify two conditional clinical and laboratory variants of the acute otitis media (AOM) course in the examined children. The first variant (purulent AOM) is characterized by moderate neutrophilosis (+II), pronounced hyporegenerative nuclear shift due to rod-shaped neutrophils, eosinophilic granulocytes and a significant increase in intoxication indices. Such blood changes indicate the predominance of the bacterial component (purulent process in the middle ear), pronounced severity of inflammation against the background of increased cellular and immune reactivity, corresponding activation of resistance and sensitization of the organism with a predominance of immediate-type hypersensitivity. In these children, a specific humoral immune response begins to form.

The second variant of the AOM course (catarrhal) is characterized by relative and absolute rod-shaped neutrophilosis (less pronounced than in the purulent AOM), higher lymphocytosis and monocytosis, with an increase

in nonspecific and immune resistance indices, which prove sensitization of the organism with the development of delayed-type hypersensitivity, against the background of moderately pronounced intoxication. The revealed pattern indicates the predominance of lymphocytic activation with the development of specific cellular defence.

Prospects for further research

To study the immunological mechanisms of nonspecific anti-infective protection in AOM children, taking into account the age.

The study was conducted as part of the comprehensive research project of the Family Medicine Department of BSMU, titled «Improvement of Diagnosis and Prediction of Hypertensive-Mediated Target Organ Damage and Symptom Control in Comorbid Pathology Considering Clinical-Metabolic and Molecular-Genetic Predictors» (State Registration Number 0124U002524, implementation period: 01.01.2024-31.12.2028).

List of references

1. Danishyar A, Ashurst JV. Acute Otitis Media [Internet]. Treasure Island (FL): StatPearls Publishing; 2023[cited 2025 Jun 20]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK470332/>
2. Jamal A, Alsabea A, Tarakme M, Safar A. Etiology, Diagnosis, Complications, and Management of Acute Otitis Media in Children. Cureus [Internet]. 2022[cited 2025 Jun 18];14(8): e28019. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC9471510/pdf/cureus-0014-00000028019.pdf> doi: 10.7759/cureus.28019
3. Tuzger N, Milani GP, Folino F, Aldè M, Agostoni C, Torretta S, et al. Referrals for Recurrent Acute Otitis Media With and Without Spontaneous Tympanic Membrane Perforation Through COVID-19: A Cross-Sectional Comparative Study. *Pediatr Infect Dis J*. 2023;42(9): e356-7. doi: 10.1097/inf.0000000000003970
4. Russell CD, Parajuli A, Gale HJ, Bulteel NS, Schuetz P, de Jager CPC, et al. The utility of peripheral blood leucocyte ratios as biomarkers in infectious diseases: a systematic review and meta-analysis. *J Infect*. 2019;78(5):339-48. doi: 10.1016/j.jinf.2019.02.006
5. Forget P, Khalifa C, Defour JP, Latinne D, Van Pel MC, De Kock M. What is the normal value of the neutrophil-to-lymphocyte ratio? *BMC Res Notes* [Internet]. 2017[cited 2025 Jun 18];10(1):12. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC5217256/pdf/13104_2016_Article_2335.pdf doi: 10.1186/s13104-016-2335-5
6. Boztepe OF, Demir M, Gün T, Bilal N, Ensari NA, Doğru H. A novel predictive marker for the viscosity of otitis media with effusion. *Int J Pediatr Otorhinolaryngol*. 2015;79(12):2355-8. doi: 10.1016/j.ijporl.2015.10.043
7. Wasano K, Kawasaki T, Yamamoto S, Tomisato S, Shinden S, Ishikawa T, et al. Pretreatment hematologic findings as novel predictive markers for facial palsy prognosis. *Otolaryngol Head Neck Surg*. 2016;155(4):581-7. doi: 10.1177/0194599816646552
8. Ha R, Lim BW, Kim DH, Park JW, Cho CH, Lee JH. Predictive values of neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), and other prognostic factors in pediatric idiopathic sudden sensorineural hearing loss. *Int J Pediatr Otorhinolaryngol*. 2019;120:134-9. doi: 10.1016/j.ijporl.2019.02.023
9. Curbelo J, Rajas O, Arnalich B, Galván-Román JM, Luquero-Bueno S, Ortega-Gómez M, et al. Neutrophil count percentage and neutrophil-lymphocyte ratio as prognostic markers in patients hospitalized for community-acquired pneumonia. *Arch* ISSN 1727-4338 <https://www.bsmu.edu.ua>
10. Bronconeumol (Engl Ed). 2019;55(9):472-7. doi: 10.1016/j.arbres.2019.02.005
11. de Jager CPC, van Wijk PTL, Mathoera RB, de Jongh-Leuvenink J, van der Poll T, Wever PC. Lymphocytopenia and neutrophil-lymphocyte count ratio predict bacteremia better than conventional infection markers in an emergency care unit. *Crit Care* [Internet]. 2010[cited 2025 Jun 20];14(5): R192. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC3219299/pdf/cc9309.pdf> doi: 10.1186/cc9309
12. Han Q, Wen X, Wang L, Han X, Shen Y, Cao J, et al. Role of hematological parameters in the diagnosis of influenza virus infection in patients with respiratory tract infection symptoms. *J Clin Lab Anal* [Internet]. 2020[cited 2025 Jun 20];34(5): e23191. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC7246361/pdf/JCLA-34-e23191.pdf> doi: 10.1002/jcla.23191
13. Pan YJ, Su KY, Shen CL, Wu YF. Correlation of Hematological Indices and Acute-Phase Reactants in Rheumatoid Arthritis Patients on Disease-Modifying Antirheumatic Drugs: A Retrospective Cohort Analysis. *J Clin Med* [Internet]. 2023[cited 2025 Jun 18];12(24):7611. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC10744259/pdf/jcm-12-07611.pdf> doi: 10.3390/jcm12247611
14. İşlek A, Balcı MK, Şimşek S. Correlation of the Neutrophil-to-Lymphocyte Ratio with the Middle Ear Risk Index in Patients with Chronic Otitis Media. *Indian J Otolaryngol Head Neck Surg*. 2022;74(Suppl 3):4603-7. doi: 10.1007/s12070-021-02898-x
15. Міністерство охорони здоров'я України. Гострий середній отит. Клінічна настанова, заснована на доказах. Київ: МОЗ України; 2021. 94 с.
16. Міністерство охорони здоров'я України. Уніфікований клінічний протокол первинної, вторинної (спеціалізованої) та третинної (високоспеціалізованої) медичної допомоги. Гострий середній отит. Затверджено Наказом Міністерства охорони здоров'я України від 09 квітня 2021 року № 688. Київ: МОЗ України; 2021. 34 с.
17. Marchisio P, Galli L, Bortone B, Ciarcià M, Motisi MA, Novelli A, et al. Updated Guidelines for the Management of Acute Otitis Media in Children by the Italian Society of Pediatrics: Treatment. *Pediatr Infect Dis J*. 2019;38(12S Suppl): S10-S21. doi: 10.1097/inf.0000000000002452
18. Соколенко МО, Сидорчук ЛП, Соколенко ЛС, Соколенко АА. Загальна імунологічна реактивність організму хворих на COVID-19 та її зв'язок з поліморфізмом генів, тяжкістю клінічного перебігу хвороби та поєднанням із супутньою патологією. Медичні перспективи. 2024;29(3):108-17. doi: 10.26641/2307-0404.2024.3.313570
19. Sydoruk LP, Syrota BS, Sydoruk AR, Gerush OV, Muzyka NY, Sheremet MI, et al. Clinical markers of immune disorders in the pathogenesis of Escherichia coli enteritis. *Archives of the Balkan Medical Union*. 2019;54(1):89-96. doi: 10.31688/ABMU.2019.54.1.12
20. Івашук СІ, Сидорчук ЛП, Коровенкова ОМ. Рівень клітинної реактивності організму і ступінь тяжкості інтоксикації у хворих на гострий панкреатит і з загостренням хронічного панкреатиту залежно від поліморфізму генів CFTR, PRSS1, IL-4 і TNF-α. Вісник Клубу Панкреатологів. 2017;35(1):21-7. doi: 10.33149/vkp.2017.01
21. Kara A, Guven M, Yilmaz MS, Demir D, Elden H. Are neutrophil, platelet and eosinophil-to-lymphocyte ratio and red blood cell distribution width can be used for nasal polyposis? *Eur Arch Otorhinolaryngol*. 2018;275(2):409-13. doi: 10.1007/s00405-017-4821-3
22. Peng J, Qi D, Yuan G, Deng X, Mei Y, Feng L, Wang D, et al. Diagnostic value of peripheral hematologic markers for coronavirus disease 2019 (COVID-19): A multicenter, cross-sectional study. *J Clin Lab Anal* [Internet]. 2020[cited 2025 Jun 18];34(10): e23475. Available from: <https://pmc.ncbi.nlm.nih.gov/> Клінічна та експериментальна патологія. 2025. Т.24, № 2 (92)

- articles/PMC7404368/pdf/JCLA-34-e23475.pdf doi: 10.1002/jcla.23475
22. Milovanovic Alempijevic T, Stojkovic Lalosevic M, Dumic I, Jovic N, Pavlovic Markovic A, Dragasevic S, et al. Diagnostic accuracy of platelet count and platelet indices in noninvasive assessment of fibrosis in nonalcoholic fatty liver disease patients. *Can J Gastroenterol Hepatol* [Internet]. 2017[cited 2025 Jun 20];2017: e6070135. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC5804372/pdf/CJGH2017-6070135.pdf> doi: 10.1155/2017/6070135
 23. Serrano CV Jr, de Mattos FR, Pitta FG, Nomura CH, de Lemos J, Ramires JAF, et al. Association between neutrophil-lymphocyte and platelet-lymphocyte ratios and coronary artery calcification score among asymptomatic patients: data from a cross-sectional study. *Mediators Inflamm* [Internet]. 2019 cited 2025 Jun 18];2019: e6513847. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC6458900/pdf/MI2019-6513847.pdf> doi: 10.1155/2019/6513847
 24. Bilen MA, Martini DJ, Liu Y, Lewis C, Collins HH, Shabto JM, et al. The prognostic and predictive impact of inflammatory biomarkers in patients who have advanced-stage cancer treated with immunotherapy. *Cancer*. 2019;125(1):127-34. doi: 10.1002/cncr.31778
 25. Ivashchuk SI, Sydorchuk LP. Level of reactive response of peripheral blood neutrophil granulocytes of patients with acute pancreatitis depending on genes polymorphism of CFTR (delF508C), PRSS1 (R122H), IL-4 (C-590T) and TNF- α (G-308A). *The Pharma Innovation Journal*. 2016;5(9):96-100.
 26. Yenigün A. Assessment of patients with nasal polyposis by the neutrophil-to-lymphocyte ratio and eosinophil-to-lymphocyte ratio. *Kulak Burun Bogaz Ihtis Derg*. 2015;25(4):193-9. doi: 10.5606/kbbihtisas.2015.10734
 27. Szilasi Z, Jósá V, Zrubka Z, Mezei T, Vass T, Merkel K, et al. Neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios as prognostic markers of survival in patients with head and neck tumours-results of a retrospective multicentric study. *Int J Environ Res Public Health* [Internet] [cited 2025 Jun 20]. 2020;17(5):1742. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC7084240/pdf/ijerph-17-01742.pdf> doi: 10.3390/ijerph17051742
- ### References
1. Danishyar A, Ashurst JV. *Acute Otitis Media* [Internet]. Treasure Island (FL): StatPearls Publishing; 2023[cited 2025 Jun 20]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK470332/>
 2. Jamal A, Alsabea A, Tarakme M, Safar A. Etiology, Diagnosis, Complications, and Management of Acute Otitis Media in Children. *Cureus* [Internet]. 2022[cited 2025 Jun 18];14(8): e28019. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC9471510/pdf/cureus-0014-00000028019.pdf> doi: 10.7759/cureus.28019
 3. Tuzger N, Milani GP, Folino F, Aldè M, Agostoni C, Torretta S, et al. Referrals for Recurrent Acute Otitis Media With and Without Spontaneous Tympanic Membrane Perforation Through COVID-19: A Cross-Sectional Comparative Study. *Pediatr Infect Dis J*. 2023;42(9): e356-7. doi: 10.1097/inf.0000000000003970
 4. Russell CD, Parajuli A, Gale HJ, Bulteel NS, Schuetz P, de Jager CPC, et al. The utility of peripheral blood leucocyte ratios as biomarkers in infectious diseases: a systematic review and meta-analysis. *J Infect*. 2019;78(5):339-48. doi: 10.1016/j.jinf.2019.02.006
 5. Forget P, Khalifa C, Defour JP, Latinne D, Van Pel MC, De Kock M. What is the normal value of the neutrophil-to-lymphocyte ratio? *BMC Res Notes* [Internet]. 2017[cited 2025 Jun 18];10(1):12. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC5217256/pdf/13104_2016_Article_2335.pdf doi: 10.1186/s13104-016-2335-5
 6. Boztepe OF, Demir M, Gün T, Bilal N, Ensari NA, Doğru H. A novel predictive marker for the viscosity of otitis media with effusion. *Int J Pediatr Otorhinolaryngol*. 2015;79(12):2355-8. doi: 10.1016/j.ijporl.2015.10.043
 7. Wasano K, Kawasaki T, Yamamoto S, Tomisato S, Shinden S, Ishikawa T, et al. Pretreatment hematologic findings as novel predictive markers for facial palsy prognosis. *Otolaryngol Head Neck Surg*. 2016;155(4):581-7. doi: 10.1177/0194599816646552
 8. Ha R, Lim BW, Kim DH, Park JW, Cho CH, Lee JH. Predictive values of neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), and other prognostic factors in pediatric idiopathic sudden sensorineural hearing loss. *Int J Pediatr Otorhinolaryngol*. 2019;120:134-9. doi: 10.1016/j.ijporl.2019.02.023
 9. Curbelo J, Rajas O, Arnalich B, Galván-Román JM, Luquero-Bueno S, Ortega-Gómez M, et al. Neutrophil count percentage and neutrophil-lymphocyte ratio as prognostic markers in patients hospitalized for community-acquired pneumonia. *Arch Bronconeumol (Engl Ed)*. 2019;55(9):472-7. doi: 10.1016/j.arbres.2019.02.005
 10. de Jager CPC, van Wijk PTL, Mathoera RB, de Jongh-Leuvenink J, van der Poll T, Wever PC. Lymphocytopenia and neutrophil-lymphocyte count ratio predict bacteremia better than conventional infection markers in an emergency care unit. *Crit Care* [Internet]. 2010[cited 2025 Jun 20];14(5): R192. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC3219299/pdf/cc9309.pdf> doi: 10.1186/cc9309
 11. Han Q, Wen X, Wang L, Han X, Shen Y, Cao J, et al. Role of hematological parameters in the diagnosis of influenza virus infection in patients with respiratory tract infection symptoms. *J Clin Lab Anal* [Internet]. 2020[cited 2025 Jun 20];34(5): e23191. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC7246361/pdf/JCLA-34-e23191.pdf> doi: 10.1002/jcla.23191
 12. Pan YJ, Su KY, Shen CL, Wu YF. Correlation of Hematological Indices and Acute-Phase Reactants in Rheumatoid Arthritis Patients on Disease-Modifying Antirheumatic Drugs: A Retrospective Cohort Analysis. *J Clin Med* [Internet]. 2023[cited 2025 Jun 18];12(24):7611. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC10744259/pdf/jcm-12-07611.pdf> doi: 10.3390/jcm12247611
 13. İşlek A, Balcı MK, Şimşek S. Correlation of the Neutrophil-to-Lymphocyte Ratio with the Middle Ear Risk Index in Patients with Chronic Otitis Media. *Indian J Otolaryngol Head Neck Surg*. 2022;74(Suppl 3):4603-7. doi: 10.1007/s12070-021-02898-x
 14. Ministerstvo okhorony zdorov'ia Ukrainy. Hostryi serednii otyt. Klinichna nastanova, zasnovana na dokazakh [Acute average otitis. An evidence-based clinical guideline]. Kyiv: MOZ Ukrainy; 2021. 94 p. (in Ukrainian)
 15. Ministerstvo okhorony zdorov'ia Ukrainy. Unifikovanyi klinichniy protokol pervynnoi, vtorynnoi (spetsializovanoi) ta tretynnoi (vysokospetsializovanoi) medychnoi dopomohy. Hostryi serednii otyt. Zatverdzheno Nakazom Ministerstva okhorony zdorov'ia Ukrainy vid 09 kvitnia 2021 roku № 688 [Unified clinical protocol for primary, secondary (specialized) and tertiary (highly specialized) medical care. Acute otitis media. Approved by the Order of the Ministry of Health of Ukraine dated April 9, 2021 № 688]. Kyiv: MOZ Ukrainy Kyiv: MOZ Ukrainy; 2021. 34 p. (in Ukrainian)
 16. Marchisio P, Galli L, Bortone B, Ciarcià M, Motisi MA, Novelli A, et al. Updated Guidelines for the Management of Acute Otitis Media in Children by the Italian Society of Pediatrics: Treatment. *Pediatr Infect Dis J*. 2019;38(12S Suppl): S10-S21. doi: 10.1097/inf.0000000000002452
 17. Sokolenko MO, Sydorchuk LP, Sokolenko LS, Sokolenko AA. Zahal'na imunolohichna reaktyvnist' orhanizmu khvorykh na COVID-19 ta yii zv'iazok z polimorfizmom heniv, tiazhkistiu klinichnoho perebihu khvoroby ta poiednanniam iz suputn'oiu patolohieiu [General immunologic reactivity of patients with COVID-19 and its relation to gene polymorphism, severity of

- clinical course of the disease and combination with comorbidities]. *Medicini perspektivi*. 2024;29(3):108-17. doi: 10.26641/2307-0404.2024.3.313570 (in Ukrainian)
18. Sydorhuk LP, Syrota BS, Sydorhuk AR, Gerush OV, Muzyka NY, Sheremet MI, et al. Clinical markers of immune disorders in the pathogenesis of *Escherichia coli* enteritis. *Archives of the Balkan Medical Union*. 2019;54(1):89-96. doi: 10.31688/ABMU.2019.54.1.12
 19. Ivashchuk SI, Sydorhuk LP, Korovenkova OM. Riven' klitynnoi reaktivnosti orhanizmu i stupin' tiazhkosti intoksykatsii u khvorykh na hostryi pankreatyt i z zahostrenniam khronichnoho pankreatytu zalezno vid polimorfizmu heniv CFTR, PRSS1, IL-4 i TNF- α [Level of cellular reactivity of organism and extent of intoxication severity in patients with acute pancreatitis and exacerbation of chronic pancreatitis depending on genes polymorphism CFTR, PRSS1, IL-4 and TNF- α]. *Herald of Pancreatic Club*. 2017;35(1):21-7. doi: 10.33149/vkp.2017.01 (in Ukrainian)
 20. Kara A, Guven M, Yilmaz MS, Demir D, Elden H. Are neutrophil, platelet and eosinophil-to-lymphocyte ratio and red blood cell distribution width can be used for nasal polyposis? *Eur Arch Otorhinolaryngol*. 2018;275(2):409-13. doi: 10.1007/s00405-017-4821-3
 21. Peng J, Qi D, Yuan G, Deng X, Mei Y, Feng L, Wang D, et al. Diagnostic value of peripheral hematologic markers for coronavirus disease 2019 (COVID-19): A multicenter, cross-sectional study. *J Clin Lab Anal* [Internet]. 2020[cited 2025 Jun 18];34(10): e23475. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC7404368/pdf/JCLA-34-e23475.pdf> doi: 10.1002/jcla.23475
 22. Milovanovic Alempijevic T, Stojkovic Lalošević M, Dumic I, Jocić N, Pavlovic Markovic A, Dragasevic S, et al. Diagnostic accuracy of platelet count and platelet indices in noninvasive assessment of fibrosis in nonalcoholic fatty liver disease patients. *Can J Gastroenterol Hepatol* [Internet]. 2017[cited 2025 Jun 20];2017: e6070135. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC5804372/pdf/CJGH2017-6070135.pdf> doi: 10.1155/2017/6070135
 23. Serrano CV Jr, de Mattos FR, Pitta FG, Nomura CH, de Lemos J, Ramires JAF, et al. Association between neutrophil-lymphocyte and platelet-lymphocyte ratios and coronary artery calcification score among asymptomatic patients: data from a cross-sectional study. *Mediators Inflamm* [Internet]. 2019 cited 2025 Jun 18];2019: e6513847. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC6458900/pdf/MI2019-6513847.pdf> doi: 10.1155/2019/6513847
 24. Bilen MA, Martini DJ, Liu Y, Lewis C, Collins HH, Shabto JM, et al. The prognostic and predictive impact of inflammatory biomarkers in patients who have advanced-stage cancer treated with immunotherapy. *Cancer*. 2019;125(1):127-34. doi: 10.1002/cncr.31778
 25. Ivashchuk SI, Sydorhuk LP. Level of reactive response of peripheral blood neutrophil granulocytes of patients with acute pancreatitis depending on genes polymorphism of CFTR (delF508C), PRSS1 (R122H), IL-4 (C-590T) and TNF- α (G-308A). *The Pharma Innovation Journal*. 2016;5(9):96-100.
 26. Yenigün A. Assessment of patients with nasal polyposis by the neutrophil-to-lymphocyte ratio and eosinophil-to-lymphocyte ratio. *Kulak Burun Bogaz Ihtis Derg*. 2015;25(4):193-9. doi: 10.5606/kbbihtisas.2015.10734
 27. Szilasi Z, Jóna V, Zrubka Z, Mezei T, Vass T, Merkel K, et al. Neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios as prognostic markers of survival in patients with head and neck tumours-results of a retrospective multicentric study. *Int J Environ Res Public Health* [Internet] [cited 2025 Jun 20]. 2020;17(5):1742. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC7084240/pdf/ijerph-17-01742.pdf> doi: 10.3390/ijerph17051742

Information about the authors:

Sakovets O. P. – Medical ENT Doctor, Postgraduate Student, Family Medicine Department, Bukovinian State Medical University, Chernivtsi, Ukraine.

E-mail: oleksii.sakovets@gmail.com

ORCID ID: <https://orcid.org/0009-0004-7215-3820>

Sydorchuk L. P. – Doctor of Medicine, Full Professor, Head of the Family Medicine Department, Bukovinian State Medical University, Chernivtsi, Ukraine.

E-mail: lsydorchuk@bsmu.edu.ua

ORCID ID: <https://orcid.org/0000-0001-9279-9531>

Kazantseva T. V. – PhD, Associate Professor, Bukovinian State Medical University, Family Medicine Department, Chernivtsi, Ukraine.

E-mail: tanya-kazantseva@bsmu.edu.ua

ORCID ID: <https://orcid.org/0000-0002-2540-2976>

Petrynych O. A. – PhD, Associate Professor, Department of Family Medicine, Bukovinian State Medical University, Chernivtsi, Ukraine.

E-mail: petrynych.oksana@bsmu.edu.ua

ORCID ID: <https://orcid.org/0000-0001-6858-4469>

Semianiv M. M. – PhD, Associate Professor, Department of Family Medicine, Bukovinian State Medical University, Chernivtsi, Ukraine.

E-mail: m.semianiv@bsmu.edu.ua

ORCID ID: <https://orcid.org/0000-0003-4169-7142>

Repchuk Yu. V. – PhD, Assistant, Department of Family Medicine, Bukovinian State Medical University, Chernivtsi, Ukraine.

E-mail: repchuk@bsmu.edu.ua

ORCID ID: <https://orcid.org/0000-0002-5156-8814>

Voroniuk K. O. – PhD, Assistant, Department of Family Medicine, Bukovinian State Medical University, Chernivtsi, Ukraine.

E-mail: voroniuk.kseniiia@bsmu.edu.ua

ORCID ID: <https://orcid.org/0000-0002-7233-5112>

Відомості про авторів:

Саковець О. П. – ЛОР лікар, аспірант кафедри сімейної медицини Буковинського державного медичного університету, м. Чернівці, Україна.

E-mail: oleksii.sakovets@gmail.com

ORCID ID: <https://orcid.org/0009-0004-7215-3820>

Сидорчук Л. П. – доктор медичних наук, професор, завідувач кафедри сімейної медицини Буковинського державного медичного університету м. Чернівці, Україна.

E-mail: lsydorchuk@bsmu.edu.ua

ORCID ID: <https://orcid.org/0000-0001-9279-9531>

Казанцева Т. В. – кандидат медичних наук, доцент кафедри сімейної медицини Буковинського державного медичного університету м. Чернівці, Україна.

E-mail: tanya-kazantseva@bsmu.edu.ua

ORCID ID: <https://orcid.org/0000-0002-2540-2976>

Петринич О. А. – кандидат медичних наук, доцент кафедри сімейної медицини Буковинського державного медичного університету м. Чернівці, Україна.

E-mail: petrynych.oksana@bsmu.edu.ua

ORCID ID: <https://orcid.org/0000-0001-6858-4469>

Сем'янів М. М. – доктор філософії, доцент кафедри сімейної медицини Буковинського державного медичного університету, м. Чернівці, Україна.

E-mail: m.semianiv@bsmu.edu.ua

ORCID ID: <https://orcid.org/0000-0003-4169-7142>

Репчук Ю. В. – доктор філософії, асистент кафедри сімейної медицини Буковинського державного медичного університету м. Чернівці, Україна.

E-mail: repchuk@bsmu.edu.ua

ORCID ID: <https://orcid.org/0000-0002-5156-8814>

Воронюк К. О. – доктор філософії, асистент кафедри сімейної медицини Буковинського державного медичного університету м. Чернівці, Україна.

E-mail: voroniuk.kseniia@bsmu.edu.ua

ORCID ID: <https://orcid.org/0000-0002-7233-5112>

Стаття надійшла до редакції 16.05.2025

*© О. П. Саковець, Л. П. Сидорчук, Т. В. Казанцева,
О. А. Петринич, М. М. Сем'янів, Ю. В. Репчук,
К. О. Воронюк*

