УДК 616.284-002-053.2:612.017.1:575.113.2 Original research

PATTERN OF IMMUNOLOGICAL PROTECTION IN CHILDREN WITH ACUTE OTITIS MEDIA TAKING INTO ACCOUNT THE HSP70-2 GENE (rs1061581) ALLELIC STATE

Sakovets O.P., Sydorchuk L.P.

Bukovinian State Medical University, Chernivtsi, Ukraine

Key words: *acute otitis, inflammation, immunity, immune defense, immunological resistance, intoxication, children, HSP70-2 gene polymorphism.*

Bukovinian Medical Herald. 2026. V. 30, № 1 (117). P. 3-8.

DOI: *10.24061/2413-0737.30.1.117.2026.1*

E-mail: *oleksii.sakovets@gmail.com lsydorchuk@ukr.net*

Objective *– to assess immune-haematological indices as integrative markers of cellular immune reactivity and nonspecific anti-infective defence in children with acute otitis media (AOM), taking into account the heat-shock protein gene polymorphism 70-2 (HSP70-2, rs1061581).*

Material and methods. *This prospective cross-sectional "case-control" study included 95 children aged 7-18 years with diagnosed AOM (34.74% girls, 65.26% boys). The study adhered to Good Clinical Practice, Good Laboratory Practice, and international ethical standards. The control group comprised 50 healthy children (40% girls, 60% boys). Cellular and general immunological reactivity, resistance, and neutrophil responses were evaluated using complete blood counts and calculated integral indices. The HSP70-2 (rs1061581) gene polymorphism was studied by polymerase chain reaction method.*

Results. *In children with AOM, the immunological defense pattern varies according to the allelic state of the HSP70-2 gene (rs1061581): GG-genotype carriers demonstrate higher levels of cellular and immunological reactivity and resistance, as well as more efficient activation of nonspecific cellular effector immunity (particularly lymphocytic responses), compared with mutant A-allele carriers. This enhanced cellular response is associated with a substantial reduction in the intoxication index by 32.82% (p=0.005), indicating more effective physiological apoptosis, compensatory cellular protection, the humoral immune response development, and increased immunological sensitization. Most indices of neutrophil reactive response did not show genotype-dependent HSP70-2 (rs1061581) differences.*

Conclusion. *Immune protection in children with AOM and the mutant A-allele of HSP70-2 gene is predominantly mediated by monocyte-driven effector pathways, accompanied by a more pronounced inflammatory response, and lower cellular and overall immunological reactivity and resistance. These features contribute to a higher level of exogenous intoxication.*

ПАТЕРН ІМУНОЛОГІЧНОГО ЗАХИСТУ У ДІТЕЙ ІЗ ГОСТРИМ СЕРЕДНІМ ОТИТОМ З УРАХУВАННЯМ АЛЕЛЬНОГО СТАНУ ГЕНА HSP70-2 (rs1061581)

Саковець О.П., Сидорчук Л.П.

Ключові слова: *гострий отит, запалення, імунітет, імунний захист, імунологічна резистентність, інтоксикація, діти, поліморфізм гена HSP70-2.*

Буковинський медичний вісник. 2026. Т. 30, № 1 (117). С. 3-8.

Мета роботи *– оцінити імуногематологічні показники як інтегративні маркери клітинної імунної реактивності та неспецифічного протиінфекційного захисту у дітей із гострим середнім отитом (ГСО), залежно від поліморфізму гена білка теплового шоку 70-2 (HSP70-2, rs1061581).*

Матеріал і методи*. Проспективним крос-секційним дослідженням "контроль-випадок" охоплено 95 дітей із діагнозом ГСО віком від 7 до 18 років: 34,74% (n=33) дівчаток та 65,26% (n=62) хлопчиків. Дослідження проводили згідно з принципами належної клінічної та лабораторної практик і встановлених етичних стандартів для біомедичних досліджень за участю людей. Контрольну групу склали 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. Поліморфізм гена HSP70-2 (rs1061581) досліджували методом полімеразної ланцюгової реакції.*

Результати*. У дітей, хворих на ГСО, формується імунологічний патерн захисту залежно від алельного стану гена HSP70-2 (rs1061581): у носіїв GG-генотипу розвивається вища клітинна та імунологічна реактивність*

та резистентність, а також краща активність неспецифічної клітинної афекторної (лімфоцитарної) імунної відповіді, ніж у власників мутаційного А-алеля, що зумовлює вагоме зниження показника інтоксикації на 32,82% (p=0,005) і засвідчує кращий природний апоптоз та компенсаторний клітинний захист, формування гуморальної відповіді та додаткову сенсибілізацію організму. Реактивна відповідь нейтрофілів за більшістю показників не має залежності від поліморфних варіантів гена HSP70-2 (rs1061581).

***Висновок**. У власників мутаційного А-алеля гена HSP70-2 переважає активність ефекторної (моноцитарної) клітинної ланки імунологічного захисту із більш вираженою запальною реакцією, зниженою клітинною та загальною імунною реактивністю і резистентністю, що зумовлює високий показник екзоінтоксикації.*

Introduction. Acute otitis media (AOM) is one of the most common infectious diseases in children worldwide, with millions of new cases diagnosed annually [1, 2]. Its high prevalence makes AOM a major public health issue, particularly due to its contribution to antimicrobial resistance and frequent recurrences in early childhood. AOM is characterized by inflammation of the mucosal lining of the middle ear, including the tympanic cavity and tympanic membrane [3]. Although the key immunological pathways involved in AOM have been broadly described, the role of non-specific immune mechanisms, especially innate and inflammatory responses, remains insufficiently explored and often overlooked in clinical practice and research [4]. A deeper understanding of these pathways may improve early diagnostic approaches and therapeutic management.

Among potential early biomarkers, hematologic parameters such as absolute counts of neutrophils, lymphocytes, monocytes, and platelets, as well as derived indices including the neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), and platelet-to-lymphocyte ratio (PLR), have been proposed as useful tools for infection screening, early detection of disease progression, and risk stratification [5]. The NLR is a basic inflammatory marker obtained from a complete blood count (CBC), typically ranging between 0.78 and 3.58 [6]. Elevated NLR values have been associated with several otolaryngologic disorders, such as otitis media with effusion [7], idiopathic sudden sensorineural hearing loss [8], and have shown prognostic value in viral facial palsy [9]. NLR also serves as a helpful indicator in diagnosing and assessing the severity of community-acquired pneumonia and bacteraemia [10, 11]. Similarly, MLR and PLR have been recognized as surrogate biomarkers for inflammatory activity in rheumatoid arthritis [12] and for influenza infection in respiratory illness [13]. However, data on the diagnostic relevance of these hematologic indices in paediatric otitis media, as well as taking into account genetic markers, remain limited [4, 13-15].

The present study therefore aimed to evaluate the absolute and relative counts of key immunocompetent cells (neutrophils, lymphocytes, monocytes, platelets, etc.) and to calculate immuno-hematologic indices such as NLR, MLR, and PLR in children with AOM, depending on heat-shock protein 70-2 subfamily type gene's polymorphism (HSP70-2, rs1061581) in order to determine their diagnostic significance and impact in disease severity.

Objective of the study: to assess immune-hematological indices as integrative markers of cellular immune reactivity and nonspecific anti-infective defense in children with acute otitis media (AOM), taking into account the allelic variants of the HSP70-2 gene (rs1061581).

Material and methods. Clinical data were collected at the Municipal Non-profit Enterprise "Multidisciplinary Hospital of Intensive Care" Kitsman (Chernivtsi region, UA), during 2023-2024. This prospective cross-sectional case-control study initially included 100 paediatric patients with clinically confirmed AOM; after screening, 95 children aged 7-18 years met the eligibility criteria. The control group included 50 practically healthy children. Written informed consent was obtained from parents or legal guardians prior to enrolment. All participants underwent a standardized evaluation protocol comprising medical history, physical examination, laboratory investigations, and instrumental diagnostics.

The diagnosis and severity grading of AOM followed the National Unified Clinical Protocol for Acute Otitis Media endorsed by the Ministry of Health of Ukraine (Order No. 688, April 9, 2021), relevant national guidelines (2021) [16, 17], and international recommendations [2, 18]. When clinically indicated, supplementary radiographic imaging, including mastoid, paranasal sinus, and chest X-rays was performed in two standard projections.

The study was conducted in accordance with the ethical principles of the Council of Europe Convention on Human Rights and Biomedicine, Good Clinical Practice and Good Laboratory Practice (GCP, 1996), and the Declaration of Helsinki. Ethical approval was obtained from the Biomedical Ethics Committee of Bukovinian State Medical University (BSMU).

Participants were stratified into two age cohorts: 7-11 years (n=81) and 12-18 years (n=14). Based on disease severity, 43 children (45.26%) exhibited severe AOM, whereas 52 (54.74%) presented with non-severe forms. The study group comprised 33 girls (34.74%) and 62 boys (65.26%). The control group consisted of 50 clinically healthy children (20 girls and 30 boys) matched by age and sex, with no history of acute or chronic inflammatory conditions at the time of enrolment or during the preceding six months. No significant age differences were observed between the study and control groups.

Cellular immune reactivity, neutrophil responsiveness,

and overall immunological status in children with AOM were assessed using complete blood count (CBC) parameters: absolute and relative counts of major immunocompetent cell (ICC) populations with subsequent calculation of integral immuno-haematological indices, following our previously published methodology [4, 19-21]. CBC analyses were performed using the CELL-DYN 3700 SL haematology analyzer (Abbott Laboratories, USA) at laboratory in the BSMU and "Multidisciplinary Hospital of Intensive Care" Kitsman city (Chernivtsi region, UA), following the common internal quality control program.

Genotyping of the HSP70-2 gene was conducted using qualitative Polymerase Chain Reaction (qPCR). Blood samples of approximately 5 mL of residual peripheral blood were collected from each participant for genotyping and immunological analysis. Genomic DNA was extracted from EDTA-anticoagulated whole blood using a commercial kit. HSP70-2 (rs1061581) A1267G polymorphisms was genotyped by using the DreamTaq Green PCR MasterMix Kit (Thermo Fisher Scientific, USA) with specific primers ("Metabion", DE). The PCR amplicons' products were separated by horizontal electrophoresis [14].

Statistical analyses were performed using Statistica 7.0 (StatSoft Inc., USA) and Excel® 2016™. Between-group differences for independent samples were assessed using the unpaired Student's t-test when data demonstrated near-normal distribution (verified by the Kolmogorov-Smirnov and Shapiro-Wilk tests), or the Wilcoxon-Mann-Whitney U-test for non-normally distributed data. A p-value <0.05 was considered statistically significant.

Results and Discussion

Genotypes distribution of the HSP70-2 gene polymorphism (rs1061581; *A1267G*) for the patients with AOM were as follows: *AA*-, *AG*-, *GG*-genotypes – 8 (8.42%), 52 (54.74%) and 35 (36.84%) respectively; genotypes' distribution in control group were - 1 (2.0%) person with *AA*-genotype (χ^2<1.0; p=0.164), 22 (44.0%) children with *AG*-genotype (χ^2=1.51; p=0.219) and 27 (54.0%) subjects with *GG*-genotype (χ^2=3.94; p=0.047).

The absolute and relative counts of major ICC in children with AOM, stratified by HSP70-2 (rs1061581) polymorphic variants, are presented in Table 1.

Leukocytosis was observed due to absolute granulocytosis (neutrophilia), driven by both an absolute and relative increase in immature band (rod-shaped) neutrophils, accompanied by a reduction of mature segmented neutrophils. These findings indicate an active inflammatory response predominantly of bacterial origin, regardless of HSP70-2 genotypes. Infectious inflammation of the middle ear was associated with a 2.64- and 2.08-fold increase in eosinophil counts (p<0.001), with significantly higher levels in *GG*-genotype carriers compared with *A*-allele patients – by 26.73% (p=0.033). An elevation in agranulocyte levels was also detected, primarily due to an increase in both relative and absolute lymphocyte counts – by 15.20-16.35% (p≤0.023) and 67.86–74.40% (p≤0.004), respectively, alongside a reduction in the relative proportion of monocytes (macrophages) by 33.46% (p<0.001) and 23.18% (p=0.002) respectively, with more pronounced changes in *GG*-genotype carriers (p>0.05).

Table 1

Laboratory findings based on complete blood cell count in children with acute otitis media depending on the HSP70-2 gene polymorphism (rs1061581)

Laboratory findings		Control, n=50	GG-genotype	AG-, AA-genotypes
Erythrocytes, $\times10^{12}$/L		4.25±0.15	4.29±0.18	4.14±0.16
Hemoglobin, g/L		128.94±5.42	125.95±4.60	123.02±3.31
WBC (leukocytes), $\times10^9$/L		5.80±0.14	8.43±0.39 p<0.001	8.85±0.55 p<0.001
Granulocytes	%	66.35±0.53	63.44±3.63	63.36±2.40
	$\times10^9$/L	3.85±0.17	5.35±0.40 p=0.004	5.61±0.31 p=0.001
NEU	%	64.71±0.88	59.22±2.18	60.03±2.80
	$\times10^9$/L	3.75±0.26	4.99±0.34 p=0.002	5.31±0.26 p<0.001
RNEU	%	2.50±0.18	8.67±0.91 p<0.001	7.55±0.83 p<0.001
	$\times10^9$/L	0.14±0.06	0.73±0.11 p<0.001	0.67±0.15 p=0.004
SNEU	%	62.21±1.05	50.56±2.02 p=0.001	52.44±3.14 p=0.002
	$\times10^9$/L	3.62±0.34	4.26±0.28 p=0.051	4.64±0.47 p=0.041
EOS, %		1.60±0.10	4.22±0.28 p<0.001	3.33±0.39 p<0.001; p_1=0.033
Agranulocytes	%	34.09±0.21	36.96±1.36 p=0.02	37.0±2.15 p=0.046
	$\times10^9$/L	2.0±0.16	3.12±0.24 p=0.003	3.27±0.19 p<0.001
LYM	%	28.74±0.20	33.44±2.31 p=0.023	33.11±1.94 p=0.014
	$\times10^9$/L	1.68±0.15	2.82±0.21 p<0.001	2.93±0.33 p<0.001
Mono	%	5.35±0.18	3.56±0.19 p<0.001	4.11±0.24 p=0.002
	$\times10^9$/L	0.31±0.03	0.30±0.03	0.36±0.05
ESR, mm/h		5.78±0.12	14.89±0.62 p<0.001	17.55±2.34 p<0.001

Note. WBC (leukocytes) – white blood cell; NEU - neutrophil; RNEU – rod-shaped neutrophil; SNEU – segmented neutrophil; EOS – eosinophil; LYM – lymphocyte; Mono – monocyte; ESR – erythrocyte sedimentation rate; P – significance of differences with control group; p_1 – significance of differences with group of children with GG-genotype.

Our findings suggest a more severe disease course and a higher degree of nonspecific anti-infective immune activation in children with *GG*-genotype, potentially leading to greater depletion of monocyte-macrophage cellular defence mechanisms compared with *A*-allele carriers of gene HSP70-2 (rs1061581).

The immuno-hematological indices reflecting the activity of nonspecific anti-infective defenses in children with AOM, stratified by HSP70-2 (rs1061581) genotypes, are presented in Table 2.

Table 2

Hematological indices of immunological resistance and reactivity in children with acute otitis media depending on the HSP70-2 gene (rs1061581)

N	Immuno-hematological indices, unit	GG-genotype	AG-, AA- genotypes
Indices of inflammation, cellular reactivity and cellular resistance			
1	Leukocytes Intoxication Index (LII) after Kalf-Kalif	0.51±0.09	0.63±0.07
2	LII after R.A. Reys	1.51±0.12	1.60±0.10
3	Intoxication Index	0.88±0.08	1.31±0.14 p=0.005
4	Index of Endotoxicosis degree (Neutrophil shift index)	0.18±0.04	0.16±0.03
5	Cellular reactivity index	183.16±27.85	157.95±33.75
6	Cellular resistance index	24.39±0.84	22.57±2.25
7	Nonspecific resistance index (Harkavi)	0.69±0.07	0.67±0.10
Reactive response of Neutrophils			
1	Lymphocyte-to-granulocytic index	5.47±0.25	5.50±0.40
2	Neutrophil-to-lymphocyte ratio (NLR)	1.92±0.14	2.0±0.16
3	Leukocyte shift index	1.95±0.13	1.88±0.09
4	NEU shift index, yo	0.18±0.02	0.16±0.03
5	Neutrophil-to-monocyte ratio (NMR)	24.43±4.67	21.40±1.01
6	Leukocyte-ESR ratio	1.27±0.07	1.61±0.11 p=0.005
7	Nonspecific reactivity index	68.72±2.18	67.49±4.53
General immunological reactivity			
8	Immune reactivity index	15.86±0.56	13.65±0.80 p=0.014
9	Immune resistance index	7.29±0.22	6.38±0.30 p=0.009
10	Index of immunological reactivity growth	2.38±0.18	2.58±0.15
11	Allergy index	1.50±0.12	1.22±0.11 p=0.044
12	Lymphocyte index	0.52±0.05	0.58±0.07
13	Lymphocyte-to-monocyte ratio (LMR)	13.34±0.61	11.66±0.58 p=0.04
14	Lymphocytes-to-eosinophils ratio	19.22±1.03	22.05±1.29 p=0.045
15	Agranulocytes-to-ESR ratio	4.47±0.48	3.23±0.39 p=0.024

Note. AOM – acute otitis media; LII – Leukocytes Intoxication Index; NEU - neutrophil; 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 GG-genotype.

No significant differences in the Leukocyte Intoxication Index (LII) were observed between the genotype groups. However, children with GG-genotype demonstrated a significantly lower LII compared with A-allele carriers – by 32.82% (p=0.005). This was accompanied by a non-significant trend toward lower LII values (by 19.05% and 5.62%; p>0.05) and higher endotoxicosis nuclear index (by 12.5%) as well as increased cellular reactivity and resistance (by 15.96% and 8.06%, respectively; p>0.05). These results indicate that GG-genotype carriers exhibit stronger cellular reactivity and resistance in response to predominantly endogenous intoxication during AOM, which likely contributes to the significantly reduced intoxication index in this group.

The leukocyte-to-erythrocyte sedimentation rate (ESR) ratio was significantly lower in GG-genotype carriers than in A-allele carriers by 21.12% (p=0.005), indicating the presence of infection-induced intoxication. No genotype-dependent differences were identified for the remaining indices of neutrophil reactive response.

Indices of immunological reactivity and resistance were elevated in AOM children with *GG*-genotype carriers, exceeding those of A-allele by 16.19% (p_{AA}=0.014) and 14.26% (p_{AA}=0.009), respectively (Table 2). These children also demonstrated higher allergization indices by 22.95% (p_{AA}=0.044), as well as increased lymphocyte-to-monocyte and agranulocyte-to-ESR ratios by 14.41% (p_{AA}=0.04) and 38.39% (p_{AA}=0.024), respectively. Conversely, the lymphocyte-to-eosinophil ratio was lower by 12.83% (p_{AA}=0.045).

It is important to note that neutrophils are capable of phagocytosis. However, they are markedly less efficient in this process compared to macrophages (monocytes). Unlike macrophages, neutrophils lack effective membrane-repair mechanisms and therefore undergo rapid apoptosis or necrosis when overloaded with pathogenic or opportunistic microorganisms. Under conditions ofsubstantial microbial contamination, neutrophils are forced to release excessive amounts of reactive oxygen species (ROS). When antioxidant systems fail to neutralize these molecules, oxidative damage leads to the destruction of the neutrophils themselves. Despite this vulnerability, through active cytokine production and phagocytic activity, neutrophils provide a highly effective first-line, nonspecific defense against infection, often at the expense of their own survival. Importantly, the activity of most enzymatic

systems and the functional properties of ICC, including neutrophils and monocytes, are genetically determined and additionally modulated by epigenomic regulatory structures. In our study, the leukocyte-to-ESR ratio was significantly lower in patients with *GG*-genotype compared with *A*-allele carriers, indicating the presence of infection-related intoxication. Conversely, the increased ratio observed in *A*-allele carriers may reflect an additional mechanism involving autoimmune-type inflammation. Changes in immunological reactivity indices indicate dominant activation of nonspecific cellular effector immunity (primarily lymphocytic responses) in children with *GG*-genotype of HSP70-2 gene (rs1061581), accompanied by increased sensitization driven by an allergic component and the development of immediate-type hypersensitivity associated with humoral immune activation. In contrast, the mutant *A*-allele carriers demonstrated a predominance of monocyte-mediated effector mechanisms with a more pronounced inflammatory response and less significant allergic reaction consistent with delayed-type hypersensitivity. These children exhibited reduced cellular and immune reactivity and resistance, contributing to a higher degree of exogenous intoxication.

Hematologic markers like NLR, MLR and PLR have recently gained attention for their diagnostic and prognostic value across numerous infectious (e.g., sepsis, urinary tract infections, COVID-19, bacteraemia) and non-infectious conditions (e.g., coronary artery disease, liver cirrhosis, advanced-stage cancer, nasal polyposis, chronic pancreatitis) [5, 22-28].

Studies demonstrate that NLR increases with the severity of infections or systemic inflammation and correlates with poorer clinical outcomes [10, 11]. In otolaryngology, NLR is an important marker used in disorders such as otitis media, facial paralysis, sudden sensorineural hearing loss, and head and neck cancers [6-9, 29, 30]. However, only limited research has evaluated NLR specifically in otitis media [15], highlighting the need for further investigation. Therefore, the diagnostic relevance of CBC-derived markers in infection-related diseases, including AOM, requires additional study.

Conclusions. In children with acute otitis media (AOM), the immunological defence pattern varies according to the allelic state of the HSP70-2 gene (rs1061581): GG-genotype carriers demonstrate higher levels of cellular and immunological reactivity and resistance, as well as more efficient activation of nonspecific cellular effector immunity (particularly lymphocytic responses), compared with mutant A-allele carriers. This enhanced cellular response is associated with a substantial reduction in the intoxication index, indicating more effective physiological apoptosis, compensatory cellular protection, the humoral immune response development, and increased immunological sensitization.

Most indices of neutrophil reactive response did not show genotype-dependent HSP70-2 (rs1061581) differences. However, the leukocyte-to-ESR ratio was 21.12% lower in *GG*-genotype carriers, reflecting intoxication primarily driven by an infectious agent. In contrast, a higher ratio in A-allele carriers may suggest an additional mechanism involving autoimmune-type inflammation.

Immune protection in children with AOM and the mutant *A*-allele of HSP70-2 gene (rs1061581) is predominantly mediated by monocyte-driven effector pathways, accompanied by a more pronounced inflammatory response, delayed-type hypersensitivity, and overall lower cellular and immunological reactivity and resistance. These features contribute to a higher level of exogenous intoxication.

Prospects for further research are to study the cellular and humoral immunity activity in children with AOM, depending on the clinical course severity, age and genetic marker HSP70-2 (rs1061581).

Conflict of interest: The authors declare no conflict of interest.

Funding: The authors received no financial support for the research, authorship, and/or publication of this article.

References

1. Jamal A, Alsabea A, Tarakmeh M, Safar A. Etiology, Diagnosis, Complications, and Management of Acute Otitis Media in Children. Cureus. 2022;14(8):e28019. DOI: 10.7759/cureus.28019.

2. Danishyar A, Ashurst JV. Acute Otitis Media. [Updated 2023 Apr 15]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; Accessed December 12.2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470332/

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-e57. DOI: 10.1097/INF.0000000000003970.

4. Sakovets OP, Sydorchuk LP, Kazanceva TV, Petrynych OA, Semianiv MM, Repchuk YV, et al. Immunohematological indices as markers of inflammation, cellular and nonspecific immunological defense in children with acute otitis media. Clinical & experimental pathology. 2025;24(2):27-35. DOI: 10.24061/1727-4338.xxiv.2.92.2025.05.

5. 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.

6. 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. 2017;10(1):12. DOI: 10.1186/s13104-016-2335-5.

7. 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):2355-58. DOI: 10.1016/j.ijporl.2015.10.043.

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;120:134-39. DOI: 10.1016/j.ijporl.2019.02.023.

9. 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):581-87. DOI: 10.1177/0194599816646552.

10. de Jager CP, van Wijk PT, Mathoera RB, de Jongh-Leuvenink J, van der Poll T, Wever PC, et al. Lymphocytopenia and neutrophil-lymphocyte count ratio predict bacteremia better than conventional infection markers in an emergency care unit. Crit Care. 2010;14(5):R192. DOI: 10.1186/cc9309.

11. 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. 2019;55(9):472-77. DOI: 10.1016/j.arbres.2019.02.005.

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. 2023;12(24):7611. DOI: 10.3390/jcm12247611.

13. 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. 2020;34(5):e23191. DOI: 10.1002/jcla.23191.

14. Sydorchuk LP, Sakovets OP. The heat shock protein 70-2 gene (rs1061581) associates with the acute otitis medium in children. Neonatology, surgery and perinatal medicine. 2025;XV(1):37-43. http://neonatology.bsmu.edu.ua/article/view/326008

15. 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):4603-07. DOI: 10.1007/s12070-021-02898-x.

16. Ministry of Health of Ukraine. State Expert Center of the Ministry of Health of Ukraine [Evidence-based clinical guideline, "Acute otitis media"] [Internet]. Kyiv: Ministry of Health of Ukraine; 2021. 94 p. [cited 2025 December 10]. Available: https://www.dec.gov.ua/wp-content/uploads/2021/04/2021_688_kn_gso.pdf

17. Ministry of Health of Ukraine [Unified clinical protocol for primary, secondary (specialized) and tertiary (highly specialized) medical care "Acute otitis media"] [Internet]. Kyiv: Ministry of Health of Ukraine. 2021. 34 p. [cited 2025 December 10]. Available: https://www.dec.gov.ua/wp-content/uploads/2021/04/2021_688_ykpmd_gso_dd.pdf

18. 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.

19. Sydorchuk LP, Syrota BS, Sydorchuk AR, Gerush OV, Muzyka NY, Sheremet MI, et al. Clinical markers of immune disorders in the pathogenesis of Escherichia coli enteritis. Arch Balk Med Union. 2019;54(1):89-96. Available: https://umbalk.org/clinical-markers-of-immune-disorders-in-the-pathogenesis-of-escherichia-coli-enteritis/

20. Sokolenko MO, Sydorchuk LP, Sokolenko LS, Sokolenko AA. General Immunological reactivity of the organism of patients to COVID-19 and its relationship with gene polymorphism, severity of the clinical course of the disease and association with common pathology. Medical Perspectives. 2024;29(3):108-17. DOI: 10.26641/2307-0404.2024.3.313570.

21. Ivashchuk SI, Sydorchuk LP, Korovenkova OM. Level of cellular reactivity of organism and extent of intoxication severity in patients with acute 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.2017.01.04.

22. 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.

23. Milovanovic Alempijevic T, Stojkovic Lalosevic M, Dumic I, Jocic 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. 2017;2017:e6070135. DOI: 10.1155/2017/6070135.

24. Peng J, Qi D, Yuan G, Deng X, Mei Y, Feng L, Wang D. Diagnostic value of peripheral hematologic markers for coronavirus disease 2019 (COVID-19): A multicenter, cross-sectional study. J Clin Lab Anal. 2020;34(10):e23475. DOI: 10.1002/jcla.23475.

25. Serrano CV, 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. 2019;2019:e6513847. DOI: 10.1155/2019/6513847.

26. 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.

27. 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(8):96-100. Available: https://www.thepharmajournal.com/archives/2016/vol5issue9/PartB/5-8-29-206.pdf

28. 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.

29. Szilasi Z, Jósa 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. 2020;17(5):1742. DOI: 10.3390/ijerph17051742.

30. Zahorec R. Neutrophil-to-lymphocyte ratio, past, present and future perspectives. Bratisl Lek Listy. 2021;122(7):474-88. DOI: 10.4149/BLL_2021_078.

Відомості про авторів

Саковець О.П. – ЛОР-лікар, аспірант кафедри сімейної медицини, Буковинський державний медичний університет, м. Чернівці, Україна. ORCID ID: https://orcid.org/0009-0004-7215-3820

Сидорчук Л.П. – д-р мед. наук, професор, завідувач кафедри сімейної медицини, Буковинський державний медичний університет, м. Чернівці, Україна. ORCID ID: https://orcid.org/0000-0001-9279-9531

Information about the authors

Sakovets O.P. – ENT doctor, Postgraduate Student, Department of Family Medicine, Bukovinian State Medical University, Chernivtsi, Ukraine. ORCID ID: https://orcid.org/0009-0004-7215-3820

Sydorchuk L.P. – Doctor of Science, Professor, Head of Family Medicine Department, Bukovinian State Medical University, Chernivtsi, Ukraine. ORCID ID: https://orcid.org/0000-0001-9279-9531

Дата першого надходження рукопису до видання: 10.12.2025 р.
Дата прийнятого до друку рукопису після рецензування: 24.12.2025 р.
Дата публікації: 19.03.2026 р.