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Association of systemic inflammatory markers and serum immunoglobulin E levels with severity of atopic dermatitis

Wenty Septa Aldona[a], Nopriyati[a*], Rusmawardiana[a], Debby Handayati Harahap[b], Inda Astri Aryani[a], Muhammad Athuf Thaha[a]

[a] *Department of Dermatology, Venereology and Aesthetics, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia*
[b] *Department of Pharmacology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia*
**Corresponding Authors: nopriyati@fk.unsri.ac.id*

Abstract

Atopic dermatitis (AD) is a chronic inflammatory skin disease with multifactorial pathogenesis and variable clinical manifestations that significantly impair quality of life. Scoring atopic dermatitis (SCORAD) index is widely used to assess severity but remains subjective and dependent on trained assessors. Systemic inflammatory markers such as neutrophil-to-lymphocyte ratio (NLR), eosinophil-to-lymphocyte ratio (ELR), eosinophil-to-neutrophil ratio (ENR), platelet-to-lymphocyte ratio (PLR), and serum immunoglobulin E (IgE) may serve as more objective indicators. This study aimed to evaluate the association between these systemic inflammatory markers, serum IgE levels, and AD severity. An analytic cross-sectional study was conducted on 36 AD patients attending the Dermatology and Venereology outpatient clinic at Mohammad Hoesin Hospital Palembang from April to June 2025. Disease severity was assessed using the SCORAD index and categorized as mild–moderate or severe. Systemic inflammatory markers were derived from complete blood count results, and serum IgE levels were measured using immunoserological assays. ELR and serum IgE levels showed significant associations with AD severity, with higher mean values in the severe group ($p<0.05$). Multivariate analysis indicated that ELR >0.217 and serum IgE >418.65 IU/mL were associated with 22.3-fold and 42-fold increased risks of severe AD, respectively. The Th2-dominant immune response in AD, involving IL-4, IL-5, and IL-13, underlies elevated eosinophil activity and IgE overproduction. ELR and serum IgE levels are significantly associated with AD severity and may serve as objective markers for assessing disease severity.

***Keywords*:** *Atopic dermatitis, Systemic inflammatory markers, Immunoglobulin E, SCORAD, Eosinophil-to-lymphocyte ratio*

Abstrak

Hubungan penanda inflamasi sistemik dan kadar serum imunoglobulin e terhadap derajat keparahan dermatitis atopik. Dermatitis atopik (DA) merupakan penyakit kulit inflamasi kronis dengan patogenesis multifaktorial dan manifestasi klinis yang bervariasi, yang dapat menurunkan kualitas hidup secara signifikan. Scoring atopic dermatitis (SCORAD) sering digunakan untuk menilai derajat keparahan, namun bersifat subjektif dan memerlukan pemeriksa terlatih. Penanda inflamasi sistemik seperti rasio neutrofil-limfosit (NLR), eosinofil-limfosit (ELR), eosinofil-neutrofil (ENR), trombosit-limfosit (PLR), serta kadar serum imunoglobulin E (IgE) berpotensi menjadi indikator yang lebih objektif. Penelitian ini bertujuan menilai hubungan antara penanda inflamasi sistemik, kadar IgE serum, dan derajat keparahan DA. Metode penelitian analitik dengan desain potong lintang dilakukan pada 36 pasien DA di Poliklinik Kulit dan Kelamin RS Mohammad Hoesin Palembang periode April–Juni 2025. Derajat keparahan dinilai dengan indeks SCORAD dan dikategorikan menjadi ringan–sedang dan berat. Penanda inflamasi sistemik diperoleh dari pemeriksaan darah lengkap, sedangkan kadar IgE diukur dengan uji imunoserologi. ELR dan kadar IgE menunjukkan hubungan signifikan dengan derajat keparahan DA ($p<0,05$), dengan nilai rerata lebih tinggi pada kelompok DA berat. Analisis multivariat menunjukkan bahwa ELR >0,217 dan kadar IgE >418,65 IU/mL masing-masing meningkatkan risiko DA berat sebesar 22,3 kali dan 42 kali. Respons imun dominan Th2 pada DA, melibatkan interleukin-4 (IL-4), interleukin-5 (IL-5), dan interleukin-13 (IL-13), berperan dalam peningkatan aktivitas

eosinofil dan produksi IgE yang berlebihan. ELR dan kadar serum IgE berhubungan signifikan dengan keparahan DA dan dapat digunakan sebagai penanda objektif dalam menilai tingkat keparahan penyakit.

Kata Kunci: *Dermatitis atopik, Penanda inflamasi sistemik, Imunoglobulin E, SCORAD, Rasio eosinofil-limfosit*

Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin disease that primarily begins in childhood and continues through adulthood with a diverse clinical course.[1] Atopic dermatitis negatively impacts the patient's overall quality of life, and the intensity of itching impacts psychosocial well-being.[2]

Atopic Dermatitis severity can be assessed using the SCORing Atopic Dermatitis (SCORAD) index.[3] However, in clinical practice, SCORAD assessment is relatively time-consuming, requires trained examiners, and interpretation of lesion and body surface area (BSA) involvement can vary (tends to be subjective) among examiners.[4] Therefore, more objective severity parameters are needed to ensure that AD patients receive effective treatment according to their severity.

Immunological abnormalities frequently associated with AD include elevated serum levels of immunoglobulin E (IgE), along with an increased risk of anaphylaxis and dysregulation of cytokine mediators.[5] Intrinsic atopic dermatitis presents with normal serum total and specific IgE levels, while extrinsic AD presents with high to very high IgE levels (>20,000 IU/mL).[6]

In addition to immunoglobulin E (IgE), studies have examined the role of as neutrophil-to-lymphocyte ratio (NLR), eosinophil-to-lymphocyte ratio (ELR), eosinophil-to-neutrophil ratio (ENR and platelet-to-lymphocyte ratio (PLR) as markers of systemic inflammation in patients with AD.[7] In AD, eosinophils produce cytotoxic mediators, neutrophils form neutrophil extracellular traps (NETs) that exacerbate inflammation, Th2 lymphocytes trigger IgE production, and platelets play a role in leukocyte migration. Therefore, these hematologic parameters can be considered as non-invasive markers to help assess AD severity more objectively.[8,9]

This study aimed to analyze the association of systemic inflammatory markers such as NLR, ELR, ENR, PLR and serum IgE levels with severity of AD also to identify the cutoff point and risk level for increasing NLR, ELR, ENR, PLR, and serum IgE levels with AD severity.

Methods

This observational analytical study with a cross-sectional design was conducted at the Dermatology, Venereology, and Aesthetics (DVE) Polyclinic, in Allergy and Immunology Division, Mohammad Hoesin Hospital Palembang, Indonesia from April 2025 to June 2025, with a sample of 36 AD patients.

The dependent variable was AD severity, determined based on the SCORAD index into mild, moderate, and severe. The independent variables were systemic inflammatory markers determined from complete blood count (CBC), including NLR, ELR, ENR, PLR, as well as serum IgE levels determined from immunoserological assays, for which a cutoff point was determined using ROC curve analysis. Covariates analyzed included age, gender, education, and occupation.

The association between each variable, NLR, ELR, ENR, PLR, serum IgE levels and AD severity was analyzed using the Chi-Square/Fisher Exact test. Logistic regression was used to determine the most influential variables affecting AD severity. All data analyses were conducted using SPSS version 25.0. Ethical approval for this study was obtained from the Health Research Ethics Committee of Mohammad Hoesin Hospital Palembang, Indonesia (Approval No. 04.03/D.XVIII.06.08/ETIK/072/2025).

Results

Characteristics of atopic dermatitis patients

In this study, most patients were female (70.6%), aged 27–35 years (38.2%), with a mean age of 37.71 years (range 18 to 68 years). The majority had a higher education or at least a high school diploma (97.1%), and the majority were students (44.1%) (**Table 1**).

Table 1. Characteristics of the research sample

Variable	Mean±SD/ Median (Min-Max)	n (%)
Age (Years)	37.71 ± 14.50/ 34.5 (18 – 68)	--
Age Category		
- 18 – 26 years	-	7 (20.6)
- 27 – 35 years		13 (38.2)
- 36 – 44 years		5 (14.7)
- 45 – 53 years		3 (14.7)
- 54 – 62 years		3 (14.7)
- 63 - 71 years		3 (14.7)
Gender		
- Male	-	10 (29.4)
- Female		24 (70.6)
Education		
- Low	-	1 (2.9)
- High		33 (97.1)
Occupation		
- Housewives	-	4 (11.8)
- Civil Servants		6 (17.6)
- Private Employees		2 (5.9)
- Self-Employed		3 (8.8)
- Traders/Laborers		4 (11.8)
- Students		15 (44.1)

Severity of Atopic Dermatitis

The mean SCORAD index of AD patients in this study was 37.76, with a range of 17 to 75. Twenty-four (64.7%) patients with mild-moderate AD were found, while 12 (35.3%) patients with severe AD (**Table 2**).

Table 2. Degree of severity of AD

Variable	Mean±SD/Median (Min-Max)	n (%)
SCORAD	37.76 ± 17.43/29.5 (17 – 75)	--
Severity		
- Severe	-	12 (35.4)
- Mild - Moderate		24 (64.7)

Numeric variables are presented as mean±SD/median (minimum-maximum). Categorical variables are presented as numbers (percentages).

Systemic inflammatory markers and serum immunoglobulin E

This study found that the mean systemic inflammatory markers and serum IgE levels included NLR of 2.115 ± 1.413, ELR of 0.237 ± 0.125, ENR of 0.128 ± 0.079, PLR of 141.75 ± 66.01, and serum IgE levels showed a mean of 1011.95 ± 2036.93 IU/mL (**Table 3**).

Table 3. Systemic inflammatory markers and serum immunoglobulin E.

Parameters	Mean	Standard Deviation	Median	Minimun	Maximum
NLR	2.115	1.413	1.775	0.08	7.82
ELR	0.237	0.125	0.204	0.095	0.546
ENR	0.128	0.079	0.105	0.02	0.33
PLR	141.75	66.01	133.32	24.79	400.57
IgE Serum	1011.5	2036.93	184.25	400.57	9887.4

Comparison of sample characteristics based on AD severity

Statistical analysis revealed differences in age (p = 0.026); but no differences in gender (p = 0.714); education (p = 0.353); and occupation (p = 0.602) between mild-moderate and severe AD patients. AD patients aged ≥ 38 years had a 6.3 times greater risk of suffering from severe AD (PR = 6.300 (95% CI 1.3 – 30.533); p = 0.026) (**Table 4**).

Table 4 Comparison of research sample characteristics based on AD severity

Variabel	Atopic Dermatitis Severity		P value
	Severe (n = 12)	Mild-Moderate (n = 24)	
Age Category			
- ≥ 38 years	7 (58.3)	4 (18.2)	0.026[a]*
- < 38 years	5 (41.7)	18 (81.8)	
Gender			
- Male	4 (33.3)	6 (27.3)	0.714[a]
- Female	8 (66.7)	16 (72.7)	
Education			
- Low	1 (8.3)	0 (0)	0.353[a]
- High	11 (91.7)	22 (100)	
Occupation			
- Housewives	3 (25)	1 (4.5)	0.602[b]
- Civil Servants	2 (16.7)	4 (18.2)	
- Private Employees	1 (8.3)	1 (4.5)	
- Self-Employed	1 (8.3)	2 (9.1)	
- Traders/Laborers	1 (8.3)	3 (13.6)	
- Students	4 (33.3)	11 (50.0)	

[a]Fisher Exaxt Test, [b]Pearson Chi Square Test, *p < 0.05

Differences in systemic inflammatory markers based on AD severity

Statistical analysis revealed differences in ELR and serum IgE between patients with mild-moderate and severe AD (P < 0.05). The eosinophil-lymphocyte ratio and serum IgE were higher in patients with severe AD than in patients with mild-moderate AD. However, there were no differences in NLR, ENR, and PLR between patients with mild-moderate and severe AD (P > 0.05) (**Table 5**).

Systemic inflammatory marker cutoffs based on AD severity

Systemic inflammatory markers cutoffs and serum IgE were analyzed using receiver operating characteristic (ROC) curves. The cutoffs for systemic inflammatory markers (NLR, ELR, ENR, PLR) and serum IgE based on AD severity were obtained with the best sensitivity (Sn) and specificity (Sp) values, respectively, of 1.865, 0.217, 0.105, 135.2, and 418.65 (**Figure 1**). The NLR cutoff had a good area under the curve (AUC) value (AUC = 0.617 (95% CI 0.411 – 0.824); p = 0.264); and the ELR cutoff had a good AUC value (AUC = 0.769 (95% CI 0.612 – 0.926); p = 0.011). The ENR cut-off point had a good AUC value (AUC = 0.657 (95% CI 0.453 –

0.861); p = 0.135), the PLR cut-off point had a good AUC value (AUC = 0.606 (95% CI 0.385 – 0.827); p = 0.313) and the serum IgE cut-off point had a very good AUC value (AUC = 0.864 (95% CI 0.710 – 1.000); p = 0.001) (**Table 6**).

Table 5. Differences in systemic inflammatory markers based on AD severity

Parameters	Atopic Dermatitis Severity		P value
	Severe (n = 12)	Mild-Moderate (n = 24)	
NLR	2.659 ± 2.002 2.02 (0.67-7.82)	1.819 ± 0.882 1.69 (0.08-3.63)	0.264[a]
ELR	0.305±0.135 0.228 (0.171-0.545)	0.200±0.105 0.164 (0.095-0.5)	0.010[a]*
ENR	0.160±0.096 0.145 (0.04-0.33)	0.111±0.065 0.09 (0.02-0.28)	0.083[b]
PLR	140.35±96.71 121.39 (24.79-400.57)	142.52±44.13 137.69 (81.32-257.05)	0.313[a]
IgE Serum	2506.1±293.1 1465.4 (24.9-9887.4)	196.99±189.68 126.5 (15.7-629.2)	0.001[a]*

[a]Mann Whitney Test; [b]Independent T Test, *p < 0.05

Table 6. Cutoff points for systemic inflammatory markers based on AD severity

Parameters	Severe vs Mild-Moderate					
	Cut off	AUC	CI95%	P value	Sensitivity	Specificity
NLR	1,865	0,617	0,411-0,824	0,264	58,3%	63,6%
ELR	0,217	0,769	0,612-0,926	0,011	66,7%	68,2%
ENR	0,105	0,657	0,453-0,861	0,135	75,0%	63,6%
PLR	135,2	0,606	0,385-0,827	0,313	66,7%	54,5%
IgE Serum	418,65	0,864	0,710-1,000	0,001	75,0%	81,8%

Analisis ROC Curve

Association of systemic inflammatory markers with AD severity

Neutrophil-lymphocyte ratio

Statistical analysis revealed an insignificant relationship between NLR and AD severity. Patients with NLR ≥ 1.865 had a 2.45-fold increased risk of severe AD compared to patients with NLR < 1.865, but this was not statistically significant (PR = 2.450 (95% CI 0.581 – 10.334); p = 0.383).

Eosinophil-lymphocyte ratio

Statistical analysis revealed a significant relationship between ELR and AD severity. Patients with an ELR ≥ 0.217 had a significantly higher risk of developing severe AD, 10.2 times greater than patients with an ELR < 0.217 (PR = 10.2 (95% CI 1.971 – 52.775); p = 0.005).

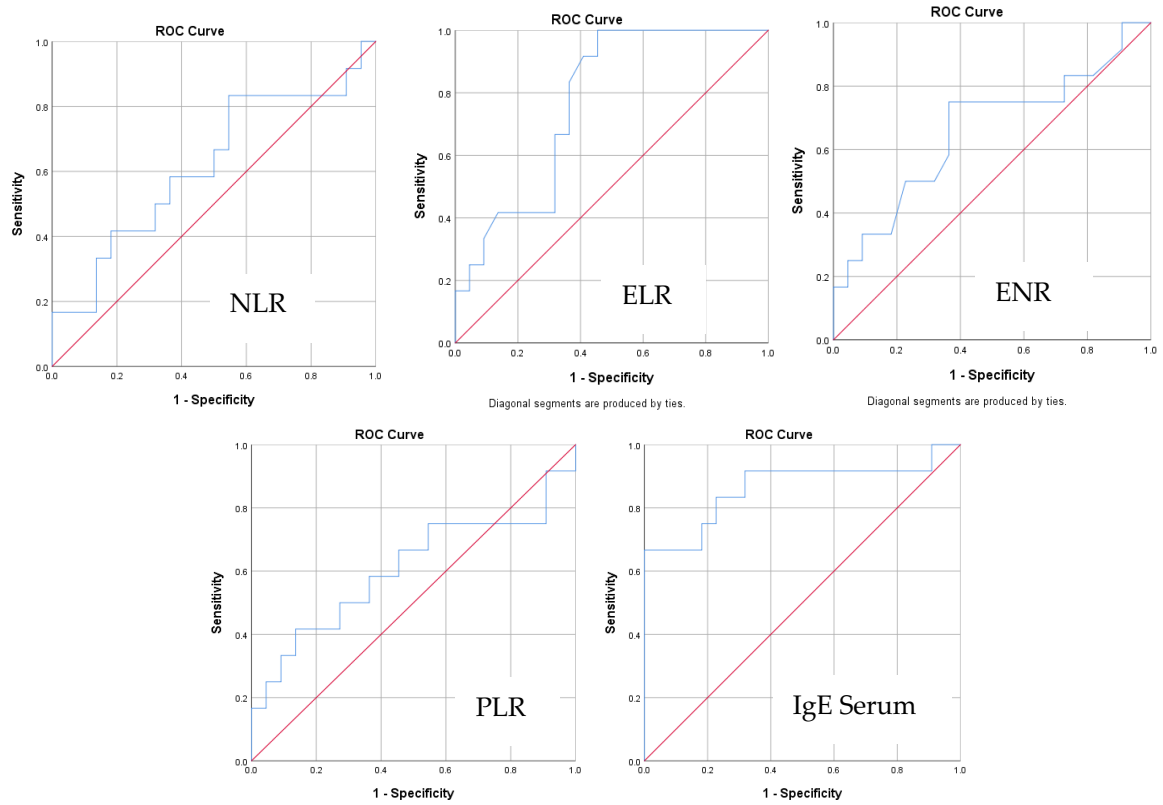

Figure 1. ROC curve of systemic inflammatory marker cutoff points based on AD severity

Eosinophil neutrophil ratio

Statistical analysis showed an insignificant association between ENR and AD severity. Patients with an ENR ≥ 0.106 had a 5.3 times greater risk of developing severe AD than patients with an ENR < 0.105, but this was not statistically significant (PR = 5.250 (95% CI 1.093 – 25.211); p = 0.073).

Platelet lymphocyte ratio

Statistical analysis showed an insignificant association between PLR and AD severity. Patients with PLR ≤ 135.2 had a 2.4 times greater risk of developing severe AD compared to patients with PLR < 135.2, but this was not statistically significant (PR = 2.400 (95% CI 0.555 – 10.381); p = 0.297).

Serum immunoglobulin E

Statistical analysis revealed a significant association between serum IgE and AD severity. Patients with serum IgE levels ≥ 418.65 had a 19 times greater risk of developing severe AD compared to patients with serum IgE levels < 418.65 (PR = 19.000 (95% CI 3.185 – 113.351); p = 0.001).

Based on multivariate analysis using logistic regression, it was found that age, ELR, and serum IgE played a role in the severity of AD in this study. Patients with serum IgE ≥ 418.65 significantly had a 42- fold risk, patients with ELR ≥ 0.217 had a 22.3-fold risk, and patients aged ≥ 38 years had an 18.6-fold risk of having severe AD (**Table 8**).

Table 7. Association of systemic inflammatory markers with AD severity

Parameters	Atopic Dermatitis Severity		PR (CI95%)	P value
	Severe	Mild-Moderate		
NLR				
- ≥ 1.865	7 (58.3)	8 (36.4)	2.450	0.383[a]
- < 1.865	5 (41.7)	14 (63.6)	(0.581-10.334)	
ELR				
- ≥ 0.217	9 (75.0)	5 (22.7)	10.200	0.005[b]
- < 0.217	3 (25.0)	17 (77.3)	(1.971-52.775)	
ENR				
- ≥ 0.105	9 (75.0)	8 (36.4)	5.250	0.073[a]
- < 0.105	3 (25.0)	14 (63.6)	(1.093-25.211)	
PLR				
- ≤ 135.2	8 (66.7)	10 (45.5)	2.400	0.297[b]
- > 135.2	4 (33.3)	12 (54.5)	(0.555-10.381)	
IgE Serum				
- ≥ 0.217	9 (75.0)	3 (13.6)	19.000	0.001[b]*
- < 0.217	3 (25.0)	19 (86.4)	(3.185-113.351)	

[a]Chi Square Test, [b]Fisher Exact Test *p<0.05

Table 8. Systemic inflammatory markers of AD severity

Parameters	CrudePR*	P value	AdjustedPR**	P value
Age	6,300	0,026*	18,667	0,043*
ELR	10,200	0,005*	22,349	0,037*
ENR	5,250	0,073	0,305	0,521
IgE Serum	19,000	0,001*	42,703	0,025*

*Chi Square Test, **Logistic Regression, *p<0.05

Discussions

The prevalence of AD varies by country, ranging from 1 to 40%. Atopic dermatitis can affect all races, with prevalence ranging from 10 to 30% in children and 2 to 10% in adults.[10] Data collected from January 2022 to December 2023 from 13 Dermatology and Venereology Polyclinics at Specialist Medical Education Institution Hospitals in Indonesia recorded 243 (0.9%) cases of AD in children and 223 (0.86%) in adults out of a total of 25,930 new patients.[11] Sociodemographic characteristics and gender in this study revealed a female predominance (70.6%). These results align with studies by Munthaha et al. and Johansson et al. which reported that AD is significantly more common in girls than in boys.[12, 13]

Menarche and pregnancy are physiological states in which sex steroids change endogenously. Atopic dermatitis worsens during the premenstrual phase in 33% to 64% of subjects and during pregnancy in 52% to 61% of subjects. This suggests that hormonal factors, such as the effects of estrogen and progesterone on the Th2 immune response and skin barrier integrity, may exacerbate AD predisposition in women.[14]

This study found that the majority of AD patients were aged 27–35 years (38.2%), with a mean age of 37.71 years (range 18 to 68). A study by Blauvelt et al. reported that AD patients had a mean age of 36 years, with a range of 18 to 76 years.[15] A study by Silverberg et al. reported that the majority of AD patients were aged 18–40 years (63%).[16] The prevalence and incidence of AD in the adult population show an increase, both in cases with new onset in adulthood without a previous history, and in patients experiencing relapses after a long remission since childhood.[17]

SCORing Atopic Dermatitis is one of the most frequently used parameters and is a validated scoring system for AD.[3, 4] In this study, based on the SCORAD index, 12 (35.3%) patients with severe AD were found, while 24 (64.7%) patients with mild-moderate AD were found. A cross-sectional study by Maspero et al. reported that mild and moderate AD patients were more common than severe AD patients, with the highest percentage being moderate (67.89%).[18]

There was an age difference between severe and mild-moderate AD patients in this study. Severe AD patients were older than mild-moderate AD patients. AD patients aged ≥ 38 years had a 19-fold increased risk of developing severe AD compared to patients aged <38 years. The results of this study are similar to the observational cross-sectional study by Salava et al. reported that older age was significantly associated with severe AD, with the majority of severe AD patients having a mean age of 37 years ($p = 0.020$).[19] As age increases, skin barrier function decreases due to reduced levels of filaggrin, ceramide, and natural moisturizing factor (NMF), leading to increased TEWL, skin pH, and susceptibility to irritation and allergens.[20] The inflammatory response also becomes more persistent and slow to subside due to the accumulation of oxidative stress and increased proinflammatory mediators such as IL-6, IL-1β, and TNF-α, which are often increased in elderly AD patients.[21, 22]

Platelets and leukocyte subsets have been reported to play a role in the systemic inflammatory process in AD patients.[7] The neutrophil-lymphocyte ratio, ELR, ENR, and PLR reflect the balance of the innate and adaptive immune systems.[23, 24] This study found that systemic inflammatory markers that differed based on AD severity were ELR and serum IgE. Patients with severe AD had significantly higher ELR and serum IgE levels. Meanwhile, NLR, ENR, and PLR levels in severe AD patients were higher than those in mild-moderate AD patients, but this was not statistically significant. Systemic inflammatory markers ELR ≥ 0.217 and serum IgE ≥ 418.65 can be considered a more objective parameter for assessing the severity of AD.

Patients with ELR ≥ 0.217 significantly increased their risk of developing severe AD by 22 times. A cross-sectional, analytical observational study by Sakata et al. reported that ELR correlated significantly with AD severity ($p = 0.002$).[25] These results are also consistent with a population-based retrospective cohort study by Weissmann et al. which reported that high ELR values were identified as a high-risk indicator for developing severe AD.[8] Eosinophils play a central role in the pathogenesis and severity of AD through cytotoxic and neuroimmunological activities.[26] Eosinophils release granule proteins such as eosinophil cationic protein (ECP), eosinophil peroxidase (EPO), and major basic protein (MBP) that damage keratinocytes and trigger the release of alarmins such as IL-33.[27] This activation stimulates basophils, mast cells, and eosinophils themselves, amplifying type 2 inflammation in the skin. Eosinophils also play a role in the neuroimmune pruritus circuit, where IL-31 and brain-derived neurotrophic factor (BDNF) released by eosinophils stimulate the growth and activation of sensory nerve fibers. The activated neurons then release substance P, which enhances eosinophil recruitment and produces the sensation of itching. This bidirectional interaction between eosinophils and sensory nerves creates a chronic inflammatory pruritic cycle, which is a hallmark of severe AD.[26,28]

Elevated serum IgE levels are an immunological response frequently associated with AD. Elevated IgE levels are associated with an increased risk of anaphylaxis and dysregulation of cytokine mediators.[5] In this study, the serum IgE levels in AD patients ranged from 400.57 to 9887.4, indicating high serum IgE levels. These results are similar to a cross-sectional study by Salava et al. which reported serum IgE levels in severe AD patients ranging from 271.25 to 9888.[19] This study also reported that patients with serum IgE levels ≥ 418.65 had a significantly 42-fold increased risk of developing severe AD.

Immunoglobulin E plays a major role in allergen-induced inflammatory processes in various atopic diseases by binding to various immune cells through different FcεRIs and acting as effectors for the release of chemical mediators and regulating cytokine production.[6] Severe AD patients have the highest serum IgE levels and it has been reported that serum IgE correlates with the severity, the more severe the AD, the higher the patient's serum IgE levels. Immunoglobulin E plays a central role in the pathogenesis of AD through the activation of allergic and inflammatory type 2 immune pathways. Immunoglobulin E binds to FcεRIs on the surface of mast cells and basophils, which are activated upon re-exposure to specific allergens. This activation triggers mast cell degranulation and the release of pro-inflammatory mediators such as histamine, prostaglandins, and leukotrienes, which contribute to itching, erythema, and edema in the skin. The

involvement of IgE also enhances eosinophil activation and Th2 responses through interactions with cytokines such as IL-4 and IL-13, which exacerbate skin barrier damage and prolong the inflammatory phase.[29,30] Therefore, IgE not only plays a role as an immunological marker, but also as an important clinical marker for assessing prognosis and response to therapy in patients with AD.

Conclusions

This study is novel compared to previous studies because it identified a cutoff point for ELR and serum IgE as markers of AD severity. Furthermore, the risk of severe AD was determined based on ELR and serum IgE levels. Patients with ELR ≥ 0.217 had a 22-fold increased risk, and patients with serum IgE ≥ 418.65 had a 42-fold increased risk of severe AD. Systemic inflammatory markers that showed a significant association with AD severity is ELR, and serum IgE levels were also significantly associated with AD severity, suggesting their potential as objective evaluation for assessing AD severity.

Conflict of Interest

The authors declare no conflict of interest.

Acknowledgment

The authors declare that there are no acknowledgments to be made.

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