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Original Article / Özgün Araştırma

Relationship Between Allergen Sensitivity, Laboratory Values, and Inflammatory Markers in Patients with Asthma and/or Allergic Rhinitis

Halil Alkaya[1], Uğur Altaş[1], Seda Çevik[1], Alican Sarısaltık[2], Mehmet Yaşar Özkars[1]

1 University of Health Sciences, Ümraniye Training and Research Hospital, Department of Pediatric Allergy and Immunology, Istanbul, Türkiye

2 Marmara University School of Medicine, Department of Public Health, Istanbul, Türkiye

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Abstract

Objective: This study aimed to examine the clinical value of inflammation-related markers in pediatric asthma and to explore how these parameters are associated with the development of allergic conditions.

Methods: In this retrospective analysis, 2028 children diagnosed with asthma (0–18 years) who were evaluated at the Pediatric Allergy and Immunology Clinic, Umraniye Training and Research Hospital, University of Health Sciences, between January 1, 2023, and January 1, 2024, were included. Information regarding demographic features, clinical asthma findings, coexisting allergic rhinitis, medications, allergen sensitization profiles, and laboratory data—such as complete blood count parameters, serum total IgE levels, and skin prick test outcomes—was extracted from medical records. Inflammation-related hematologic ratios, including the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic inflammation response index (SIRI), were computed. All statistical procedures were conducted using SPSS software (version 25.0).

Results: Of the 2028 patients, 64.3% were diagnosed with AR, and 39.9% showed allergen sensitization, predominantly to house dust mite, cat dander, and pollen. Patients with allergen sensitization exhibited significantly higher total IgE, eosinophil counts, and inflammatory indices. Those with AR also had elevated IgE and eosinophil levels, with higher inflammatory indices ($p < 0.001$).

Conclusion: Asthma frequently coexists with allergic rhinitis in children. Sensitization to common allergens is common, and inflammatory markers such as total IgE, eosinophil count, NLR, SIRI, and PLR may serve as useful indicators of disease severity and allergic inflammation. These parameters may contribute to more effective evaluation and management of pediatric asthma.

Keywords: Asthma; Allergic rhinitis; Allergen sensitization; NLR; PLR; ELR; SIRI; PIV; Inflammatory hematologic indices; Pediatrics

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Correspondence / Yazışma Adresi: *Halil Alkaya, University of Health Sciences, Ümraniye Training and Research Hospital, Department of Pediatric Allergy and Immunology, Istanbul, Türkiye e-mail: halilalkaya2910@gmail.com*

Astım ve Alerjik Rinitli Hastalarda Alerjen Duyarlılığı, Laboratuvar Değerleri ve İnflamatuar Belirteçler Arasındaki İlişki

Öz

Amaç: Bu çalışma, pediatrik astımda inflamasyona bağlı belirteçlerin klinik değerini incelemeyi ve bu parametrelerin alerjik durumların gelişimiyle ilişkisini değerlendirmeyi amaçlamıştır.

Yöntemler: Bu retrospektif analizde, 1 Ocak 2023 – 1 Ocak 2024 tarihleri arasında Sağlık Bilimleri Üniversitesi Ümraniye Eğitim ve Araştırma Hastanesi Çocuk Alerji ve İmmünoloji Kliniği'nde değerlendirilen, astım tanılı 0–18 yaş arası 2028 çocuk çalışmaya dâhil edildi. Tıbbi kayıtlardan demografik özellikler, astımın klinik bulguları, eşlik eden alerjik rinit varlığı, kullanılan ilaçlar, alerjen duyarlılık profilleri ve hem tam kan sayımı parametreleri, serum total IgE düzeyleri ile deri prik testi sonuçlarını içeren laboratuvar verileri elde edildi. İnflamasyonla ilişkili hematolojik oranlar—nötrofil/lenfosit oranı (NLR), trombosit/lenfosit oranı (PLR) ve sistemik inflamasyon yanıt indeksi (SIRI) hesaplandı. Tüm istatistiksel analizler SPSS 25.0 yazılımı ile gerçekleştirildi.

Bulgular: Çalışmaya dâhil edilen 2028 hastanın %64,3'ünde alerjik rinit (AR) saptandı; %39,9'unda ise alerjen duyarlılığı mevcuttu. En sık saptanan duyarlılıklar ev tozu akarı, kedi epiteli ve polen alerjenlerine karşıydı. Alerjen duyarlılığı olan hastalarda total IgE düzeyleri, eozinofil sayıları ve inflamatuar indeksler belirgin olarak daha yüksekti. Alerjik rinitli çocuklarda da IgE ve eozinofil düzeyleri artmış olup inflamatuar indekslerde anlamlı yükselmeler mevcuttu ($p < 0.001$).

Sonuç: Çocuklarda astım sıklıkla alerjik rinit ile birlikte görülmektedir. Yaygın inhalan alerjenlere duyarlılık oldukça yaygındır ve total IgE, eozinofil sayısı, NLR, SIRI ve PLR gibi inflamatuar belirteçler hastalığın şiddeti ve alerjik inflamasyon hakkında değerli bilgiler sunabilir. Bu parametreler, pediatrik astımın daha etkili değerlendirilmesine ve yönetimine katkı sağlayabilir.

Anahtar kelimeler: Astım; Alerjik rinit; Alerjen duyarlılığı; NLR; PLR; ELR; SIRI; PIV; İnflamatuvar hematolojik indeksler; Pediatri.

INTRODUCTION

Asthma is a complex, multi-faceted condition in which ongoing inflammation of the airways leads to fluctuating degrees of airflow obstruction and is clinically defined by recurrent episodes of cough, wheezing, and shortness of breath[1]. Approximately 80% of childhood asthma cases are classified as allergic (atopic) asthma[2]. A range of triggers—including exposure to allergens or irritants, physical activity, shifts in weather conditions, and respiratory infections—may lead to worsening of asthma symptoms[3].

In addition to airway inflammation, asthma involves systemic inflammatory responses. Increased concentrations of circulating pro-inflammatory cytokines—such as interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α)—contribute significantly to disease pathophysiology by enhancing the activation of neutrophils and natural killer cells[4,5]. Identifying an allergic asthma phenotype involves assessing atopic status, which is generally confirmed by skin prick testing and by measuring serum specific IgE levels to common allergens[6].

Several hematologic parameters have been proposed in earlier research as indirect markers of systemic inflammation. Elevated neutrophil-to-lymphocyte (NLR) and platelet-to-lymphocyte (PLR) ratios have been reported in children with atopic dermatitis compared with healthy peers, and both indices have demonstrated associations with disease severity[7]. In the same way, ratio such as NLR has been linked to several chronic inflammatory conditions, including atopic dermatitis[8]. Doğru and colleagues also demonstrated that children with allergic rhinitis exhibit significantly higher NLR values compared with healthy controls[9]. In that study, 85.1% of patients exhibited sensitization to house dust mites, while another investigation found such sensitization in 52.9%

of allergic rhinitis cases, indicating a strong association between allergen exposure and airway inflammation[10].

"In children with allergic asthma, sensitization is most frequently directed toward house dust mites, a variety of pollens originating from grasses, grains, trees, and weeds, as well as certain fungal allergens. According to the findings of Ay et al., pollen was the leading sensitizing agent in both asthmatic children and those presenting with asthma accompanied by allergic rhinitis[11]. The distribution of allergen sensitivities varies among regions and countries, largely influenced by environmental conditions such as climate, vegetation, humidity, and living standards[12].

In recent years, two emerging inflammatory indices—the Systemic Inflammation Response Index (SIRI) and the Pan-Immune-Inflammation Value (PIV)—have been proposed as useful measures for evaluating systemic inflammatory status. SIRI, defined by the formula (neutrophil × monocyte) / lymphocyte, illustrates the interplay between inflammatory activity and immune regulation. This index has demonstrated prognostic significance in patients with severe COVID-19, neonatal sepsis, and certain rheumatologic and cardiovascular diseases[13-15]. PIV, defined as (neutrophil × platelet × monocyte) / lymphocyte, has been studied in malignancies and correlated with disease prognosis[16].

These indices, together with routinely used hematologic measures such as NLR, ELR, PLR, mean platelet volume (MPV), plateletcrit (PCT), and platelet distribution width (PDW), are readily accessible, low-cost, and highly reproducible, making them practical tools in clinical evaluation.

This study sought to characterize inflammation-associated biomarkers in pediatric asthma, compare hematologic indices according to allergic rhinitis status, and assess differences in peripheral blood cell profiles between allergen-sensitized and non-sensitized children. The study further aimed to determine whether these indices could contribute to the phenotyping of allergic rhinitis and help identify potential diagnostic biomarkers.

METHODS

Study Design and Population

"This retrospective analysis included all children diagnosed with asthma who were evaluated at the Pediatric Allergy and Immunology Clinic, Umraniye Training and Research Hospital, University of Health Sciences, between January 1, 2023, and January 1, 2024. Medical files of patients aged 0–18 years were screened, and those with a confirmed asthma diagnosis and complete clinical documentation were eligible for inclusion. Patients with incomplete or missing medical records were excluded from the analysis.

In total, 2028 children met the criteria and were assessed. Data regarding demographic features (age and sex), clinical findings (asthma symptoms and coexisting allergic rhinitis), hematologic measurements, and allergen sensitization status were systematically retrieved and analyzed.

Asthma Diagnosis and Clinical Characteristics

Asthma diagnosis was confirmed retrospectively from medical records based on the documented diagnosis of a pediatric allergy/immunology specialist and in accordance with guideline-based criteria (GINA). Diagnosis was supported by a compatible clinical history, including recurrent wheezing, cough, dyspnea, and/or chest tightness with variability over time, and, when available, objective evidence of variable airflow limitation (e.g., bronchodilator responsiveness

on spirometry) or a documented clinical response to asthma treatment.

Follow-up duration was defined as the time interval between the initial asthma diagnosis and the index outpatient visit during the study period and was extracted from patient records. Information regarding current asthma treatment at the index visit, including controller and reliever medications, was recorded. In addition, the latest available asthma control status documented in routine clinical practice (well-controlled, partly controlled, or uncontrolled), when available, was retrieved from medical files. Coexisting allergic rhinitis and related treatments were also identified based on physician documentation.

Laboratory Measurements

"Laboratory evaluations included complete blood count parameters, serum total immunoglobulin E (IgE) concentrations, and specific IgE (sIgE) measurements targeting common aeroallergens such as house dust mite, cat dander, and various pollens. Results from skin prick testing (SPT) were also examined. Standardized allergen extracts used for skin prick testing included house dust mite species (Dermatophagoides pteronyssinus and Dermatophagoides farinae), grass pollen mixture, tree pollen mixture, weed pollen mixture, cat dander, dog dander, cockroach, and mold allergens (Alternaria alternata and Cladosporium herbarum).

A range of inflammation-associated hematologic indices was calculated, including the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), eosinophil-to-lymphocyte ratio (ELR), and the Systemic Inflammation Response Index (SIRI), defined as (neutrophils × monocytes) / lymphocytes. Additional indices included the neutrophil–lymphocyte–platelet ratio (NLPR), calculated as (neutrophils × 100) / (lymphocytes × platelets), and the Pan-Immune-Inflammation Value (PIV), derived from (neutrophils × platelets × monocytes) / lymphocytes.

Specific IgE levels were determined using the ImmunoCAP system (Thermo Fisher Scientific, Uppsala, Sweden), with values ≥ 0.35 kU/L considered positive. Skin prick testing was performed using standardized allergen extracts, and a wheal at least 3 mm greater than the negative control—without dermographism or induration—was interpreted as a positive reaction.

Statistical Analysis

Statistical analyses were conducted using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed through both visual methods—such as histograms and Q–Q plots—and formal normality tests, including the Kolmogorov–Smirnov and Shapiro–Wilk tests. Continuous variables were summarized as medians with their minimum and maximum values, while categorical data were presented as frequencies and percentages. Comparisons between two independent groups for non-normally distributed variables were performed using the Mann–Whitney U test, and categorical comparisons were evaluated with the Chi-square test. A p-value below 0.05 was regarded as statistically significant. The study adhered to the principles of the Declaration of Helsinki and all applicable national ethical guidelines. The study protocol was approved by the Scientific Research Ethics Committee of Umraniye Training and Research Hospital, University of Health Sciences (Decision No: 329; Date: October 17, 2024).

RESULTS

The study population consisted of 2028 children with a confirmed diagnosis of asthma. The median age was 5 years, with ages ranging from infancy to 18 years. Among them, 58.6% (n = 1189) were male. Allergic rhinitis (AR) was diagnosed in 64.3% (n = 1305) of the patients

Allergen Sensitivity Profile

Assessment of allergen sensitization showed that 39.9% of the children (n = 810) were reactive to at least one allergen. Multiple allergen sensitivities were detected in 11.6% of patients (n = 235). The most frequent sensitizations were to house dust mite (36.8%, n = 746), followed by cat dander (11.1%, n = 226) and pollen allergens (6.1%, n = 123) (Table 1).

Table I: Allergen sensitivities of patients

		n	%
Allergen Sensitivity	Poly	235	11.6
	Mono	575	28.3
	None	1218	60.1
Sensitivity to House Dust Mites		746	36.8
Sensitivity to Cat Allergens		226	11.1
Sensitivity to Pollen		123	6.1

Comparison According to Allergen Sensitization Status

Patients with allergen sensitization exhibited markedly higher total IgE, eosinophil counts, and inflammatory markers, including NLR, PLR, ELR, SIRI, and NLPR, compared with those without sensitization ($p < 0.05$). PIV levels also tended to be higher in the sensitized group; however, this increase was not statistically significant ($p > 0.05$) (Table 2).

Table II: Relationship between allergen sensitivity, laboratory values, and inflammatory markers with asthma

	Allergen Sensitivity						*P-value*
	None			Present			
	Median	Minimum	Maximum	Median	Minimum	Maximum	
Total IgE[a]	53.0	0	3977.0	290.0	3.0	5165.0	<0.001
Eosinofil[b]	210	0	2170	400	0	2400	<0.001
Eosinofil %[c]	2.5	0	23.2	4.7	0	23.4	<0.001
NLR[d]	1.10	0.12	1410.00	1.23	0.15	315.00	<0.001
ELR[e]	0.06	0	0.72	0.13	0	0.73	<0.001
NLPR[f]	0.32	0.04	2.76	0.37	0.05	3.84	<0.001
SIRI[c]	0.58	0	11.78	0.63	0	11.12	0.008
PIV[g]	201.06	0.32	3581.93	218.40	1.12	4168.58	0.071
PLR[h]	95.85	22.00	278.84	104.18	33.13	253.67	<0.001

[a]Total IgE: Immunoglobulin E, total serum level [b]Eosinophil: Absolute eosinophil count (cells/µL) [c]Eosinophil %: Eosinophil percentage in total leukocyte count SIRI: Systemic Inflammation Response Index [d]NLR: Neutrophil-to-Lymphocyte Ratio [e]ELR: Eosinophil-to-Lymphocyte Ratio [f]NLPR: Neutrophil-Lymphocyte Platelet Ratio [g]PIV: Pan-Immune-Inflammation Value [h]PLR: Platelet-to-Lymphocyte Ratio

Comparison According to the Presence of Allergic Rhinitis

Likewise, children with allergic rhinitis showed significantly higher total IgE and eosinophil levels compared with those without AR ($p < 0.05$). Furthermore, all inflammatory indices—including NLR, PLR, ELR, SIRI, NLPR, and PIV—were markedly elevated in the AR group ($p < 0.001$) (Table 3).

Table III: Relationship between allergen sensitivity and laboratory values with asthma

	Allergic Rhinitis						*P-value*
	None			Present			
	Median	Minimum	Maximum	Median	Minimum	Maximum	
Total IgE[a]	75.5	0	5165.0	127.0	0	5023.0	<0.001
Eosinofil[b]	260	0	2400	270	0	2330	0.030
Eosinofil %[c]	2.9	0	18.5	3.2	0	23.4	0.002
NLR[d]	1.03	0.12	11.78	1.21	0.15	1410.00	<0.001
ELR[e]	0.06	0	0.72	0.08	0	0.73	<0.001
NLPR[f]	0.30	0.04	2.33	0.36	0.05	3.84	<0.001
SIRI[c]	0.55	0.05	9.22	0.63	0	11.78	<0.001
PIV[g]	187.39	20.41	2757.30	220.29	0.32	4168.58	<0.001
PLR[h]	91.75	30.50	278.84	102.44	22.00	253.67	<0.001

[a]Total IgE: Immunoglobulin E, total serum level [b]Eosinophil: Absolute eosinophil count (cells/µL) [c]Eosinophil % / SIRI: Systemic Inflammation Response Index [d]NLR: Neutrophil-to-Lymphocyte Ratio [e]ELR: Eosinophil-to-Lymphocyte Ratio [f]NLPR: Neutrophil-Lymphocyte Platelet Ratio [g]PIV: Pan-Immune-Inflammation Value [h]PLR: Platelet-to-Lymphocyte Ratio

DISCUSSION

A total of 2,028 children with asthma were included in the analysis, and the median age of the cohort was 5 years (0–18 years). In the report by Atla et al., the mean patient age was 4.5 years[17]. Both findings underscore that asthma is a prevalent childhood disease and highlight the importance of early diagnosis and management.

In our cohort, 64.3% (n = 1305) of patients had concomitant allergic rhinitis (AR). Consistent with the Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update, allergic rhinitis is present in a substantial proportion of patients with asthma, with reported prevalence ranging from approximately 40% to 80%[18]. This high coexistence underscores the concept of "one airway, one disease," emphasizing the close pathophysiological link between the upper and lower airways. Differences in prevalence rates across studies may be attributed to variations in patient characteristics, geographic factors, age distribution, and study design.

Of all participants, 58.6% (n = 1189) were male, and 41.4% were female. Another study found similar findings, with 58.2% of allergic asthma cases occurring in males and 41.8% in females[19]. These findings reinforce the widely recognized pattern that allergic asthma occurs more frequently in boys—a disparity that may be shaped by genetic, hormonal, and anatomical factors, as well as differences in sample characteristics or population demographics across studies.

Evaluation of allergen sensitivities revealed that 39.9% (n = 810) of patients exhibited at least one allergen sensitivity, while 11.6% (n = 235) showed multiple sensitivities. The most frequent sensitizations were to house dust mites (36.8%, n = 746), cat dander (11.1%, n = 226), and pollens (6.1%, n = 123). In a study by Akçal and Atakul, 40.2% of children showed no aeroallergen sensitivity, 46.2% had single sensitivity, and 13.6% had multiple sensitivities[20]. The most common sensitizations in that study were to house dust mites (44.3%), pollen (23.5%), and cat dander (5.9%). These consistent results emphasize that aeroallergens are frequent triggers of asthma, and the predominance of house dust mite sensitivity underscores the significance of indoor allergen exposure. Minor differences between studies may arise from geographical and climatic variations, differences in allergen panels, and population characteristics.

Our findings indicate that total IgE and eosinophil levels serve as important biomarkers of allergic inflammation in asthma patients with allergen sensitivities. Both parameters were significantly elevated in sensitized patients, suggesting a more pronounced immune activation and inflammatory response. This observation has also been evaluated by Sayar, who reported mean total IgE and eosinophil counts in children with aeroallergen sensitivities[21]. While total IgE reflects the intensity of allergic responses, eosinophil levels indicate the degree of allergic inflammation. Taken together, these results highlight the clinical utility of these biomarkers in assessing and managing allergic asthma and suggest that they may aid in identifying children who are at higher risk for more severe disease.

In our study, NLR, SIRI, and NLPR values were significantly higher in patients with allergen sensitivities, whereas PIV showed no statistically significant difference. In a study by Söğütlü and Altaş, inflammatory indices such as NLR, SIRI, PIV, and NLPR were significantly higher in children with febrile seizures compared with both febrile and healthy controls[22]. These indices, derived from neutrophil, monocyte, lymphocyte, and platelet

counts, provide valuable insight into systemic inflammation and immune activation. The elevated NLR, SIRI, and NLPR in our study suggest that allergen sensitivity augments systemic inflammatory responses. Conversely, the lack of a significant difference in PIV may indicate that this marker reflects different inflammatory dynamics. To the best of our knowledge, no prior study has specifically evaluated these inflammatory indices in the context of allergen sensitization among children with asthma.

"In our analysis, ELR levels were markedly elevated in children with allergen sensitization. This finding is consistent with the report by Altaş et al., who demonstrated significantly increased ELR values in children with allergic rhinitis and positive allergy test results[23]. These findings suggest that ELR may serve as an indirect marker of allergic inflammation and reflect the degree of immune activation triggered by allergen exposure. Although current evidence remains limited, ELR may represent a promising, readily accessible biomarker in the evaluation of allergic diseases. Larger, well-designed studies are warranted to further clarify its clinical utility.

In the subgroup of patients with allergic rhinitis, total IgE levels and eosinophil counts were markedly higher compared with those without AR. This aligns with findings by Sharma et al., who demonstrated elevated serum total IgE and eosinophil counts in allergic rhinitis compared to controls[24]. These results reinforce that IgE-mediated inflammation and eosinophilic infiltration play a central role in AR pathophysiology and can serve as diagnostic and prognostic indicators in allergic airway diseases.

NLR values were also markedly elevated in asthmatic children with allergic rhinitis, a finding that aligns with the meta-analysis by Khanzadeh et al., which demonstrated higher NLR levels in individuals with allergic rhinitis compared with healthy controls[25]. This suggests that the coexistence of AR and asthma enhances systemic inflammation and immune activation. Similarly, ELR was significantly elevated in asthma patients with AR. Selçuk and Keren11 also reported elevated ELR values in individuals with allergic rhinitis, further supporting its potential usefulness as a marker of inflammation severity. In our cohort, PLR levels were also elevated in asthmatic children with allergic rhinitis, a pattern that mirrors the findings of Cansever and Sari, who reported significantly higher PLR values in pediatric patients with allergic rhinitis compared with healthy controls[26]. This supports the hypothesis that PLR reflects systemic inflammatory load and may assist in evaluating the severity of allergic airway diseases.

Finally, NLPR values were higher in asthma patients with AR. Pantea et al. found significantly elevated NLPR in neonates with systemic inflammatory response syndrome (SIRS), supporting its predictive value for systemic inflammation[27]. Similarly, our results suggest that coexisting AR and asthma may amplify systemic inflammatory responses, and NLPR could represent a useful marker for identifying inflammation severity in these patients.

In conclusion, this large retrospective study demonstrates that allergen sensitization and coexisting allergic rhinitis are strongly associated with increased systemic inflammation in children with asthma. Elevated levels of total IgE, eosinophils, and inflammation-related hematologic indices such as NLR, SIRI, ELR, PLR, and NLPR reflect enhanced immune activation in these patients. These readily available and low-cost biomarkers may support routine clinical assessment and contribute to more precise phenotyping and risk stratification in pediatric asthma. Similarly, our previous study evaluating hemogram parameters in patients

with atopic dermatitis also identified eosinophil count and total IgE levels as markers associated with allergic inflammation and disease severity[28]. Nevertheless, prospective studies are warranted to further clarify their prognostic value and potential role in guiding personalized management strategies.

Limitations

The study's main limitation lies in its single-center retrospective design, which may restrict generalizability. Additionally, only the most common allergens known to cause sensitization in children were evaluated, potentially overlooking regional variations in allergen exposure. Future multicenter studies with larger and more diverse populations could provide broader insights.

Ethical approval: The study adhered to the principles of the Declaration of Helsinki and all applicable national ethical guidelines. Approval for the research protocol was granted by Ethics Committee of Ümraniye Training and Research Hospital (Decision No: 329; Date: October 17, 2024).

Conflict of Interest: The authors declared no conflicts of interest.

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