Cukurova Medical Journal
ÇUKUROVA ÜNİVERSİTESİ TIP FAKÜLTESİ

Cukurova Med J 2026;51(1):349-360
DOI: 10.17826/cumj.1840817

RESEARCH

Role of serum albumin and inflammatory markers in predicting anaphylaxis severity in the emergency department

Acil serviste anafilaksi şiddetini öngörmede serum albümin ve inflamatuar belirteçlerin rolü

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Abstract

Purpose: This study investigates whether routinely measured hematological and biochemical parameters can help predict severe anaphylaxis in emergency department (ED) patients.

Materials and Methods: This retrospective study analyzed patients diagnosed with anaphylaxis who presented to the ED between 2018 and 2023. Clinical severity was categorized as mild, moderate, or severe. Data included demographic characteristics, clinical findings, and laboratory parameters: serum albumin, C-reactive protein (CRP), hemoglobin, neutrophil-to-lymphocyte ratio, and mean platelet volume to platelet count ratio (MPV/PC). The predictive accuracy of significant variables was assessed through receiver operating characteristic analysis, with corresponding area under the curve (AUC) values reported.

Results: Among the 104 patients, 28 (26.9%) were classified as having severe anaphylaxis. The serum albumin concentration was significantly lower in this group ($p = 0.004$). A cutoff of ≤40.8 g/L yielded an AUC of 0.714 (95% confidence interval: 0.614–0.814), with 85.7% sensitivity and 56.6% specificity. In multivariate analysis, serum albumin, CRP, hemoglobin levels, and the MPV/PC ratio were independently associated with anaphylaxis severity.

Conclusion: The findings suggest that serum albumin, a widely accessible and cost-effective laboratory parameter, is associated with severe anaphylaxis and may support risk stratification in ED settings.

Keywords: Anaphylaxis, biomarkers, serum albumin, emergency department, risk assessment

Öz

Amaç: Bu çalışma, acil servis (AS) hastalarında şiddetli anafilaksiyi tahmin etmede rutin olarak ölçülen hematolojik ve biyokimyasal parametrelerin yardımcı olup olamayacağını araştırmaktadır.

Gereç ve Yöntem: Bu retrospektif çalışmada, 2018–2023 yılları arasında AS'e başvuran ve anafilaksi tanısı alan hastalar analiz edilmiştir. Klinik şiddet; hafif, orta ve şiddetli olarak sınıflandırılmıştır. Veriler; demografik özellikler, klinik bulgular ile serum albümin, C-reaktif protein (CRP), hemoglobin, nötrofil/lenfosit oranı ve ortalama trombosit hacmi/trombosit sayısı oranı (MPV/PC) gibi laboratuvar parametrelerini içermektedir. Anlamlı değişkenlerin öngörücü doğruluğu, alıcı işletim karakteristiği analizi ile değerlendirilmiş ve karşılık gelen eğri altındaki alan (AUC) değerleri raporlanmıştır.

Bulgular: 104 hastadan 28'i (%26,9) şiddetli anafilaksi olarak sınıflandırıldı. Bu grupta serum albümin konsantrasyonu anlamlı derecede daha düşüktü ($p = 0,004$). ≤40,8 g/L albümin kesim noktası için AUC değeri 0,714 (%95 güven aralığı: 0,614–0,814) olup, duyarlılık %85,7 ve özgüllük %56,6 olarak saptandı. Çok değişkenli analizde, serum albümin, CRP, hemoglobin düzeyleri ve MPV/PC oranı, anafilaksi şiddeti ile bağımsız olarak ilişkiliydi.

Sonuç: Bulgular, yaygın olarak erişilebilir ve uygun maliyetli bir laboratuvar parametresi olan serum albüminin şiddetli anafilaksi ile ilişkili olduğunu ve AS ortamlarında risk sınıflandırmasını destekleyebileceğini göstermektedir.

Anahtar kelimeler: Anafilaksi, acil servis, biyobelirteçler, risk değerlendirmesi, serum albumin

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Received: 12.12.2025 Accepted: 09.03.2026

INTRODUCTION

Anaphylaxis is a systemic allergic reaction that can emerge immediately or a few minutes after exposure to an allergen. The severity of the resulting reactions can range from mild to life-threatening[1]. It represents 0.04% and 0.33% of all emergency department (ED) presentations[2]. Severe anaphylaxis has been reported in 12.2-42.3% of all anaphylaxis cases and approximately 0.01-0.03% of the total population[3]. Epidemiological data over recent years have demonstrated a gradual increase in the incidence of anaphylaxis, which may be attributed not only to improved recognition and documentation but also to a true rise in the global prevalence of allergic diseases[4].

Anaphylaxis may involve multiple organ systems and present with a wide range of clinical manifestations[5,6]. Given its potential for rapid progression, early recognition and timely intervention are crucial. However, marked variability in clinical presentation can complicate severity assessment. Current diagnostic systems, including those proposed by the World Allergy Organization (WAO), are largely based on clinical findings and lack support from standardized laboratory biomarkers[7]. This limitation is particularly evident in patients without cutaneous symptoms, such as urticaria or angioedema, which are absent in approximately 10% of cases[8]. Although several scoring systems have been developed, their applicability in emergency settings remains limited due to symptom variability and reliance on clinical judgment[9].

Recent immunopathological studies have highlighted the central role of immune and inflammatory pathways in anaphylaxis[10]. While mast cells are traditionally regarded as key effector cells, other immune components—including eosinophils, basophils, neutrophils, and platelets—also contribute to systemic reactions. Despite this complex immunological background, no widely accepted laboratory biomarker currently exists for objectively assessing the severity of anaphylactic episodes[11]. Although several potential markers have been explored, their routine use remains limited due to issues such as cost, availability, and delayed turnaround times, particularly in emergency settings[11].

Given the increasing number of anaphylaxis-related visits to EDs, early identification of patients at risk for severe reactions is essential. Readily available and cost-effective laboratory markers may facilitate timely treatment and appropriate follow-up[9,11]. Few studies in the literature examine the relationship between the clinical severity of anaphylaxis and laboratory parameters. This study aimed to evaluate the association of routinely measured inflammatory and acute-phase markers and complete blood count–derived indices with the severity of anaphylaxis. We hypothesized that these routinely available hematological and biochemical parameters are independently associated with severe anaphylaxis.

MATERIAL AND METHODS

Sample

This retrospective study included patients aged 18 years and older who were admitted to the Aksaray Training and Research Hospital Department of Emergency Medicine with a diagnosis of anaphylaxis or anaphylactic shock (ICD diagnostic codes T78.0 and T78.2) between January 2018 and January 2023. Individuals were excluded if essential clinical or laboratory data were unavailable, if they had been transferred from another medical institution, or if prehospital cardiac arrest had occurred.

Patients with prior systemic corticosteroid use before presentation, hepatic or renal failure, bronchial asthma, cardiac arrhythmias, rheumatic diseases, or hematological and solid organ malignancies were also excluded because these conditions could interfere with systemic inflammatory responses and laboratory parameters. One hundred four patients aged 18–75 years were included. Patients diagnosed with anaphylaxis were classified into mild, moderate, and severe groups. The patient selection process is summarized in the flow diagram (Figure 1).

Procedure

Ethical approval for the study was obtained from the clinical research ethical committee of Aksaray University Faculty of Medicine (decision number: 2022/16-02; approval date: 13 October 2022). The research was conducted in conformity with the principles of the Declaration of Helsinki. Patients' sociodemographic data, personal histories, allergy histories, presentation time, length of hospital stay, suspected triggers, clinical signs, vital findings, and laboratory parameters were retrieved retrospectively from the electronic database.

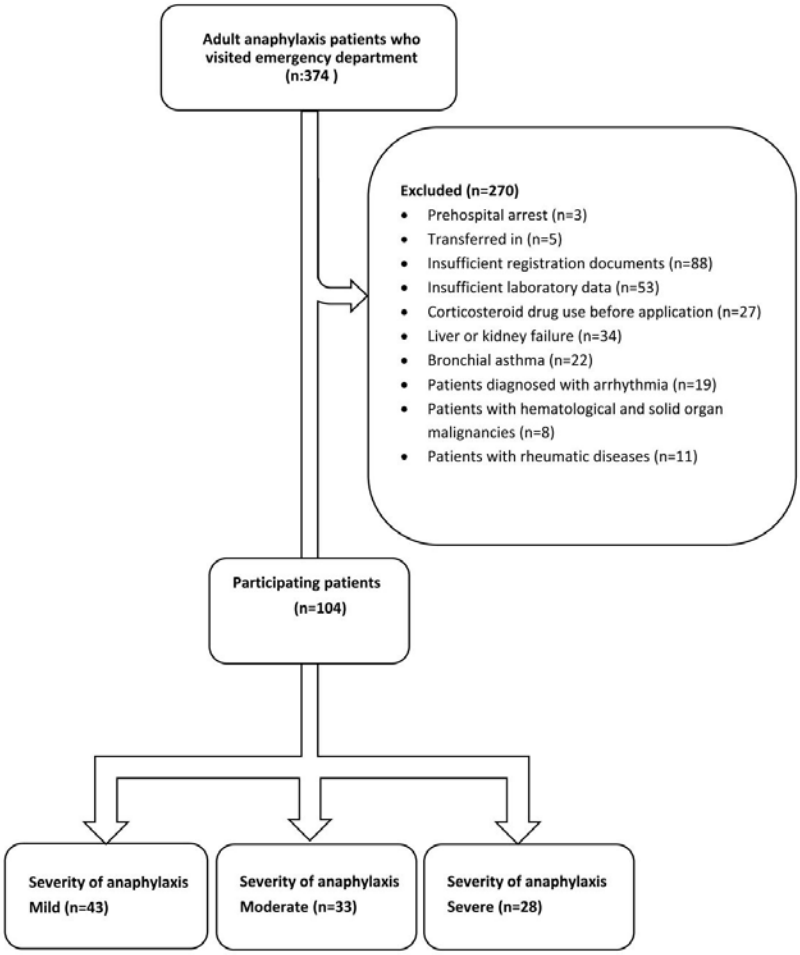

Figure 1. Study flow diagram

Definition of anaphylaxis and assessment of the clinical severity of anaphylaxis

Anaphylaxis was defined in accordance with the diagnostic criteria proposed by the European Academy of Allergy and Clinical Immunology (EAACI)[12]. For this retrospective analysis, ED records were reviewed to verify that patients fulfilled the EAACI criteria based on documented clinical manifestations at presentation.

Clinical severity was determined retrospectively using predefined criteria derived from the EAACI recommendations. Severity assessment relied on objective clinical information recorded at the time of admission, including vital signs, the extent of organ system involvement, and evidence of respiratory or cardiovascular compromise. Based on these standardized criteria, patients were classified into mild, moderate, or severe anaphylaxis categories. The criteria employed to determine disease severity are shown in Table 1[12,13].

Hematological and biochemical parameters

Peripheral venous blood samples were taken from the patients at admission to the ED. Dry tubes were used for biochemical analysis, and EDTA tubes were used for hematological tests. The Coulter Counter LH Series (Beckman Coulter Inc., Hialeah, FL, USA), an automated hematology device, analyzed patients' hematinic parameters. The biochemical measurements were determined by an automated biochemistry analyzer (Abbott Laboratories, Abbott

Park, IL, USA). Routine laboratory parameters such as aspartate aminotransferase (AST, 0-50 U/L), alanine aminotransferase (ALT, 0-50 U/L), creatinine (0.51- 0.95 mg/dl), CRP (0-5 mg/L), serum albumin (35–52 g/L), hemoglobin (11-16 g/dl), leukocyte (4-10 10^9/L), neutrophil (2-7 10^9/L), lymphocyte (0.8-4 10^9/L), eosinophil (0.02- 0.50 10^9/L), monocyte (0.12-1.20 10^9/L), platelet count (PC, 100-400 10^9/L), and mean platelet volume (MPV, 6.5-12 fl) were recorded. The neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), and MPV/PC were calculated from those data.

Table 1. Severity of anaphylaxis

Grade	Clinical features
Mild (skin and mucosal findings only)	Generalized erythema, urticaria, periorbital edema, or angioedema
Moderate (features suggesting respiratory, cardiovascular, or gastrointestinal findings)	Dyspnea, stridor, wheeze, chest or throat tightness, diaphoresis, abdominal pain, nausea, vomiting, dizziness (presyncope)
Severe (hypoxia, hypotension, or especially neurologic findings)	Cyanosis or SpO_2 < 92% at any stage, hypotension (SBP < 90 mm Hg in adults), confusion, collapse, loss of consciousness or incontinence

SBP: Systolic blood pressure; SpO_2: Peripheral oxygen saturation.

Statistical analysis

Categorical variables are presented as frequency (percentage); numerical variables are presented as mean±standard deviation if distributed normally and as median (minimum-maximum) otherwise. The assumption of normality was tested using Shapiro–Wilk's test. The chi-square goodness of fit test was used to test the effect of season on the distribution of anaphylaxis cases. Categorical variables were compared with Pearson's Chi-Square and Fisher's Exact test between the anaphylaxis severity groups. The comparison of numerical variables between the study groups was made using the One-Way Analysis of Variance (ANOVA) test when the parametric test assumptions were met and the Welch (violation of homogeneity of variances)/Kruskal-Wallis (violation of normality) test when the assumptions were violated. Bonferroni corrected Dunn's test, and Games-Howell tests were used for post-hoc comparisons of the Kruskal-Wallis and Welch's test results, respectively. Spearman's correlation coefficient was used to assess the correlation between anaphylaxis severity and numerical variables. The risk factors of severe anaphylaxis were determined using the Binary Logistic Regression Model, and variables with a significance level less than 0.20 were included in the Multiple Binary Logistic Model. The Forward Likelihood Ratio method was used for variable selection. The diagnostic ability of the variables found to be significant in group comparisons was assessed with Receiver Operating Characteristic Curve (ROC) analysis, and Youden's index was used to determine the cut-off value. All statistical analyses were performed using Statistical Package for Social Sciences (SPSS, Version 21.00. Armonk, NY: IBM Corp.), and p-values less than 0.05 were considered statistically significant.

Sample size adequacy was additionally evaluated using post hoc power analyses based on the main statistically significant findings. In the multivariable logistic regression model, hemoglobin level was identified as an independent predictor of severe anaphylaxis (OR=1.827). After standardization to a one–standard deviation increase (SD=2.3), the estimated effect size corresponded to an approximate OR of 4.00. Post hoc power analysis using G*Power (version 3.1) indicated a statistical power of 0.99 ($1-\beta$). In addition, the statistical power of the ROC analysis for serum albumin was 0.935, calculated using the pROC package in R (version 4.4.3) based on an AUC of 0.714 with 28 cases and 76 controls ($\alpha = 0.05$). These findings indicate that the sample size was sufficient for the primary analyses.

RESULTS

One hundred four patients with a mean age of 47.2 ± 13.8 years, 55 males (M: 52.9%) were enrolled in the study. Anaphylaxis was mild in 43 (41.3%) patients, moderate in 33 (31.7%), and severe in 28 (26.9%). Anaphylaxis was triggered by drugs in 53 patients (51.0%), venom in 27 (26.0%), and

foodstuffs in seven (6.7%). No triggering agent could be identified in eight (7.7%) patients. In terms of seasonal distribution, 13 (12.5%) cases occurred in spring, 38 (36.5%) in summer, 21 (20.2%) in the fall, and 32 (30.8%) in winter, with a statistically significant increase in numbers being observed during the summer (p=0.002).

Analysis of vital findings revealed a significant decrease in systolic and diastolic blood pressure and significantly higher heart rate elevation in the severe group than in the other groups (p<0.001 for all). Oxygen saturation was significantly lower and respiratory rate significantly higher in the moderate and severe groups compared to the mild group (p<0.001 for both, Table 2). Evaluation of system involvements in terms of disease severity revealed significant differences. The most common system involvement in all the groups was cutaneous-mucosal involvement, and the rate of such involvement was significantly lower in the severe group (7.1%) than in the other groups. The cardiovascular system (CVS) was the second most involved system. The incidence of CVS findings was significantly higher in the severe group (53.6%) than in the mild-moderate group. The least frequently detected findings were neurological findings. The incidence of neurological findings in severe anaphylaxis was significantly higher than in moderate anaphylaxis (p<0.001, Table 2).

As anticipated, intensive care requirements were highest in the severe disease group (p<0.001). While no mortality occurred in the mild and moderate disease groups, one patient from the severe group died from drug-induced anaphylaxis.

Table 2. Comparison of clinical findings according to the severity of anaphylaxis

Parameters		**Severity of anaphylaxis**			
	Total (n=104)	**Mild (n=43)**	**Moderate (n=33)**	**Severe (n=28)**	**p-value**
Gender, n (%)					
Male	55 (52.9)	17 (39.5)	21 (63.6)	17 (60.7)	0.071*
Female	49 (47.1)	26 (60.5)	12 (36.4)	11 (39.3)	
Age (years)	47.2 ± 13.8	46.6 ± 13.7	47.9 ± 13.1	47.3 ± 15.3	0.918##
Allergy history, n(%)	30 (28.8)	16 (37.2)	8 (24.2)	6 (21.4)	0.279*
Trigger agent, n(%)					
Food	7 (6.7)	5 (11.6)	1 (1.0)	1 (3.6)	
Drug	53 (51.0)	18 (41.9)	20 (60.6)	15 (53.6)	
Venom	27 (26.0)	11 (25.6)	7 (21.2)	9 (32.1)	
Unknown	8 (7.7)	5 (11.6)	2 (6.1)	1 (3.6)	
Other	9 (8.7)	4 (9.3)	3 (9.1)	2 (7.1)	
Systolic BP, mmHg	115 (60-180)	125 (90-180)[a]	120 (90-165)[a]	80 (60-150)[b]	<0.001#
Diastolic BP, mmHg	75 (30-100)	75 (50-100)[a]	75 (40-100)[a]	50 (30-100)[b]	<0.001#
Heart rate, per/minute	95 (55-130)	89 (67 -115)[a]	95 (55-125)[a]	110 (65-110)[b]	<0.001#
Saturation, %	94 (65-100)	95 (92-100)[a]	93 (83-99)[b]	90 (65-96)[b]	<0.001#
Respiratory rate, per/minute	28 (20-88)	25 (20-30)[a]	28 (20-35)[b]	30 (25-88)[b]	<0.001#
System involved, n(%)					
Respiratory	16 (15.4)	3 (7.0)[a]	9 (27.3)[b]	4 (14.3)[a,b]	<0.001**
Cardiovascular	21 (20.2)	2 (4.7)[a]	4 (12.1)[a]	15 (53.6)[b]	
Gastrointestinal	11 (10.6)	4 (9.3)	6 (18.2)	1 (3.6)	
Neurological	10 (9.6)	4 (9.3)[a,b]	0 (0.0)[b]	6 (21.4)[a]	
Cutaneous-Mucosal	46 (44.2)	30 (69.8)[a]	14 (42.4)[a]	2 (7.1)[b]	
Intensive care, n(%)	14 (13.5)	2 (4.7)[a]	1 (3.0)[a]	11 (39.3)[b]	<0.001**
Mortality, n(%)	1 (1.0)	0 (0.0)	0 (0.0)	1 (3.6)	0.269**

Numerical variables are presented as mean±standard deviation if distributed normally and as median (minimum-maximum) otherwise.
[a,b]: Groups with different superscripts indicate Bonferroni-corrected statistical significance at the 0.05 level.
*: Pearson Chi-Square Test, **: Fisher's Exact Test, #: Kruskal-Wallis Test, ##: One Way Analysis of Variance (ANOVA)
BP: Blood pressure; mmHg: millimeters of mercury; n: number of patients.

Evaluation of biochemical parameters revealed that albumin and CRP significantly affected disease severity. Albumin levels were significantly lower in the severe group than in the other groups (p=0.004, Table 3). A moderate negative correlation was observed between disease severity and albumin (ϱ(rho)=-0.606; p=0.001, Table 4, Figure 2). Although no significant intergroup difference was determined in CRP levels, a 1 mg/L increase in CRP resulted in a 4.4% rise in the risk of severe anaphylaxis [OR (95% CI):1.045 (1.010-1.081), p=0.012, Table 5].

Examination of hematological parameters showed that hemoglobin, leukocyte, neutrophil, eosinophil, and platelet values significantly affected disease severity (Tables 3 and 4). Mean hemoglobin was significantly lower in the mild disease group than in the moderate and severe groups (p=0.002). A significant weak positive correlation was observed between hemoglobin levels and the severity of anaphylaxis (ϱ(rho)=0.223; p=0.023).

White blood cell levels were significantly higher in the moderate and severe groups than in the mild group (p=0.001). Neutrophil levels were higher in the severe group than in the other groups (p=0.005, Table 3). Disease severity was positively correlated with leukocyte and neutrophil levels, with these values rising in line with severity (ϱ(rho)=0.236; p=0.016, ϱ(rho)=0.295; p=0.002, respectively, Table 4). A one-unit increase in neutrophil levels increased the risk of severe anaphylaxis by 14.2% [OR (95% CI): 1.142 (1.020-1.279), p=0.022, Table 5].

No significant difference was observed between the groups' eosinophil or platelet levels. A weak, negative correlation was found between eosinophil and platelet levels and disease severity, these values decreasing as severity increased (ϱ(rho)=-0.245; p=0.012, and ϱ(rho)=-0.195; p=0.047, respectively). A 50 10^9/ul unit decrease in platelet levels increased the severity of anaphylaxis by 31.5% [OR(95% CI): 0.685 (0.501-0.937), p=0.018, Table 5].

Table 3. Comparison of laboratory findings according to the severity of anaphylaxis

Parameters		Severity of anaphylaxis			
	Total (n=104)	**Mild (n=43)**	**Moderate (n=33)**	**Severe (n=28)**	**p-value**
Creatinine (mg/dl)	0.82 (0.46-4.52)	0.76 (0.50-4.51)	0.91 (0.56-1.64)	0.94 (0.46-4.52)	0.039#
Albumin (g/L)	40.3 (28.1-48.1)	41.2 (33.8-47.8)[a]	41.0 (32.8-48.1)[a]	39.3 (28.1-42.4)[b]	0.004#
ALT (U/L)	16.6 (4.7-171.1)	17.2 (4.7-123.5)[a]	16.7 (7.8-171.1)[a,b]	12.9 (7.0-33.4)[b]	0.033#
AST (U/L)	19 (10-90)	20 (10-33)	20 (14-90)	18.5 (13-42)	0.257#
CRP (mg/L)	4.1 (0.1-167.6)	4.1 (0.3-35.1)	2.2 (0.1-52.3)	6.2 (0.3-167.6)	0.279#
Leukocyte (x10^9/L)	9.95 (4.70-27.65)	9.11 (4.70-23.21)[a]	11.38 (6.15-27.65)[b]	11.52 (6.76-21.00)[b]	0.001#
Lymphocyte (x10^9/L)	3.39 ± 1.67	3.03 ± 1.26[a]	4.05 ± 1.95[b]	3.17 ± 1.71[a,b]	0.021##
Monocyte (x10^9/L)	0.51 (0.09-1.41)	0.48 ± 0.18	0.58 ± 0.29	0.59 ± 0.29	0.093###
Neutrophil (x10^9/L)	5.95 (0.26-25.24)	5.38 (2.20-19.52)[a]	5.96 (0.26-25.24)[a,b]	7.29 (3.27-15.71)[b]	0.005#
Eosinophil (x10^9/L)	0.13 (.00-0.58)	0.13 (0.01-0.58)	0.15 (0.01-0.52)	0.09 (0.00-0.38)	0.045#
Hemoglobin (gr/dL)	14.8 ± 2.3	14.0 ± 1.7[a]	15.2 ± 1.8[b]	15.7 ± 2.9[b]	0.002###
Platelet count (x10^9/L)	282 ± 74	287 ± 62	300 ± 70	253 ± 87	0.081###
MPV (fL)	9.9 ± 1.1	10.1 ± 0.9	9.6 ± 1.0	9.9 ± 1.3	0.075###
NLR	1.68 (0.06-20.63)	1.69 (0.47-20.63)[a,b]	1.24 (0.06-17.41)[a]	2.49 (0.91-20.63)[b]	0.030#
PLR	84.47 (29.61-382.56)	95.32 (54.77-382.56)	74.43 (29.61-344.17)	80.71 (38.16-330.23)	0.074#
MPV/PC	0.03 (0.02-0.12)	0.04 (0.02-0.12)	0.03 (0.02-0.05)	0.04 (0.02-0.12)	0.184#

Numerical variables are presented as mean±standard deviation if distributed normally and as median (minimum-maximum) otherwise.
[a,b]: Groups with different superscripts indicate Bonferroni-corrected statistical significance at the 0.05 level.
*: Pearson Chi-Square Test, **: Fisher's Exact Test, #: Kruskal-Wallis Test, ##: One Way Analysis of Variance (ANOVA), ###: Welch Test.; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; CRP: C-reactive protein; MPV: Mean platelet volume; MPV/PC: Mean platelet volume to platelet count ratio; NLR: Neutrophil-to-lymphocyte ratio; PC: Platelet count; PLR: Platelet-to-lymphocyte ratio.

Table 4. Severity of anaphylaxis and correlations with laboratory finding

Anaphylaxis Severity	Spearman's rho (ϱ)	p-value
Creatinine	0.174	0.077
Albumin	-0.329	0.001
ALT	-0.254	0.009
AST	-0.155	0.116
CRP	0.139	0.159
Leukocyte	0.236	0.016
Lymphocyte	-0.076	0.444
Monocyte	0.099	0.319
Neutrophil	0.295	0.002
Eosinophil	-0.245	0.012
Hemoglobin	0.223	0.023
Platelet count	-0.195	0.047
MPV	0.013	0.896
NLR	0.100	0.310
PLR	-0.187	0.058
MPV/PC	0.039	0.694

ϱ: Spearman correlation coefficient; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; CRP: C-reactive protein; MPV: Mean platelet volume; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; MPV/PC: Mean platelet volume to platelet count ratio.

Table 5. Predictive parameters for severe anaphylaxis

Parameter	Univariate		Multiple	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (1-year increase)	1.001 (0.970-1.033)	0.957		
Gender (Female)	0.647 (0.268-1.563)	0.333		
Allergy history	0.591 (0.212-1.645)	0.314		
Creatinine (0.1 mg/dL increase)	1.041 (0.968-1.120)	0.280		
Albumin (1 unit increase)	0.804 (0.699-0.925)	0.002	0.793 (0.668-0.942)	0.008
ALT (1 U/L increase)	0.934 (0.872-1.000)	0.049		
AST (1 U/L increase)	0.972 (0.917-1.032)	0.352		
CRP (1 mg/L increase)	1.045 (1.010-1.081)	0.012	1.044 (1.007-1.082)	0.019
Leukocyte (1 unit increase)	1.117 (1.001-1.246)	0.048		
Lymphocytes (1 unit increase)	0.894 (0.683-1.169)	0.894		
Monocyte (0.1 unit increase)	1.116 (0.943-1.321)	0.202		
Neutrophil (1 unit increase)	1.142 (1.020-1.279)	0.022		
Eosinophil (0.1 unit increase)	0.646 (0.429-0.974)	0.037		
Hemoglobin (1 g/dL increase)	1.282 (1.044-1.574)	0.018	1.827 (1.330-2.508)	<0.001
Platelet (50 unit increase)	0.685 (0.501-0.937)	0.018		
MPV (1 unit increase)	0.989 (0.666-1.467)	0.955		
NLR (1 unit increase)	1.094 (0.991-1.208)	0.074		
PLR (1 unit increase)	1.000 (0.993-1.006)	0.927		
MPV/PC (0.01 unit increase)	1.371 (1.057-1.779)	0.018	1.738 (1.192-2.534)	0.004

Abbreviations: ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; CI: Confidence interval; CRP: C-reactive protein; MPV: Mean platelet volume; MPV/PC: Mean platelet volume to platelet count ratio; NLR: Neutrophil-to-lymphocyte ratio; OR: Odds ratio; PLR: Platelet-to-lymphocyte ratio.

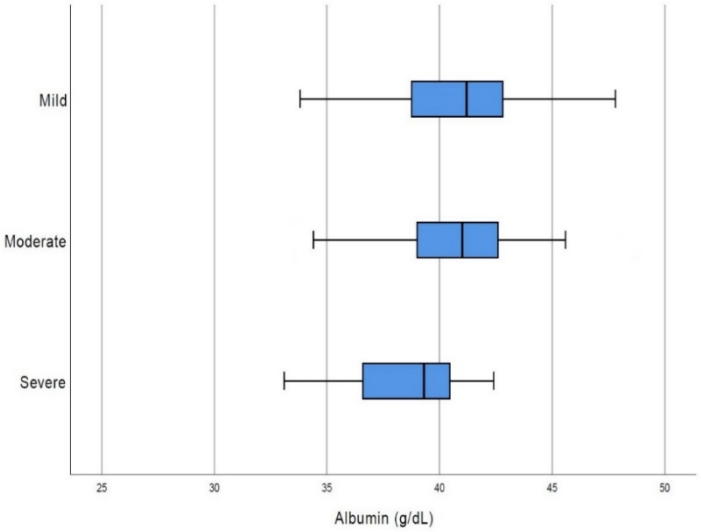

Figure 2. Correlation between albumin level and disease severity.

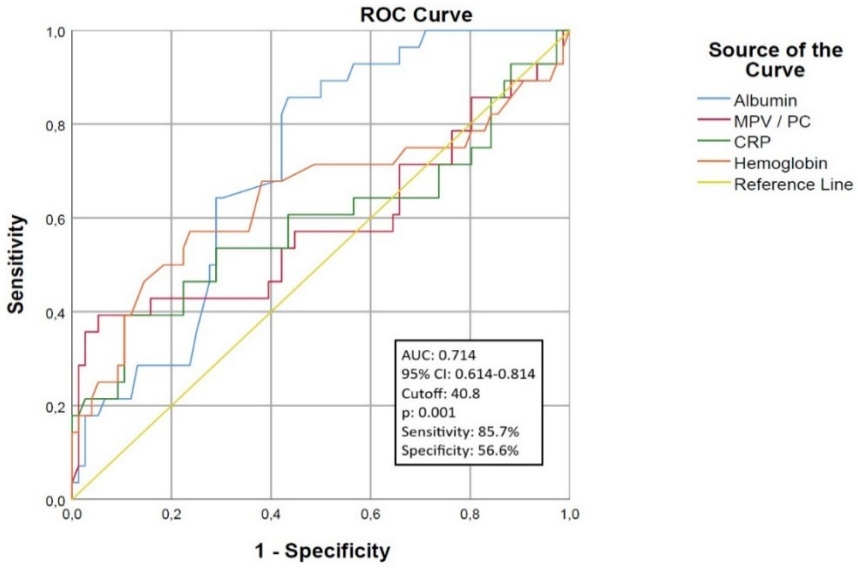

Figure 3. Receiver operating characteristic (ROC) curve analysis for anaphylaxis severity prediction.

AUC: Area under the curve; CI: Confidence interval; CRP: C-reactive protein; MPV/PC: Mean platelet volume to platelet count ratio.

The NLR was significantly higher in the severe group than the moderate group (p=0.03). A 0.01 unit increase in the MPV/PC ratio increased the risk of severe anaphylaxis by 37.1% in the univariate logistic regression model, while the risk in the multivariate model including the albumin, CRP, and hemoglobin variables increased that risk by 73.8% [OR(95% CI): 1.738 (1.192-2.534), p=0.004]. The ROC analysis was used to see how well the variables that were significantly different between the groups could tell

the difference between mild and severe anaphylaxis. The AUC values were found to be between 0.549 and 0.714. Of these variables, only the AUC value for albumin reached the acceptable level of discrimination [AUC (95% CI): 0.714 (0.614-0.814); p=0.001], and with the help of the Youden index, the cut-off value was obtained as ≤40.8. This cut-off value provides 85.7% sensitivity, 56.6% specificity, 42.1% positive predictive value, and 91.5% negative predictive value (Figure 3).

DISCUSSION

This study evaluated anaphylaxis patients presenting to the ED within the previous five years in terms of etiologies, clinical findings, and hematinic and biochemical parameters. Biomarkers capable of predicting the severity of anaphylaxis were investigated by examining their association with disease severity. We suggest that albumin, CRP, hemoglobin, NLR, and MPV/PC values are essential for detecting severe anaphylaxis. Our study emphasized that low albumin levels may be an independent indicator of severe anaphylaxis. The findings are valuable in predicting severe disease because the ability to predict severe anaphylaxis is important in deciding on treatment, the length of observation in the hospital, and reducing morbidity and mortality.

Severe anaphylaxis accounts for many anaphylaxis cases presenting to the ED. Kim et al. also determined severe anaphylaxis in 37.6% of their patients, the most common determinants being drugs, age, and male gender[3]. Brown et al. determined a prevalence of severe anaphylaxis of 17% and suggested a correlation between advanced age and severe disease[13]. Another cohort study involving a large patient population observed severe anaphylaxis at a rate of 11.6% and reported an association between drug-induced anaphylaxis and severe anaphylaxis[14]. Worm et al. identified advanced age, male gender, and accompanying mastocytosis as determinants of severe anaphylaxis[15]. The prevalence of severe anaphylaxis in the present study was greater, at 26.9%. In contrast to previous studies, no significant associations were detected between age or gender and the severity of anaphylaxis, although severe anaphylaxis was more common in males. Additionally, recent meta-analytic data have shown that the global incidence of anaphylaxis has been steadily increasing over time, with considerable variation across regions, likely influenced by differences in allergen exposure patterns, diagnostic criteria, and healthcare system structures[16]. Such variability may also contribute to the inconsistent associations between demographic factors and anaphylaxis severity reported in different cohorts.

The diagnosis and severity of anaphylaxis are established based on clinical symptoms[12]. There are no objective biomarkers for clearly determining the severity of the disease. The classification of clinical severity may, therefore, vary depending on the experience of the physician[17]. Our study observed that the most common involvement was cutaneous-mucosal (e.g., urticaria, angioedema, erythema, pruritus), consistent with the literature[18,19]. Observing the lowest involvement in the neurological system also supports previous studies[20,21]. A low level (7.1%) of cutaneous findings was observed in severe anaphylaxis, while CVS and neurological findings were more common. Cutaneous symptoms may not be observed or may emerge subsequently in approximately 10% of cases[21]. This shows that the level of severe anaphylaxis without cutaneous involvement is negligible.

CRP, widely used as a marker of systemic inflammation, may increase in infectious, autoimmune, and allergic conditions[22-24]. Importantly, CRP levels can also increase significantly in severe anaphylaxis, which may be overlooked in clinical practice. Elevated CRP in the context of anaphylaxis—especially when cardiovascular symptoms predominate and skin involvement is absent—can mimic septic shock, potentially leading to misdiagnosis and inappropriate treatment[24]. Clinicians should be aware that a combination of increased CRP and hypotension is not exclusive to infection and may indicate severe anaphylaxis. Moreover, recent research suggests that increased CRP levels during anaphylaxis may reflect endothelial activation in addition to systemic inflammation, particularly in severe cases involving cardiovascular compromise[25]. In our study, we further demonstrated that a one-unit increase in CRP corresponds to a 4.4% increase in the risk of severe anaphylaxis.

The use of the NLR for determining the prognosis of allergic diseases has been investigated in several studies. NLR elevation has been linked to disease severity in asthma, allergic rhinitis, and atopic dermatitis[26-28]. A recent study examined the relationship between NLR and the development of epinephrine-resistant refractory anaphylaxis.

Significantly low NLR, high lymphocyte count, and low neutrophil count were observed in the refractory anaphylaxis group compared to the non-anaphylactic group[29]. In our study, however, neutrophil levels and the NLR were significantly higher in severe disease, while no significant difference was observed in lymphocyte levels in the severe group. In another study, Yanagawa et al. reported high lymphocyte and hemoglobin levels in patients with anaphylactic shock. The authors reported that the presence of lymphocytosis without anemia at a routine complete blood count (CBC) is indicative of anaphylactic shock and that this can thus be differentiated from hemorrhagic, septic, and cardiogenic shocks[30].

MPV/PC values, the ratio of MPV to the platelet count, can be easily calculated from CBC. This study is the first to examine the MPV/PC ratio, one of the biomarkers we wish to emphasize in anaphylaxis, in particular. Platelet and MPV values have previously been examined in diseases such as asthma, chronic urticaria, and atopic dermatitis. However, MPV values have only been found to be significant in patients with urticaria[31,32]. Based on the results of this study, the severity of anaphylaxis increases with a decrease in platelet level and an increase in the MPV/PC ratio.

A global increase is observed in all-cause anaphylaxis rates and general hospital presentations[7]. However, despite that increase, anaphylaxis-related mortality rates are known to remain at the same levels or to exhibit a decreasing tendency. Anaphylaxis-related mortality is reported to be rare, with a prevalence of 0.5-1%[33]. Today's lower rate of anaphylaxis-related mortality may be attributable to the improved provision of emergency interventions or to the epinephrine autoinjectors that are prescribed. Mortality associated with drug-induced severe anaphylaxis occurred in one patient (0.96%) in the present study.

Albumin is a vital plasma protein that contributes to maintaining acid-base balance, mitigating inflammation, preserving vascular wall integrity, and binding a variety of endogenous and exogenous substances[34]. Albumin also provides defense against inflammation-induced tissue damage. In certain critical illnesses, the administration of albumin is employed to increase the plasma volume[35]. It has been recognized as a prognostic marker in a range of diseases, including cardiovascular conditions, stroke, sepsis, and chronic kidney disease. Furthermore, hypoalbuminemia is frequently linked with poorer outcomes in patients exhibiting shock manifestations[36,37]. Nevertheless, the prognostic significance of the serum albumin concentration in anaphylaxis and anaphylactic shock has remained largely unexplored. Our findings revealed that albumin concentrations are markedly lower in severe anaphylaxis cases compared to than in milder anaphylaxis cases, with a strong inverse correlation observed between albumin levels and disease severity. These results imply that low serum albumin may be a valuable biomarker for assessing anaphylaxis severity. Furthermore, the ability of albumin to maintain endothelial function and regulate inflammatory responses underscores its potential relevance in understanding the pathophysiology of severe anaphylaxis. Additional studies have explored the use of intravenous albumin beyond its volume-expanding effect in severe inflammatory conditions; however, its role in the management of anaphylaxis remains to be clearly defined.

Although the serum albumin level identified in our study demonstrated acceptable discriminatory performance in ROC analysis, its clinical utility should be interpreted with caution. Lower albumin levels were associated with a higher risk of a severe clinical course and may help identify patients with anaphylaxis who require prolonged observation or admission to the intensive care unit. While emergency interventions such as epinephrine administration and its repetition must remain guided by clinical assessment, our findings suggest that serum albumin may serve as a supportive parameter for early risk stratification following initial clinical stabilization in the ED.

This study has certain inherent limitations. Its retrospective design and single-center scope may limit the generalizability of the findings. Laboratory parameters were assessed only at the time of ED presentation, and changes during follow-up could not be evaluated. In addition, excluding patients with incomplete clinical or laboratory data may have introduced selection bias. Laboratory markers such as serum albumin and hemoglobin may also reflect baseline patient characteristics, including hydration status, nutritional state, or unrecognized comorbidities, rather than the acute anaphylactic process alone. Therefore, residual confounding may still be present and should be taken into account when interpreting the relationship between laboratory findings and anaphylaxis severity.

In conclusion, anaphylaxis remains a significant clinical diagnosis requiring urgent intervention and effective treatment. Parameters and biomarkers that can be used in monitoring anaphylaxis, determining the situations that cause anaphylaxis, and identifying underlying factors and risks will allow better management of this serious condition. In this study, we report that lower serum albumin levels were associated with severe anaphylaxis. Our findings provide a useful basis for future prospective, multicenter studies.

Author Contributions: Concept/Design : TSM; Data acquisition: TSM; Data analysis and interpretation: TSM, ÜÖ; Drafting manuscript: TSM; Critical revision of manuscript: TSM, ÜÖ; Final approval and accountability: TSM, ÜÖ; Technical or material support: TSM; Supervision: ÜÖ; Securing funding (if available): n/a.
Ethical Approval: Approval was obtained from Aksaray University Faculty of Medicine Ethics Committee (Approval no:2022/16-02).
Peer-review: Externally peer-reviewed.
Conflict of Interest: The authors declare no competing interests to disclose.
Financial Disclosure: The authors declared that this study has received no financial support or any funding.
Meeting Presentation: A preliminary version of this study was presented as an oral presentation at the 3rd International Congress on Emergency Medicine (ICON-EM), Antalya, Türkiye, 2023, and published in the congress abstract book. The study has not been published as a full-text article in any peer-reviewed journal.

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