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The Role of Hematological Parameters in the Diagnosis of Childhood Allergic Conjunctivitis

Çocukluk Çağında Allerjik Konjunktivitin Tanısında Hematolojik Parametrelerin Rolü

Fatih Çiçek[1], Mehmet Tolga Köle[2], İbrahim Kandemir[3]

[1]University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar City Hospital, Clinic of Pediatric Allergy and Immunology, İstanbul, Turkey
[2]University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar City Hospital, Clinic of Pediatrics, İstanbul, Turkey.
[3]Biruni University Faculty of Medicine, Department of Pediatrics, İstanbul, Turkey

Abstract

Objective: We aimed to investigate the parameters of complete blood count and the levels of systemic inflammatory biomarkers in children with allergic conjunctivit and to evaluate their role in diagnosis in this study.

Method: We included 71 pediatric patients with allergic conjunctivit diagnosis referred from the ophthalmology outpatient clinics who had sensitivity to at least one allergen and 71 age- and sex-matched healthy controls and compared complete blood count results, immunoglobulin E (IgE), neutrophil/lymphocyte, and platelet/lymphocyte ratios and systemic immune-inflammation index results. We built a multivariate model with correlated results.

Results: Eosinophil counts and serum total IgE values were significantly higher in the patient group compared to the control group (p<0.001). Other parameters were not statistically different. 70.4% (n=50) of the patients had seasonal allergic conjunctivit, and 29.6% (n=21) had perennial allergic conjunctivit. In the skin prick tests performed in the patient group, 60.6% (n=43) of the patients had pollen, 54.9% (n=39) mite, 12.7% (n=9) dander, 11.3% (n=8) cockroach, and 4.2% (n=3) had alternaria sensitivities. In the multivariate analysis, every 100-cell increase in eosinophil count increased the hazard ratio of allergic conjunctivitis 1.3 times (95% confidence interval: 1.1-1.5), and every 100-units increase in total IgE levels increased 1.2 times (95% confidence interval: 1.1-1.5).

Conclusion: We found no significant relationship between neutrophil/lymphocyte and platelet/lymphocyte ratios, and SII with allergic conjunctivit. Increasing eosinophil count and serum total IgE levels increase the hazard ratio for developing allergic conjunctivit. Pollen sensitivity was the most common factor in the skin test in allergic conjunctivit-diagnosed patients.

Keywords: Allergic conjunctivitis, inflammation, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, systemic immune inflammation index

Öz

Amaç: Bu çalışmada allerjik konjonktiviti olan çocuklarda tam kan sayımı parametrelerini ve sistemik enflamatuvar biyobelirteç düzeylerini araştırmayı ve tanıdaki rollerini değerlendirmeyi amaçladık.

Yöntem: Göz polikliniklerinden başvuran ve en az bir alerjene duyarlılığı olan allerjik konjonktivit tanılı 71 çocuk hasta ile yaş ve cinsiyet uyumlu 71 sağlıklı kontrol alındı ve tam kan sayımı sonuçları, immünoglobulin E (IgE), nötrofil/lenfosit ve trombosit/lenfosit oranları ve sistemik immün-enflamasyon indeksi sonuçları karşılaştırıldı. Anlamlı korelasyon saptanan değerlerle çok değişkenli model oluşturuldu.

Bulgular: Hasta grubunda eozinofil sayısı ve serum total IgE değerleri kontrol grubuna göre anlamlı olarak yüksekti (p<0,001). Diğer parametreler açısından istatistiksel olarak anlamlı bir fark saptanmadı. Hastaların %70,4'ünde (n=50) mevsimsel, %29,6'sında (n=21) perennial allerjik konjonktivit vardı. Hasta grubunda yapılan deri delme testlerinde hastaların %60,6'sında (n=43) polen, %54,9'unda (n=39) akar, %12,7'sinde (n=9) kepek, %11,3'ünde (n=8) hamamböceği ve %4,2'sinde (n=3) alternaria duyarlılığı vardı. Multivariate analizde, eozinofil sayısındaki her 100 birim artış, allerjik konjonktivit oranını 1,3 kat (%95 güven aralığı: 1,1-1,5) ve toplam IgE seviyelerindeki her 100 birimlik artış 1,2 kat (%95 güven aralığı: 1,1-1,5) artırdı.

Sonuç: Nötrofil/lenfosit, trombosit/lenfosit oranları ve SII ile alerjik konjonktivit arasında anlamlı bir ilişki bulunamadı. Ancak eozinofil sayısı ve serum total IgE düzeylerindeki yükseklik ile alerjik konjonktivit arasında ilişkili olduğu saptandı. Alerjik konjonktivit tanısı konan hastalarda deri testinde saptanan en yaygın etken polen duyarlılığıydı.

Anahtar kelimeler: Alerjik konjonktivit, enflamasyon, nötrofil/lenfosit oranı, trombosit/lenfosit oranı, sistemik immün-enflamasyon indeksi

Address for Correspondence: Fatih Çiçek, University of Health Sciences Turkey, Kartal Dr. Lütfi Kirdar City Hospital, Clinic of Pediatric Allergy and Immunology, İstanbul, Turkey
E-mail: drfatihcck@gmail.com **ORCID:** orcid.org/0000-0001-7348-7081 **Received:** 24.07.2023 **Accepted:** 10.08.2023

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Introduction

Allergic conjunctivitis (AC) progresses with symptoms such as eye itching, watering, redness, and eyelids edema (1). Although AC is a frequently encountered disorder, many ocular diseases with overlapping clinics in their differential diagnosis create difficulties in the diagnosis phase. The classification of different forms of ocular allergy was recently revised by the European Academy of Allergy and Clinical Immunology (2). The conjunctival allergy forms with an immunoglobulin E (IgE)-mediated reaction, including benign seasonal allergic conjunctivitis (SAC) and perennial allergic conjunctivitis (PAC), as well as severe vernal keratoconjunctivitis and atopic keratoconjunctivitis involving the cornea (2,3). The most common type is SAC among AC, and PAC is the second most common (1). The frequency of AC has been increasing in recent years. There is no single reason for this increase, but many genetic/environmental factors, such as atopic susceptibility/family history, air pollution, and allergen exposure in early childhood, play a role (4). Although epidemiological studies are limited, it affects up to 25% of European children (3) and 28% of Chinese children (5).

In AC, the clinical picture develops with an IgE-mediated reaction against an allergen (1). As a result of the binding of the allergen to specific IgE, mast cells in the conjunctiva degranulate. In addition to mast cells, eosinophils, and Th2 lymphocytes play an important role in the inflammatory response that occurs in this process (3). In addition, neutrophils and platelets are blood parameters that have important functions in the inflammatory process. The easy accessibility of these blood parameters in today's conditions allows them to be used in diagnosing and following-up on many diseases. Studies have shown that neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (TLR), and systemic immune-inflammation index (SII) parameters obtained from complete blood count parameters have prognostic importance in cardiovascular diseases, chronic inflammatory diseases, and various malignancies and can be used as inflammatory markers (6-8).

Studies suggest that hemogram parameters are important in allergic diseases such as asthma, atopic dermatitis, and allergic rhinitis diagnosis and follow-up (9-11); however, studies on the use of these parameters in the diagnosis and follow-up of AC are limited (12,13). We aimed to investigate the parameters of complete blood count and the levels of systemic inflammatory biomarkers in children with AC and to evaluate their role in diagnosis in this study.

Materials and Methods

We included 71 pediatric patients referred to the pediatric allergy clinic from the ophthalmology outpatient clinics with AC diagnosis between March 2022 and May 2023 who had sensitivity to at least one allergen and 71 age- and sex-matched healthy controls. We retrospectively analyzed the complete blood count parameters, serum total IgE levels, and skin prick test results of the cases during active complaints and evaluated neutrophil, lymphocyte, eosinophil, erythrocyte, leukocyte, and platelet counts, and mean platelet volume, and hemoglobin and serum total IgE levels. We calculated NLR and PLR values by dividing the neutrophil and platelet counts by the absolute lymphocyte counts, respectively, and SII using the (neutrophil×platelet)/lymphocyte formula.

Patients whose skin prick tests showed sensitivity and developed symptoms such as itching, watering, burning, redness, and eye rubbing after exposure to these aeroallergens were defined as SAC, and patients with persistent symptoms throughout the year as PAC. Patients who received systemic or ocular/topical treatment for any reason (including AC), had systemic/ocular acute or chronic disease (including vernal keratoconjunctivitis, giant papillary conjunctivitis, allergic rhinitis, asthma, atopic dermatitis) other than AC, and had signs of active infection excluded from the study. We obtained the study approval from University of Health Sciences Turkey, Dr. Lütfi Kırdar City Hospital Ethics Committee (date: 29.03.2023, number: 2023/514/246/22) and conducted the study in adherence to the Helsinki criteria. In the skin prick test, skin reactions of 3 mm or more from the negative control at the 15th minute after application with standardized inhaled allergens were considered positive.

Statistical Analysis

We analyzed the data with JAMOVI 2.3.18 statistical package program. Values are expressed as mean ± standard deviation for presentation. Statistical comparisons were performed using the Student's t-test for parametric continuous variables, the Mann-Whitney U test for non-parametric continuous variables, and the chi-square test for categorical variables. We used a generalized linear model (GLM) for multivariate analysis with skewed data and assessed significant confounding factors ($p<0.01$ considered for significance) with the stepwise method. A type 1 error for $p<0.05$ was considered for statistical significance.

Results

We included 71 AC patients (36 females and 35 males) and 71 healthy controls (37 females and 34 males), and the mean ages of the patient and control groups were 11.3±3.7 years and 10.9±3.9 years, respectively, with no statistical differences either for gender and age (p=0.740, chi-square test, and p=0.396, Mann-Whitney U test, respectively). There was no statistical difference between the patient and control groups by hemoglobin, mean platelet volume and white blood cell, red blood cell, lymphocyte, neutrophil, and thrombocyte counts, and NLR, TLR, and SII values (p>0.05). Eosinophil counts and serum total IgE values were significantly higher in the patient group compared to the control group (p<0.001) (Table 1). A total of 70.4% (n=50) of the patients had SAC, and 29.6% (n=21) had PAC diagnosis. In the skin prick tests performed in the patient group, 60.6% (n=43) of the patients had pollen, 54.9% (n=39) mite, 12.7% (n=9) dander, 11.3% (n=8) cockroach, and 4.2% (n=3) had alternaria sensitivities.

Eosinophil count and total IgE had significant correlations with the patient group but there was no significant correlation by other laboratory parameters (Table 2).

We created a multiple regression model using laboratory parameters (eosinophils and total IgE) as possible confounders. Every 100-cell increase in eosinophil count increased the risk of AC (hazard ratio) 1.3 times (95% confidence interval: 1.1-1.5), and every 100-units increase in total IgE levels increased 1.2 times (95% confidence interval: 1.1-1.5) (GLM, R^2: 0.225). The related graph and the estimated marginal means table are presented below (Figure 1, Table 3).

Table 1. Comparison of laboratory parameters between the patient and the control group

	Control (n=71)	Patients (n=71)	p
White blood cell count (10^3/u L)	9.01±3.0	9.13±2.7	0.527*
Hemoglobin (g/dL)	12.8±1.3	12.6±0.9	0.608*
Red blood cell count (10^6/u L)	4.78±0.38	4.7±0.31	0.443**
Neutrophil count (10^3/u L)	4.8±2.5	4.4±2.2	0.388*
Lymphocyte count (10^3/u L)	3.2±1.2	3.5±1.1	0.056*
Eosinophil count (10^3/u L)	0.22±0.15	0.53±0.65	**<0.001***
Platelet counts (10^3/u L)	359.9±106.9	350.6±67.1	0.652*
Mean platelet volume (fL)	9.7±1.4	9.8±0.8	0.945*
Serum total IgE (kIU/L)	101±260	973±2.049	**<0.001***
Neutrophil/lymphocyte ratio	1.67±0.97	1.41±0.94	0.072*
Platelet/lymphocyte ratio	120±38	113±48	0.073*
Systemic immune-inflammation index	590±378	494±331	0.123*

*Mann-Whitney U test, **Student's t-test, IgE: Immunoglobulin E

Table 2. Laboratory correlations between the patient and the control group

Parameter	Kendall's tau b
White blood cell count (10^3/u L)	0.044
Hemoglobin (g/dL)	0.036
Red blood cell count (10^6/u L)	0.038
Neutrophil count (10^3/u L)	0.060
Lymphocyte count (10^3/u L)	0.133
Eosinophil count (10^3/u L)	0.280***
Platelet counts (10^3/u L)	0.031
Mean platelet volume (fL)	0.005
Serum total IgE (kIU/L)	0.427***
Neutrophil/lymphocyte ratio	0.124
Platelet/lymphocyte ratio	0.124
Systemic immune-inflammation index	0.107

***p<0.001, IgE: Immunoglobulin E

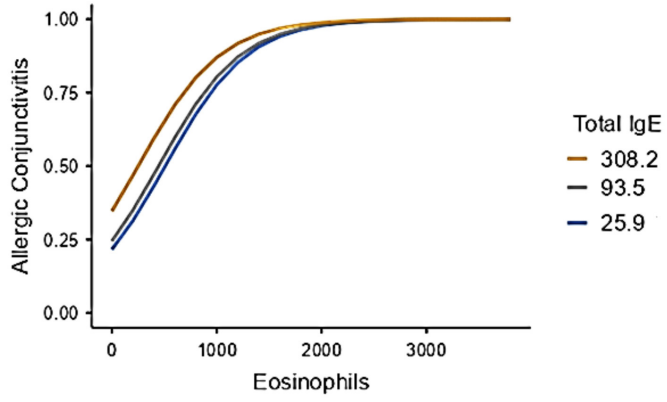

Figure 1. Eosinophil count and total IgE correlations with allergic conjunctivitis

IgE: Immunoglobulin E

Table 3. Estimated marginal means table for eosinophil count and total IgE correlations with allergic conjunctivitis

	Mean allergic conjunktivitis possibility (95%confidence interval)
Eosinophil count	
130/(10^3/u L)	55.5% (33.9-75.2)
230/(10^3/u L)	61.7% (41.9-78.2)
450/(10^3/u L)	73.8% (56.3-86.0)
Total IgE level	
25.9 kIU/L	41.8% (30.4-54.2)
93.5 kIU/L	45.7% (34.8-56.9)
308.2 kIU/L	58.0% (45.8-69.3)

R^2: 0.225, IgE: Immunoglobulin E

Discussion

The incidence of allergic diseases in childhood increases significantly, and AC is one of the most common ocular diseases in clinical practice (14). AC is divided into SAC, where symptoms occur seasonally, and PAC, where symptoms persist throughout the year (15,16). Cellular reactions, mediators, and immunological events that play a role in the pathogenesis of AC have begun to be better understood (17,18). A study stated that eosinophils are the main effective cells in AC, and their interaction between cells through physiologically active substances (for example, histamine and leukotriene), cytokines, and chemokines is influential (15). Also, innate immunity contributes to this reaction with kerato-conjunctival cells, which play a role in the etiology through chemokine production (15).

The relationship between NLR and PLR in childhood and various inflammatory diseases has been shown in many studies (19,20). Studies also emphasized that NLR and PLR can be used as markers of inflammation in many allergic diseases, such as allergic rhinitis, asthma, and atopic dermatitis (9,21,22). Faria et al. (23) showed that NLR is closely related to ocular pathologies such as macular degeneration, glaucoma, and retinal vascular diseases.

A study conducted with 26 patients and 31 healthy control in Turkey compared hemogram parameters and systemic inflammatory markers and did not find a significant difference in results between groups in this study, and high NLR, PLR, and SII levels did not have an association with AC in the pediatric age group, similar to our study (13). Also, Kurtul et al. (12) reported no significant difference between SAC-diagnosed patients and controls in terms of NLR rates. In our study, while eosinophil counts were statistically significantly higher in the patient group than in the control group, the results of other hemogram parameters and systemic inflammatory markers did not differ. We think the low number of patients and mild allergic symptoms in most cases were effective in these results.

Although AC is a clinical diagnosis, laboratory tests support the diagnosis. Cytological examination, skin prick tests, and serum total IgE antibody detection are important in AC diagnosis (24). IgE plays a role in allergic diseases like in many immunological diseases (25,26). In many studies conducted on patients with AC, serum total Ig E levels were elevated, consistent with our results (12,27). In addition, in the multiple regression model, every 100-unit increase in total IgE levels increased the hazard ratio of AC by 1.2 times. Also, studies reported that pollen sensitivity was the most common cause of skin tests in patients with AC, consistent with our result (15,28).

Study Limitations

The limitations of our study were its retrospective and single-centered design and the small number of patients.

Conclusion

We did not find a significant relationship between NLR, PLR, and SII levels between AC and the control group in the pediatric age. Multicenter, prospective and longitudinal studies are needed to evaluate this topic. In addition, increasing eosinophil count and serum total IgE levels increase the hazard ratio of developing AC, and pollen sensitivity was the most common factor in the skin test in AC-diagnosed patients.

Ethics

Ethics Committee Approval: This study was approved by the Ethics Committee of University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar City Hospital on March 29, 2023 with the decision number 2023/514/246/22.

Informed Consent: Not necessary.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: F.Ç., M.T.K., Design: F.Ç., M.T.K., Data Collection or Processing: M.T.K., İ.K., Analysis or Interpretation: F.Ç., İ.K., Writing: F.Ç., M.T.K., İ.K., Drafting Manuscript: F.Ç., M.T.K., Critical Revision of Manuscript: F.Ç., M.T.K., İ.K., Final Approval and Accountability: F.Ç., M.T.K., İ.K., Technical or Material Support: F.Ç., M.T.K., Supervision: F.Ç., M.T.K., İ.K.

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References

1. Bielory L, Delgado L, Katelaris CH, Leonardi A, Rosario N, Vichyanoud P. ICON: Diagnosis and management of allergic conjunctivitis. Ann Allergy Asthma Immunol 2020;124(2):118-134.
2. Roberts G, Pfaar O, Akdis CA, Ansotegui IJ, Durham SR, Gerth van Wijk R, et al. EAACI Guidelines on Allergen Immunotherapy: Allergic rhinoconjunctivitis. Allergy 2018;73(4):765-798.
3. Fauquert JL. Diagnosing and managing allergic conjunctivitis in childhood: The allergist's perspective. Pediatr Allergy Immunol 2019;30(4):405-414.
4. Miyazaki D, Fukagawa K, Fukushima A, Fujishima H, Uchio E, Ebihara N, et al. Air pollution significantly associated with severe ocular allergic inflammatory diseases. Sci Rep 2019;9(1):18205.
5. Feng Y, Wang X, Wang F, Liu R, Chen L, Wu S, et al. The Prevalence of Ocular Allergy and Comorbidities in Chinese School Children in Shanghai. Biomed Res Int 2017;2017:7190987.
6. Haybar H, Pezeshki SMS, Saki N. Evaluation of complete blood count parameters in cardiovascular diseases: An early indicator of prognosis? Exp Mol Pathol 2019;110:104267.
7. Zhang CL, Jiang XC, Li Y, Pan X, Gao MQ, Chen Y, et al. Independent predictive value of blood inflammatory composite markers in ovarian cancer: recent clinical evidence and perspective focusing on NLR and PLR. J Ovarian Res 2023;16(1):36.
8. OmranzadehA,BaradaranA,GhodsiA,ArekhiS,DadgarmoghaddamM, Mirshekaran A, et al. Neutrophil-to-Lymphocyte ratio as an inflammatory marker in familial mediterranean fever: a systematic review and meta-analysis. J Child Sci 2021;11(1):e100–e109.
9. Dogru M, Evcimik MF, Cirik AA. Is neutrophil-lymphocyte ratio associated with the severity of allergic rhinitis in children? Eur Arch Otorhinolaryngol 2016;273(10):3175-3178.
10. Inokuchi-Sakata S, Ishiuji Y, Katsuta M, Kharma B, Yasuda KI, Tominaga M, et al. Role of Eosinophil Relative Count and Neutrophil-to-Lymphocyte Ratio in the Assessment of Severity of Atopic Dermatitis. Acta Derm Venereol 2021;101(7):adv00491.
11. Dogru M, Aktas A, Ozturkmen S. Mean platelet volume increased in children with asthma. Pediatr Allergy Immunol 2015;26(8):823-826.
12. Kurtul BE, Kabatas EU, Boybeyi SD, Caglar AA, Ozer PA. Increased red cell distribution width levels in children with seasonal allergic conjunctivitis. Int Ophthalmol 2018;38(3):1079-1084.
13. Akçam HT. Investigation of Systemic Inflammation Biomarkers in Children with Seasonal Allergic Conjunctivitis. Düzce Üniversitesi Sağlık Bilimleri Enstitüsü Dergisi 2020;10(2):201-206.
14. Ackerman S, Smith LM, Gomes PJ. Ocular itch associated with allergic conjunctivitis: latest evidence and clinical management. Ther Adv Chronic Dis 2016;7(1):52-67.
15. Miyazaki D, Takamura E, Uchio E, Ebihara N, Ohno S, Ohashi Y, et al. Japanese guidelines for allergic conjunctival diseases 2020. Allergol Int 2020;69(3):346-355.
16. Palmares J, Delgado L, Cidade M, Quadrado MJ, Filipe HP; Season Study Group. Allergic conjunctivitis: a national cross-sectional study of clinical characteristics and quality of life. Eur J Ophthalmol 2010;20(2):257-264.
17. Fukuda K, Fujitsu Y, Seki K, Kumagai N, Nishida T. Differential expression of thymus- and activation-regulated chemokine (CCL17) and macrophage-derived chemokine (CCL22) by human fibroblasts from cornea, skin, and lung. J Allergy Clin Immunol 2003;111(3):520-526.
18. Fukagawa K, Nakajima T, Saito H, Tsubota K, Shimmura S, Natori M, et al. IL-4 induces eotaxin production in corneal keratocytes but not in epithelial cells. Int Arch Allergy Immunol 2000;121(2):144-150.
19. Kırkgöz T, Özkan B. Could Hematologic Parameters Have a Predictive Role in Pediatric Hashimoto Thyroiditis?. J Dr Behcet Uz Child Hosp 2022;12(2):159-163.
20. Elbeyli A, Kurtul BE. Systemic immune-inflammation index, neutrophil-to-lymphocyte ratio, and platelet-to-lymphocyte ratio levels are associated with keratoconus. Indian J Ophthalmol 2021;69(7):1725-1729.
21. Jiang Y, Ma W. Assessment of Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio in Atopic Dermatitis Patients. Med Sci Monit 2017;23:1340-1346.
22. Cansever M, Sari N. The association of allergic rhinitis severity with neutrophil-lymphocyte and platelet-lymphocyte ratio in children. North Clin Istanb 2022;9(6):602-609.
23. Faria SS, Fernandes PC Jr, Silva MJ, Lima VC, Fontes W, Freitas-Junior R, et al. The neutrophil-to-lymphocyte ratio: a narrative review. Ecancermedicalscience 2016;10:702.
24. Bao J, Tian L, Meng Y, Wu B, Wang J, He J, et al. Total IgE in tears accurately reflects the severity and predicts the prognosis of seasonal allergic conjunctivitis. Clin Transl Allergy 2022;12(3):e12139.
25. Mukai K, Tsai M, Starkl P, Marichal T, Galli SJ. IgE and mast cells in host defense against parasites and venoms. Semin Immunopathol 2016;38(5):581-603.
26. Platts-Mills TA, Heymann PW, Commins SP, Woodfolk JA. The discovery of IgE 50 years later. Ann Allergy Asthma Immunol 2016;116(3):179-182.
27. Pritchard DI, Falcone FH, Mitchell PD. The evolution of IgE-mediated type I hypersensitivity and its immunological value. Allergy 2021;76(4):1024-1040.
28. Yamana Y, Yamana S, Uchio E. Relationship among total tear IgE, specific serum IgE, and total serum IgE levels in patients with pollen-induced allergic conjunctivitis. Graefes Arch Clin Exp Ophthalmol 2022;260(1):281-287.