

ORIGINAL ARTICLE

Recurrent Wheezing in Preschoolers: The Association Between Peripheral Blood Cell-Derived Inflammatory Indexes and the Asthma Predictive Index

Okul Öncesi Çocuklarda Tekrarlayan Hışıltı: Periferik Kan Hücrelerinden Elde Edilen İnflamatuvar İndekslerin Astım Prediktif İndeksi ile İlişkisi

¹Yahya GÜL , ²Ahmet KAN , ¹Tuğba GÜLER 

¹MD, Division of Immunology and Allergy, Department of Pediatrics, Health Sciences University Erzurum Regional Training and Research Hospital, Erzurum, Türkiye
E-mail: yahya.palu@hotmail.com,

¹MD, Division of Immunology and Allergy, Department of Pediatrics, Health Sciences University Erzurum Regional Training and Research Hospital, Erzurum, Türkiye
E-mail: tugbacihanguler@gmail.com

²Assoc. Prof., Division of Immunology and Allergy, Department of Pediatrics, Faculty of Medicine, Dicle University, Diyarbakir, Türkiye
E-mail: rodmerrod1980@gmail.com

Correspondence

Ahmet KAN, MD,
Department of Pediatric Allergy and Immunology of Faculty of Medicine, Diyarbakir University, Diyarbakir, Türkiye,

E-Mail: rodmerrod1980@gmail.com

How to cite ?

Gül Y., Kan A., Güler T., Recurrent Wheezing in Preschoolers: The Association Between Peripheral Blood Cell-Derived Inflammatory Indexes and the Asthma Predictive Index, Genel Tıp Derg. 2025;35(4):605-612

ABSTRACT

Aim: This study aimed to evaluate the role of chronic and eosinophilic inflammation in the etiopathogenesis of recurrent wheezing in preschool children and to explore the association between peripheral blood-derived inflammatory indexes and the Modified Asthma Predictive Index (mAPI) in positive and negative groups.

Methods: Children under six years old presenting with recurrent wheezing to pediatric immunology and allergy clinics between September 2022 and September 2023 were included and had not yet started asthma treatment. Demographic data such as gender, age, atopy history, smoking exposure, complete blood count, total immunoglobulin E (IgE) levels, and aeroallergen sensitivity were assessed. The patients were grouped based on mAPI positivity and negativity.

Results: The mAPI-positive group exhibited significantly higher eosinophil count ($p=0.004$), eosinophil percentage ($p=0.035$), eosinophil/lymphocyte ratio (ELR) ($p=0.01$), ENR ($p=0.007$), and EMR ($p<0.001$). A moderate positive correlation was found between basophil and eosinophil counts ($p=0.001$, $r=0.38$). Additionally, when children with eosinophilia were excluded, monocyte count and percentage were significantly higher in the remaining mAPI-positive group compared to the mAPI-negative group ($p=0.01$, $p=0.005$). The groups did not reveal statistical differences regarding hospitalization rates, oral corticosteroid use, or emergency visits.

Conclusions: Preschool children with recurrent wheezing and mAPI positivity demonstrated an eosinophil-dominant inflammatory profile. Additionally, basophils may have a vital role in chronic inflammation alongside eosinophils. Notably, increased monocyte levels in mAPI-positive children without eosinophilia suggest that non-eosinophilic inflammatory mechanisms may also contribute to systemic inflammation in this population. Larger cohort studies are required to search for asthma risk in this patient population.

Keywords: Asthma predictive index, inflammation, monocytes, peripheral blood cells, preschool children, recurrent wheezing

ÖZ

Amaç: Mevcut çalışma okul öncesi çocuklarda tekrarlayan hışıltının etiopatogenezinde kronik ve eozinofilik inflamasyonun rolünü belirlemek ve bu inflamatuvar parametrelerin Modifiye Astım Prediktif İndeksi (mAPI) pozitif ve negatif gruplar arasındaki ilişkisini değerlendirmeyi hedefledi.

Gereç ve Yöntemler: Çalışmaya, Eylül 2022 - Eylül 2023 tarihleri arasında çocuk immünoji ve alerji polikliniklerine tekrarlayan hışıltı şikayeti ile başvuran, altı yaşından küçük, astım için herhangi bir tedaviye yeni başlayan hastalar dahil edildi. Hastaların yaş, cinsiyet, atopi öyküsü, sigara maruziyeti gibi demografik verileri ile tam kan sayımı, total IgE düzeyleri ve aeroalerjen duyarlılığı analiz edildi. Hastalar, modifiye astım prediktif indeksi pozitif ve negatif olmak üzere iki gruba ayrıldı.

Bulgular: mAPI pozitif grupta, eozinofil sayısı ($p=0.004$), eozinofil yüzdesi ($p=0.034$), eozinofil/lenfosit oranı ($p=0.01$), eozinofil/nötrofil oranı ($p=0.007$) ve eozinofil/monosit oranı ($p<0.001$) anlamlı derecede yüksek bulundu. Basofil sayısı ile eozinofil sayısı arasında anlamlı pozitif korelasyon saptandı ($p=0.001$, $r=0.31$). Gruplar arasında hastaneye yatış oranları, oral kortikosteroid kullanımı ve acil başvurular açısından istatistiksel fark bulunmadı.

Sonuçlar: Çalışmamızda, okul öncesi tekrarlayan hışıltılı çocuklarda, mAPI pozitif grupta eozinofilik inflamasyonu gösteren hematolojik parametrelerin belirgin şekilde yüksek olduğu tespit edildi. Ayrıca, bazofillerin de kronik inflamasyonda eozinofillerle birlikte rol oynayabileceği gözlemlendi. Astım riski yüksek olan bu hasta grubunda daha büyük çaplı kohort çalışmalarına ihtiyaç duyulmaktadır.

Anahtar Kelimeler: Astım prediktif indeksi, inflamasyon, okul öncesi çocuklar, tekrarlayan hışıltı

INTRODUCTION

Recurrent wheezing episodes are prevalent among preschool-aged children, with approximately one-third experiencing at least one episode within their first three years (1). Longitudinal studies have shown that 30% of these children continue to exhibit asthma symptoms by six years of age (2, 3). Although asthma frequently emerges early in life, the precise mechanisms leading to persistent airway changes in susceptible children remain poorly understood (4). The Modified Asthma Predictive Index (mAPI), developed from the Tucson Children's Respiratory Study cohort, identifies young children at high risk for developing asthma (5, 6). Children with a positive mAPI at three years have a 77% likelihood of active asthma by adolescence, compared to only 3% in those with a negative mAPI (6).

Despite the recognized utility of mAPI, the role of eosinophilic airway inflammation in preschool wheezing and asthma development is still debated. While most preschool wheezers exhibit virus-induced, non-atopic, and transient symptoms, a subset characterized by mAPI positivity demonstrates an inflammatory profile resembling that of established asthma (7, 8). Nevertheless, discrepancies exist regarding the extent of eosinophilic inflammation and its prognostic relevance in this population (9, 10). Hematological parameters such as eosinophil counts, ELR, ENR, EMR, and total immunoglobulin E (IgE) levels have been proposed as accessible biomarkers for identifying eosinophilic asthma phenotypes in older children (11-15). However, limited studies have evaluated these indices, specifically in preschoolers with recurrent wheezing.

This study primarily aims to evaluate the association between peripheral blood

cell-derived inflammatory indices and mAPI positivity in preschool children with recurrent wheezing. The secondary aims were to assess the correlation between basophil counts and eosinophilic markers and to compare clinical parameters such as hospitalization rates, emergency admissions, and corticosteroid use between mAPI-positive and mAPI-negative groups. By clarifying the inflammatory profiles in preschool children at risk of asthma, this study seeks to contribute to early identification strategies and highlight potential targets for monitoring disease progression.

MATERIALS and METHODS

Study Design

This multicenter study included patients under six years old who presented with recurrent wheezing to the Pediatric Immunology and Allergy clinics at Dicle University Hospital and Erzurum City Hospital between September 2022 and September 2023 and who had not previously initiated asthma therapy. Demographic data, including gender, age, family history of atopy, smoking exposure, complete blood count, total IgE levels, and aeroallergen sensitivities, were evaluated. Skin prick tests were performed with solutions from Lofarma®, Milan, Italy. Before the test, antihistamines were discontinued 15 days before, antidepressants were discontinued 1 week before, and medications containing montelukast were discontinued 3 days before. Histamine solution was used as a positive control, and saline solution as a negative control in the skin prick test. Allergen solutions were applied to the inner surface of the forearm with a lancet. A positive reaction was considered if edema

of 3 mm or more was observed 15 minutes after application of allergen solutions compared with the negative control (16).

Inhaled allergens used in the skin prick test included house dust mites (*Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*), pollen allergens (birch, rye, grass mix (orchard grass, tussac grass, blue fescue, grass), weed mix (cart-track, *Xanthium strumarium*, weed)), cat epithelium, dog epithelium, *Alternaria alternata*, and *Aspergillus fumigatus*.

Recurrent wheezing was defined as ≥ 3 episodes of physician-diagnosed wheezing within one year (17). Premature infants, low birth weight infants, and patients with chronic cardiac, neurological, or pulmonary diseases (e.g., cystic fibrosis, ciliary dyskinesia, bronchopulmonary dysplasia) were excluded. Additionally, children with active wheezing attacks during assessment and those whose parents had active smoking habits since birth were excluded.

The definition of mAPI: Children were considered mAPI-positive if they had ≥ 3 wheezing episodes plus at least one major criterion (physician-diagnosed eczema, parental asthma, or aeroallergen sensitization) or two minor criteria (food allergen sensitization, wheezing unrelated to infections, or peripheral eosinophilia $\geq 4\%$) (5).

Statistical Analysis

Statistical analyses were performed using SPSS version 18.0 (SPSS Inc., Chicago, IL, USA). Data distribution was assessed using histograms, Kolmogorov-Smirnov, and Shapiro-Wilk tests. Non-normally distributed continuous variables were compared using the Mann-Whitney U test, while normally distributed variables were analyzed with the

Student’s t-test. Categorical variables were analyzed with the Chi-square test or Fisher’s exact test when necessary. A p-value < 0.05 was considered statistically significant. Since peripheral eosinophilia is part of the mAPI definition, separate analyses excluding eosinophil-related parameters were also performed to prevent circular reasoning and enhance methodological robustness.

Ethical Consideration

The research received approval from the Local Ethics Committee of Atatürk University Faculty of Medicine with decision No.2023/27 dated January 26, 2023. The study adhered entirely to the principles outlined in the Declaration of Helsinki.

RESULTS

One hundred four preschool children with recurrent wheezing were enrolled, 36 of whom were mAPI-positive and 68 mAPI-negative. The sociodemographic characteristics of the groups are summarized in Table 1. No significant differences were observed between groups regarding age ($p=0.60$) and gender distribution ($p=0.96$). Smoking exposure rates were also similar between groups ($p=0.48$).

Table 1. Sociodemographic profiles of the study groups

	mAPI positive (n=36)	mAPI negative (n=68)	p
Patient age (months±SD)	31.9±17.5	32.08±18.06	0.6
Gender			
Male, n (%)	21 (58.3)	40 (58.8)	0.96
Female, n (%)	15 (41.7)	28 (41.2)	

mAPI: Modified asthma predictive index, SD: Standard deviation

Table 2 summarizes the distribution of mAPI criteria among patients who proved positive.

The results of the aeroallergen skin prick tests for mAPI-positive patients are presented in Table 3. The total number of sensitizations exceeds the number of patients because some patients have more than one aeroallergen sensitization.

Analysis of hematological parameters demonstrated that eosinophil count, eosinophil percentage, ELR, ENR, and EMR were significantly higher in the mAPI-positive group (all $p < 0.05$) (Table 4).

Table 2. Distribution of modified asthma predictive index criteria among positive patients

Criterion	Positive Patients, n (%)
Parental Asthma	14 (37)
Physician–diagnosed Atopic Dermatitis	12 (32)
Aeroallergen Sensitization	13 (34)
Food Allergen Sensitization	17 (45)
Eosinophilia ($\geq 4\%$)	16 (42)
Wheezing Unrelated to Infections	19 (50)

Note: The total number of criteria exceeds the number of patients because some patients simultaneously fulfilled more than one major or minor criterion.

Table 3. Skin prick test results

Allergen type	Sensitized Patients, n (%)
House Dust Mite	23 (22)
Grass pollen mixture	11 (11)
Weed Pollen Mixture	6 (6)
Tree Pollen Mixture	4 (4)
Mold (Alternaria)	2 (2)

Excluding mAPI positive children with eosinophilia, a statistical analysis

of hematological parameters and inflammatory indices revealed a significant difference in monocyte count and percentages between mAPI negative and mAPI positive children without eosinophilia ($p = 0.01$; $p = 0.005$). No statistically significant differences were found between the groups regarding white blood cell (WBC) count, neutrophil counts, lymphocyte counts, eosinophil count, eosinophil percentage, platelet counts, or total IgE levels ($p = 0.6$; $p = 0.71$; $p = 0.25$; $p = 0.88$; $p = 0.21$; $p = 0.59$; $p = 0.62$).

A moderate positive correlation was found between basophil counts and eosinophil counts ($r = 0.38$, $p = 0.001$). Regarding clinical outcomes, there were no significant differences between groups in emergency admissions during the previous six months ($p = 0.44$), hospitalization frequency ($p = 0.67$), or systemic corticosteroid use in the past year ($p = 0.58$) (Table 5).

DISCUSSION

In this cross-sectional study, we evaluated hematological parameters and inflammation-related indices in preschool children with recurrent wheezing, grouped according to mAPI status. Our findings revealed that mAPI-positive children exhibited significantly higher eosinophil counts and eosinophil-derived ratios—including ELR, ENR, and EMR—suggesting a prominent eosinophilic inflammatory profile in this subgroup. A moderate positive correlation was observed between eosinophil and basophil counts, highlighting a potential cooperative role of these granulocytes in early airway inflammation. Also, we compared hematological parameters, inflammatory indices, and total

Table 4. Comparative analysis of complete blood parameters and total IgE levels across the groups

	mAPI positive (n=36)	mAPI negative (n=68)	p
WBC count (x10⁹/L)	9815 (5700-22930)	9415 (4160-19200)	0.26**
Neutrophil count (x10⁹/L)	3345 (1400-13680)	3605 (1040-9290)	0.80**
Neutrophil percentage (%)	37.1±12.2	38.8±13.4	0.53*
Lymphocyte count (x10⁹/L)	5160 (2500-11150)	4510 (1430-10990)	0.2**
Lymphocyte percentage (%)	51.4±12.7	49.8±13.3	0.54*
Monocyte count (x10⁹/L)	675 (70-1360)	715 (70-2890)	0.18**
Monocyte percentage (%)	7.2 (3.5- 11.9)	7.8 (3.4- 18.7)	0.02**
Eosinophil count (x10⁹/L)	370 (10-1330)	185 (0-1440)	0.004**
Eosinophil percentage (%)	3.6 (0.5-12.9)	2.4 (0-22.4)	0.035**
Platelet count (x10⁹/L)	400333.3±108340.9	401764.7±119491.1	0.96*
Basophil count (x10⁹/L)	40 (1.3-110)	30 (0-110)	0.34**
Basophil percentage (%)	0.4 (0.1-4)	0.3 (0-1.1)	0.12**
MPV	9.2±0.7	9.2±0.8	0.81*
NLR	0.68 (0.2-2.99)	0.74 (0.2-2.99)	0.67**
ELR	0.06 (0-0.34)	0.04 (0-0.39)	0.01**
Eosinophil/ neutrophil ratio	0.11(0-0.31)	0.07 (0-0.44)	0.007**
Eosinophil/ monocyte ratio	0.58 (0.02-5.3)	0.23 (0-5)	<0.001**
Platelet/ lymphocyte ratio	79.6 (25.7-201.6)	84.3 (42.4-221.7)	0.32**
Total IgE levels (kU/L)	48.8 (0-1493)	44 (2-1874)	0.46**

*Student's t-test, ** Mann-Whitney U test. Data are presented as mean ± standard deviation or median (min-max).

ELR: Eosinophil/lymphocyte ratio, EMR: Eosinophil/monocyte ratio,

ENR: Eosinophil/neutrophil ratio, IgE: Immunoglobulin E, MPV: Mean platelet volume, NLR: Neutrophil/lymphocyte ratio,

PLR: Platelet/lymphocyte ratio, WBC: White blood cell

Table 5. Comparison of emergency admissions, hospitalization frequency, and use of OCS in the last year between groups

	mAPI positive (n=36)	mAPI negative (n=68)	p
Admissions to Emergency in the last six months, Median (min-max)	2 (0-5)	2 (0-15)	0.44
Number of Hospitalizations over the past year, Median (min-max)	2 (0-5)	2 (0-5)	0.67
Use of OCS in the last year, Median (min-max)	7 (3-17)	5.5 (0-15)	0.58

mAPI: Modified asthma predictive index, OCS: Oral corticosteroid

IgE levels between children who were API-positive but had peripheral blood eosinophil percentages <4% and those who were API-negative. While most hematological and inflammatory parameters did not differ significantly between the groups, we observed a statistically significant difference in monocyte count and percentage.

The findings align with previous studies indicating that eosinophilic inflammation plays a significant role in asthma pathophysiology (5, 18, 19). In particular, Castro-Rodriguez et al. (20) found higher eosinophil counts in preschool children with positive mAPI scores, supporting our observations. However, since eosinophilia is a defining criterion for mAPI positivity, these associations should be interpreted cautiously, and causality cannot be inferred from our cross-sectional data.

Interestingly, despite elevated eosinophil parameters, no significant differences were observed between groups regarding clinical outcomes such as emergency admissions, hospitalization rates, or corticosteroid use, consistent with previous findings (20) (21) (21, 28). This may suggest that while eosinophilic inflammation is a marker of at-risk phenotypes, it does not necessarily correlate with short-term clinical severity in this age group.

The clinical significance of eosinophil-derived indices in preschool wheezers remains a subject of ongoing investigation. Although elevated eosinophil counts and ratios were associated with mAPI positivity, our study could not establish specific predictive thresholds for future asthma development. Additionally, it is noteworthy that a subset of mAPI-negative children exhibited high levels of eosinophilic

inflammation markers. These patients may represent a distinct at-risk subgroup, potentially progressing to asthma later in childhood, underscoring the need for closer longitudinal follow-up.

The moderate positive correlation between basophil and eosinophil counts further supports the idea that basophils may contribute to early chronic airway inflammation (22). While basophil counts alone were not significantly different between groups, the observed correlation highlights their potential role as synergistic mediators alongside eosinophils. Literature suggests that basophils can promote Th2-type immune responses and enhance eosinophil activation, supporting their involvement in early inflammation processes (22). Contrary to earlier studies linking elevated total IgE levels to asthma risk (13, 23), no significant differences in total IgE levels were found between the groups. This may reflect the heterogeneity of allergic sensitization profiles among preschool wheezers. However, it should be noted that other studies, such as Altas et al., have demonstrated that elevated total IgE and absolute eosinophil levels can serve as significant predictors for allergy test positivity, supporting their potential role as early markers of atopic predisposition even if not directly linked to asthma development in every cohort (24).

The absence of eosinophilic inflammation, monocyte-driven immune responses may play a role in the pathogenesis of asthma, aligning with hypotheses in the current literature. Carr et al. reported that non-eosinophilic asthma (NEA) may arise through alternative immune pathways and that monocytes may be more prominent in this Th2-low inflammatory phenotype

(25). Similarly, Baraldo et al. demonstrated that children with NEA exhibited airway remodeling comparable to those with eosinophilic asthma, supporting the concept that structural changes may develop even in the absence of eosinophilic infiltration (26). This finding suggests that non-eosinophilic immune mechanisms, possibly associated with recurrent viral respiratory infections, may contribute to systemic inflammation in some wheezy preschoolers. These results support the view that preschool wheezing is a phenotypically heterogeneous condition, where eosinophilic and non-eosinophilic inflammation may play a role.

However, given our study's cross-sectional nature, we could not assess long-term clinical outcomes or determine whether these children will eventually develop asthma.

Future longitudinal studies are warranted to evaluate the prognostic significance of monocyte-associated inflammation in predicting asthma development, especially in children who do not exhibit classical eosinophilic patterns.

Limitations

Several limitations must be acknowledged. The study's cross-sectional nature prevents establishing causal relationships between inflammatory markers and asthma development. Furthermore, objective assessments of airway function, such as spirometry or FeNO measurements, could not be performed due to the young age of the participants. Future longitudinal studies incorporating follow-up into school age are necessary to determine the true predictive value of these biomarkers.

CONCLUSION

In conclusion, mAPI-positive preschool children with recurrent wheezing exhibited significantly higher eosinophil counts and eosinophil-related hematological indices. However, since peripheral eosinophilia is a defining component of mAPI, these findings should be interpreted cautiously. Importantly, when children with eosinophilia were excluded, monocyte count and percentage were significantly higher in the remaining mAPI-positive group, compared to mAPI-negative children. Given that monocytes play a central role in innate immune responses, this elevation may reflect an increased burden of viral respiratory infections, which are known to contribute to recurrent wheezing in early childhood. These findings suggest that monocyte-associated inflammatory activity may be present in wheezy preschoolers independent of eosinophilic pathways. Although the cross-sectional nature of our study limits prognostic interpretation, the observed hematological differences may help refine phenotypic classifications of preschool wheezers and provide insight for future longitudinal studies.

Conflict of interest: The authors confirm that there are no conflicts of interest.

Financial support: None.

REFERENCES

1. Bisgaard H, Szefler S. Prevalence of asthma-like symptoms in young children. *Pediatr Pulmonol.* 2007;42:723–8.
2. Martinez FD, Wright AL, Taussig LM, et al. Asthma and wheezing in the first six years of life. The Group Health Medical Associates. *N Engl J Med.* 1995;332:133–8.

3. Taussig LM, Wright AL, Holberg CJ, et al. Tucson Children's Respiratory Study: 1980 to present. *J Allergy Clin Immunol.* 2003;111:661–75; quiz 76.
4. Belgrave DC, Buchan I, Bishop C, et al. Trajectories of lung function during childhood. *Am J Respir Crit Care Med.* 2014;189:1101–9.
5. Castro-Rodríguez JA, Holberg CJ, Wright AL, Martinez FD. A clinical index to define the risk of asthma in young children with recurrent wheezing. *Am J Respir Crit Care Med.* 2000;162:1403–6.
6. Castro-Rodríguez JA. The Asthma Predictive Index: a very useful tool for predicting asthma in young children. *J Allergy Clin Immunol.* 2010;126:212–6.
7. Guilbert TW, Bacharier LB. Controversies in the treatment of the acutely wheezing infant. *Am J Respir Crit Care Med.* 2011;183:1284–5.
8. Ater D, Bar BE, Fireman N, et al. Asthma-predictive-index, bronchial-challenge, sputum eosinophils in acutely wheezing preschoolers. *Pediatr Pulmonol.* 2014;49:952–9.
9. Gelfand EW. Is asthma in childhood different from asthma in adults? Why do we need special approaches to asthma in children? *Allergy Asthma Proc.* 2008;29:99–102.
10. Lee DH, Kwon JW, Kim HY, et al. Asthma predictive index as a useful diagnostic tool in preschool children: a cross-sectional study in Korea. *Clin Exp Pediatr.* 2020;63:104–9.
11. Bedolla-Barajas M, Morales-Romero J, Hernández-Colín DD, et al. Beyond eosinophilia: inflammatory patterns in patients with asthma. *J Asthma.* 2022;59:255–63.
12. Talay F, Kurt B, Tuğ T. The Comparison of Clinical Characteristics and Pulmonary Functions of Allergic and Non-Allergic Asthma Patients. *Duzce Medical Journal.* 2008;10:15–20.
13. Dursun F, Koç An. IgE, Eosinophil, CRP Levels and Atopy in the Asthmatic Children. *Sağlık Bilimleri Dergisi.* 2007;16:80–5.
14. Zhang XY, Simpson JL, Powell H, et al. Full blood count parameters for the detection of asthma inflammatory phenotypes. *Clin Exp Allergy.* 2014;44:1137–45.
15. Ilmarinen P, Tuomisto LE, Niemelä O, et al. Comorbidities and elevated IL-6 are associated with negative outcomes in adult-onset asthma. *Eur Respir J.* 2016;48:1052–62.
16. Position paper: Allergen standardization and skin tests. The European Academy of Allergology and Clinical Immunology. *Allergy.* 1993;48:82.
17. Guidelines for the Diagnosis and Management of Asthma 2007 (EPR-3) [Available from: <https://www.nhlbi.nih.gov/health-topics/guidelines-for-diagnosis-management-of-asthma>].
18. Brand PL, Baraldi E, Bisgaard H, et al. Definition, assessment, and treatment of wheezing disorders in preschool children: an evidence-based approach. *Eur Respir J.* 2008; 32:1096–110.
19. Stoltz DJ, Jackson DJ, Evans MD, et al. Specific patterns of allergic sensitization in early childhood and asthma & rhinitis risk. *Clin Exp Allergy.* 2013;43:233–41.
20. Castro-Rodríguez JA, Atton I, Villarroel G, Serrano CA. Serum periostin is not related to the asthma predictive index. *Allergol Immunopathol (Madr).* 2018;46:235–40.
21. Forget P, Khalifa C, Defour JP, et al. What is the normal value of the neutrophil-to-lymphocyte ratio? *BMC Res Notes.* 2017;10:12.
22. Brooks CR, van Dalen CJ, Hermans IF, et al. Sputum basophils are increased in eosinophilic asthma compared with non-eosinophilic asthma phenotypes. *Allergy.* 2017;72:1583–6.
23. Yoo Y, Seo SC, Kim YI, et al. Bronchodilator Responses after Methacholine and Adenosine 5'-Monophosphate (AMP) Challenges in Children with Asthma: Their Relationships with Eosinophil Markers. *Journal of Asthma.* 2012;49:717–23.
24. Ozkul Saglam N, Ozkars MY, Altas U, Altas ZM. Evaluation of the predictive value of total IgE and absolute eosinophil levels on allergy test positivity. *Northern Clinics of Istanbul.* 2023;10:602–8.
25. Carr TF, Zeki AA, Kraft M. Eosinophilic and Non-Eosinophilic Asthma. *Am J Respir Crit Care Med.* 2018;197:22–37.
26. Baraldo S, Turato G, Bazzan E, et al. Non-eosinophilic asthma in children: relation with airway remodelling. *Eur Respir J.* 2011; 38:575–83.