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Hematological and inflammatory biomarkers in pediatric snakebite: Associations with laboratory-defined coagulopathy and envenomation severity

Utku Dönger, Osman Fırat Çalışkan, Ali Yağız Hüzmeli

Hatay Mustafa Kemal University Faculty of Medicine, Department of Pediatrics, Hatay, Türkiye

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Corresponding Author:
Asst. Prof. Utku Dönger, Hatay Mustafa Kemal University Faculty of Medicine, Department of Pediatrics, Hatay, Türkiye
utkudonger@gmail.com

ORCID:
orcid.org/0000-0002-7489-0136

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ABSTRACT

Aims: The present investigation characterized the clinical features of pediatric snakebite while exploring whether routinely obtainable laboratory markers, including platelet count, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and the systemic immune-inflammation index (SII), were associated with laboratory-defined coagulopathy and envenomation severity.

Methods: This retrospective study included children with snakebite at a tertiary university-affiliated pediatric emergency department in Türkiye between January 2019 and December 2025. Demographic, clinical, treatment, and laboratory data were reviewed. Patients were categorized according to envenomation severity. Laboratory-defined coagulopathy was defined by abnormalities in the available initial coagulation parameters, excluding platelet count, and platelet count, NLR, PLR, and SII were evaluated for their associations with laboratory-defined coagulopathy and envenomation severity and their discriminatory performance for these outcomes.

Results: Thirty-one children (median age, 12 years; 74.2% male) were included. Most snakebites occurred during the summer months (67.7%), and the lower extremity was the most frequently affected site (51.6%). Laboratory-defined coagulopathy was identified in 13 patients (41.9%), while 19 patients (61.3%) had moderate-to-severe envenomation. Antivenom therapy was administered to 22 patients (71.0%). Platelet counts were numerically lower in children with laboratory-defined coagulopathy, but the difference was not statistically significant (p=0.199), and platelet count did not demonstrate statistically significant discrimination for laboratory-defined coagulopathy [area under the curve (AUC)=0.684; 95% confidence interval (CI), 0.489-0.879; p=0.065]. In contrast, platelet counts were significantly lower in children with moderate-to-severe envenomation (p=0.035), with an AUC of 0.693 (95% CI, 0.505-0.880; p=0.044). NLR, PLR, and SII did not demonstrate statistically significant associations or discriminatory performance for either outcome.

Conclusions: Laboratory-defined coagulopathy was frequent in pediatric snakebite. Platelet count showed the highest discriminatory performance and was associated with moderate-to-severe envenomation, but not with laboratory-defined coagulopathy. NLR, PLR, and SII did not demonstrate statistically significant discriminatory performance for either outcome. These exploratory findings require validation in larger pediatric cohorts.

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Introduction

Snakebite envenomation remains an important global health concern, with the greatest burden observed in tropical and subtropical regions. Worldwide, millions of snakebite incidents occur annually, and a considerable proportion of these exposures result in clinically significant envenomation. Beyond the associated mortality, snakebite also leads to substantial long-term morbidity, as many survivors experience permanent disabilities including limb loss, persistent tissue injury, functional impairment, or chronic physical limitations. Owing to its substantial global health burden, the World Health Organization recognizes snakebite envenomation as a neglected tropical disease and considers it a global health priority (1).

Türkiye reflects this regional pattern, although comprehensive nationwide surveillance data remain limited. A recent descriptive epidemiological study based on provincial health directorate data documented 2,486 snakebite cases across 38 provinces between 2015 and 2020. Cases were concentrated particularly in the southeastern, Mediterranean, and Aegean regions and during the summer months, with Adana, Mersin, and Hatay reporting the highest numbers (2).

Rural populations face heightened vulnerability to snakebite due to limited access to healthcare services. Engagement in agricultural and other outdoor activities further increases the risk of human-snake encounters, which contribute to significant morbidity and mortality in many low- and middle-income countries (3).

Pediatric patients are especially susceptible to the toxic effects of snake venom because a comparable quantity of venom represents a greater dose relative to body weight than in adults. This situation can lead to more severe clinical presentations of envenomation in pediatric patients and a higher incidence of systemic complications (4).

Depending on the snake species, venom may exert predominantly hematologic, neurologic, or cytotoxic effects, often producing complex multisystem involvement. These may cause serious complications such as local tissue damage, coagulopathy, rhabdomyolysis, acute kidney failure, compartment syndrome, and, rarely, intracranial hemorrhage. Snake bites are a critical clinical condition requiring urgent intervention. Timely transport of patients to a healthcare facility is critical for prognosis (5).

Studies on pediatric snake bites indicate that clinical severity and the development of complications are closely related to the degree of envenomation. In particular, leukocytosis, metabolic changes, and increased hospital stay duration have been reported in patients with severe envenomation (6). Additionally, low platelet levels and certain hematological parameters have been noted as potential risk indicators for the development of serious complications (7).

Although several inflammatory biomarkers have recently been investigated in pediatric snakebite, their clinical utility for predicting coagulopathy and envenomation severity remains uncertain (8).

This study investigated the clinical characteristics of pediatric snakebite and examined the associations of routinely available laboratory parameters, including platelet count, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and the systemic immune-inflammation index (SII), with laboratory-defined coagulopathy and envenomation severity.

Methods

Study design and ethical approval

This retrospective observational study was conducted at the Pediatric Emergency Department of Hatay Mustafa Kemal University Faculty of Medicine, Hatay, Türkiye. The study included 31 consecutive pediatric patients who presented with snakebite between January 2019 and December 2025. Demographic characteristics, clinical presentation, envenomation grade, administered treatments, and laboratory findings were retrospectively retrieved from the hospital electronic medical record database. The study was approved by the Hatay Mustafa Kemal University Non-Interventional Clinical Research Ethics Committee (meeting no: 04, decision no: 67; date: March 25, 2026).

Eligibility criteria and data collection

Patients aged 0-18 years with a confirmed history of snakebite were eligible for inclusion. The age of the included patients ranged from 31 to 192 months. Snakebite was considered confirmed when the patient had a definite history of snakebite. Five patients were transferred from other healthcare facilities after having been diagnosed with snakebite and were accepted to our tertiary university hospital for further evaluation and management.

We retrospectively re-evaluated the medical records of all 31 patients for potential confounding conditions and medication use. None of the included patients had pre-existing hematological, infectious, inflammatory or autoimmune, renal, hepatic, malignant, or immunological disorders that could affect the investigated hematological, inflammatory, or coagulation parameters. None were receiving corticosteroids, immunosuppressive or anti-inflammatory agents, anticoagulants, or antiplatelet drugs.

All complete blood count-derived indices and other laboratory parameters included in the analyses were obtained from the first blood sample collected after presentation to our hospital and before antivenom administration. The interval between presentation to our hospital and collection of the initial blood sample was recorded for each patient. None of the five

patients transferred from other healthcare facilities had received antivenom before transfer. Four of these patients did not receive antivenom during their subsequent hospitalization, whereas one received antivenom at our institution only after the initial blood sample had been obtained. Therefore, all laboratory measurements included in the analyses represented pre-antivenom values.

Laboratory measurements

Complete blood count parameters were measured using Mindray automated hematology analyzers (Mindray, Shenzhen, China) throughout the study period, with the BC-6200 analyzer used during approximately the last two years. Biochemical parameters were previously analyzed using the ADVIA 1800 system and, during approximately the last two years, using the Atellica Solution (Siemens Healthineers, Germany). Coagulation parameters, including prothrombin time (PT), prothrombin activity, international normalized ratio (INR), activated partial thromboplastin time (aPTT), and fibrinogen, were measured using the STA Compact Max^2 coagulation analyzer (Diagnostica Stago, France) throughout the study period. D-dimer was measured using the STA Compact Max^2 before 2025 and the miniVIDAS platform in 2025.

The institutional laboratory reference intervals were INR 0.8-1.2, aPTT 24-36 seconds, fibrinogen 200-400 mg/dL, D-dimer 0-500 ng/mL, PT 11-16 seconds, and prothrombin activity 70-120%. These institutional reference intervals were not further stratified according to pediatric age.

INR and aPTT measurements were available for all 31 patients. Fibrinogen was measured in 11 of 31 patients (35.5%), and D-dimer in 3 of 31 patients (9.7%). Because laboratory testing was clinically directed in this retrospective cohort, not all coagulation parameters were available for every patient. Missing fibrinogen and D-dimer values were not imputed.

Antivenom treatment

The antivenom used at our institution was HSGM Polyvalent Snake Antivenom (General Directorate of Public Health, Ministry of Health, Türkiye; manufactured by Albila Serum Biyolojik Ürünler San. ve Tic. A.Ş., Türkiye), supplied as a 10-mL injectable solution per vial. Snake species could not be reliably identified because most patients did not bring the snake to the hospital and photographic documentation was unavailable in most cases. The decision to initiate antivenom treatment was based on the overall severity of envenomation, the presence of systemic manifestations, and the patient's clinical course. No predefined institutional protocol was used to determine the initiation of antivenom therapy; this decision was based on the clinical judgment of the treating physician. The number of bite sites alone was not used as an indication for antivenom administration or as a determinant of the number of vials administered. There was no predefined dosing protocol assigning a specific number of antivenom vials according to envenomation grade or coagulopathy status. When additional doses were administered, the total number of vials was individualized according to clinical evolution and treatment response. The exact interval between hospital presentation and antivenom administration could not be reliably retrieved from the retrospective medical records.

Classification of envenomation severity

Envenomation severity was graded using a four-level clinical classification based on local and systemic manifestations, consistent with previously published clinical approaches to snakebite severity (9-11). Laboratory parameters, including platelet count and platelet-derived indices, were not used to assign envenomation severity grades.

Grade 0 (dry bite): Presence of fang marks without evidence of local or systemic envenomation.

Grade 1 (mild envenomation): Minimal local findings, including pain, erythema, or limited edema, without systemic manifestations.

Grade 2 (moderate envenomation): Progressive local swelling, ecchymosis, or more extensive tissue involvement, with mild systemic manifestations.

Grade 3 (severe envenomation): Advanced local tissue involvement, including extensive swelling, bullous lesions, or necrosis, and/or severe systemic manifestations including organ dysfunction.

For analytical purposes, patients were subsequently grouped as mild envenomation (Grades 0-1) or moderate-to-severe envenomation (Grades 2-3). This dichotomization was based on the approach previously used by İpek et al. (9) in a pediatric snakebite cohort, in which Stages 0-1 were categorized as cases without serious complications and Stages 2-3 as cases with serious complications.

Definition of laboratory-defined coagulopathy

Coagulopathy was defined using laboratory criteria adapted from those previously applied in a pediatric snakebite cohort (9), with consideration of the institutional laboratory reference intervals.

Laboratory-defined coagulopathy was considered present when at least one of the following abnormalities was detected among the coagulation parameters available at the initial laboratory evaluation: INR >1.2, aPTT >36 seconds, fibrinogen <150 mg/dL, or D-dimer >500 ng/mL.

A patient was classified as having laboratory-defined coagulopathy if at least one measured parameter met the specified abnormality criterion. Patients without an abnormality among the coagulation parameters measured at presentation were classified as not having laboratory-defined coagulopathy.

Platelet count was excluded from the revised definition of coagulopathy to avoid incorporation bias because platelet count was evaluated separately as a laboratory marker in the present study.

PT and prothrombin activity were evaluated as descriptive laboratory variables and were not used to define laboratory-defined coagulopathy.

Calculation of inflammatory biomarkers

Inflammatory indices were derived from complete blood count results obtained from the initial blood sample collected after presentation to our hospital.

NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count.

PLR was obtained by dividing the platelet count by the absolute lymphocyte count.

The SII was calculated using the following equation:

SII = (absolute neutrophil count × platelet count)/absolute lymphocyte count

These indices were subsequently evaluated for their associations with and discriminatory performance for laboratory-defined coagulopathy and moderate-to-severe envenomation.

$$NLR = Absolute\ Neutrophil\ Count / Absolute\ Lymphocyte\ Count$$

$$PLR = Absolute\ Platelet\ Count / Absolute\ Lymphocyte\ Count$$

$$SII = (Absolute\ Neutrophil\ Count \times Absolute\ Platelet\ Count) / Absolute\ Lymphocyte\ Count$$

Statistical Analysis

All statistical analyses were conducted using IBM SPSS Statistics (IBM Corp., Armonk, NY, USA). Distributional assumptions for continuous variables were examined with the Shapiro-Wilk normality test. Variables with normal distributions are reported as mean ± standard deviation, whereas skewed variables are presented as median and interquartile range (IQR). Categorical variables are summarized as frequencies and percentages.

To compare continuous variables between groups, we used the independent-samples t-test if parametric assumptions were met, or the Mann-Whitney U test otherwise. For categorical variables, we relied on the chi-square test or Fisher's exact test, depending on the sample size in the cells.

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the discriminatory performance of platelet count, NLR, PLR, and SII for laboratory-defined coagulopathy and moderate-to-severe envenomation. For each biomarker, we calculated the area under the ROC curve (AUC), its 95% confidence interval (CI), the exploratory cut-off value determined using the Youden index, as well as sensitivity, specificity, and p-value.

Owing to the limited sample size (n=31), multivariable logistic regression analysis was not undertaken.

Results

A total of 31 children with snakebite were included in the study. The median age was 12 years (IQR, 5.2), and the mean body weight was 39.32±15.54 kg. Boys accounted for 74.2% of the cohort. Snakebites occurred predominantly during the summer (67.7%), with July (29.0%) and August (25.8%) representing the peak months. The lower extremity was the most frequent bite location (51.6%), followed by the upper extremity (45.2%), and 90.3% of patients sustained a single bite. Compartment syndrome developed in two patients (6.5%).

According to the revised definition, laboratory-defined coagulopathy was identified in 13 patients (41.9%), whereas 18 patients (58.1%) were classified as not having laboratory-defined coagulopathy. Envenomation severity was classified as Grade 0 in 7 patients (22.6%), Grade 1 in 5 (16.1%), Grade 2 in 16 (51.6%), and Grade 3 in 3 (9.7%); thus, 19 patients (61.3%) had moderate-to-severe (Grade 2-3) envenomation. Laboratory-defined coagulopathy was present in 5/12 (41.7%) patients with Grade 0-1 envenomation and 8/19 (42.1%) patients with Grade 2-3 envenomation, with no statistically significant difference between the groups (Fisher's exact test, p=1.000). Antivenom was administered to 22 patients (71.0%); nine patients received one vial, 10 received two vials, two received four vials, and one received six vials. Nine patients (29.0%) did not receive antivenom.

Age, body weight, time from snakebite to hospital presentation, and sex distribution did not differ significantly between patients with and without laboratory-defined coagulopathy (all p>0.05). Similarly, age, body weight, and sex distribution did not differ significantly between the Grade 0-1 and Grade 2-3 groups. However, the median time from snakebite to hospital presentation was longer in patients with Grade 2-3 envenomation than in those with Grade 0-1 envenomation [150 minutes (IQR, 390) vs. 90 minutes (IQR, 123); p=0.049] (Table 1).

The overall laboratory findings are presented in Table 2. The mean hemoglobin level was 13.0±1.54 g/dL, and the mean platelet count was 251,968±82,622/μL. The median NLR, PLR, and SII values were 3.65 (IQR, 5.98), 118.64 (IQR, 79.42), and 844.63 (IQR, 1003.80), respectively. The median aPTT was 28.7 seconds (IQR, 6.1), and the median INR was 1.13 (IQR, 0.16) (Table 2).

When laboratory parameters were compared according to laboratory-defined coagulopathy status, CK, NLR, PLR, and SII did not differ significantly between the groups (all p>0.05). Platelet counts were numerically lower in patients with laboratory-defined coagulopathy than in those without laboratory-defined coagulopathy (229,308±62,741/μL vs. 268,333±92,692/μL); however, this difference was not statistically significant (p=0.199) (Table 3).

Table 1. Demographic and clinical characteristics of patients presenting with snakebite

	Laboratory-defined coagulopathy		p
	No (n=18)	**Yes (n=13)**	
Age (years)[1]	11.5; 4.6	14.2; 5.8	0.167
Body weight (kg)[2]	37.56±16.11	41.77±15.00	0.466
Time from snakebite to hospital presentation (min)[1]	120; 120	120; 330	0.552
Sex[3]			
Male	12 (66.7)	11 (84.6)	0.260
Female	6 (33.3)	2 (15.4)	
	Envenomation severity		**p**
	Grade 0-1 (n=12)	**Grade 2-3 (n=19)**	
Age (years)[2]	10.3±4.69	11.5±3.45	0.429
Body weight (kg)[2]	40.75±20.53	38.42±11.94	0.726
Time from snakebite to hospital presentation (min)[1]	90; 123	150; 390	0.049
Sex[3]			
Male	10 (83.3)	13 (68.4)	0.355
Female	2 (16.7)	6 (31.6)	
Overall cohort (n=31)			
Season[3]			
Spring		4 (12.9)	
Summer		21 (67.7)	
Autumn		6 (19.4)	
Month[3]			
March		1 (3.2)	
April		1 (3.2)	
May		2 (6.5)	
June		4 (12.9)	
July		9 (29.0)	
August		8 (25.8)	
September		4 (12.9)	
October		2 (6.5)	
Bite location[3]			
Upper extremity		14 (45.2)	
Trunk		1 (3.2)	
Lower extremity		16 (51.6)	
Number of bites[3]			
Single bite		28 (90.3)	
Multiple bites		3 (9.7)	
Additional signs and symptoms[3]			
Compartment syndrome		2 (6.5)	
Dizziness		1 (3.2)	
None		28 (90.3)	
Laboratory-defined coagulopathy[3]			
Present		13 (41.9)	
Absent		18 (58.1)	

Table 1. Continued			
	Laboratory-defined coagulopathy		p
	No (n=18)	Yes (n=13)	
Envenomation grade[3]			
Grade 0		7 (22.6)	
Grade 1		5 (16.1)	
Grade 2		16 (51.6)	
Grade 3		3 (9.7)	
Number of antivenom vials administered[3]			
None		9 (29.0)	
1 vial		9 (29.0)	
2 vials		10 (32.3)	
4 vials		2 (6.5)	
6 vials		1 (3.2)	
Tetanus vaccination[3]			
Administered		29 (93.5)	
Not administered		2 (6.5)	
Mannitol treatment[3]			
Yes		3 (9.7)	
No		22 (71.0)	
Unknown		6 (19.3)	

[1]: Median; IQR, [2]: Mean ± SD, [3]: n (%), IQR: Interquartile range, SD: Standard deviation

Table 2. Laboratory findings of patients presenting with snakebite	
Hemoglobin (g/dL)[1]	**13.0±1.54**
Neutrophil count (×10^3/μL)[1]	7.805±3.909
Lymphocyte count (×10^3/μL)[2]	2.430; 1.910
Platelet count (/μL)[1]	251,968±82,622
NLR[2]	3.65; 5.98
PLR[2]	118.64; 79.42
SII[2]	844.63; 1003.80
CRP (mg/L)[2]	3.31; 0.18
Prothrombin time, s[2]	15.00; 2.40
Prothrombin activity (%)[1]	81.65±13.467
Fibrinogen (mg/dL)[1*]	272.36±61.59
D-dimer (ng/mL)[1*]	3153.67±4061.51
aPTT (s)[2]	28.7; 6.1
INR[2]	1.13; 0.16
Sodium (mmol/L)[1]	138.1±2.57
Potassium (mmol/L)[1]	4.22±0.482
Chloride (mmol/L)[1]	107.6±3.06
Calcium (mg/dL)[1]	9.35±0.588
Magnesium (mg/dL)[1]	1.90±0.265
AST (U/L)[2]	28; 9
ALT (U/L)[2]	16; 6
BUN (mg/dL)[2]	11.0; 4.51
Creatinine (mg/dL)[1]	0.53±0.152
CK (U/L)[2]	168; 110.4
pH[1]	7.36±0.063
pCO_2 (mmHg)[1]	40.9±5.688
HCO_3^- (mmol/L)[1]	22.9±4.176

[1]: Mean ± SD, [2]: Median; IQR, [*]: Fibrinogen and D-dimer values are presented for patients with available measurements only (n=11 and n=3, respectively). Missing values were not imputed. SD: Standard deviation, IQR: Interquartile range, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, SII: Systemic immune-inflammation index, CRP: C-reactive protein, aPTT: Activated partial thromboplastin time, INR: International normalized ratio, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, BUN: Blood urea nitrogen, CK: Creatine kinase, pCO_2: Partial pressure of carbon dioxide, HCO_3^-: Bicarbonate

When patients were stratified according to envenomation severity, prothrombin time (PT), prothrombin activity, aPTT, INR, CK, NLR, PLR, and SII did not differ significantly between the Grade 0-1 and Grade 2-3 groups (all p>0.05). In contrast, platelet counts were significantly lower in patients with Grade 2-3 envenomation than in those with Grade 0-1 envenomation (228,789±86,188/μL vs. 288,666±63,754/μL; p=0.035) (Table 4).

In ROC analysis for laboratory-defined coagulopathy, platelet count yielded an AUC of 0.684 (95% CI, 0.489-0.879; p=0.065). A platelet threshold of ≤252,000/μL provided 69.2% sensitivity and 72.2% specificity. NLR, PLR, and SII also did not demonstrate statistically significant discrimination for laboratory-defined coagulopathy, with AUCs of 0.585 (p=0.428), 0.491

(p=0.940), and 0.577 (p=0.490), respectively. Thus, none of the evaluated hematological or inflammatory indices demonstrated statistically significant discriminatory performance for laboratory-defined coagulopathy (Table 5; Figure 1).

For moderate-to-severe envenomation, platelet count yielded an AUC of 0.693 (95% CI, 0.505-0.880; p=0.044). A platelet threshold of ≤262,500/μL provided 63.2% sensitivity and 75.0% specificity. NLR, PLR, and SII were not statistically significant discriminators of moderate-to-severe envenomation, with AUCs of 0.596 (p=0.383), 0.583 (p=0.467), and 0.526 (p=0.819), respectively (Table 5; Figure 2). Although platelet count yielded a numerically higher AUC than the other evaluated indices, pairwise comparisons between the ROC curves showed no statistically significant differences (all p>0.05).

Finally, the interval between presentation to our hospital and collection of the initial blood sample did not differ significantly according to laboratory-defined coagulopathy status or envenomation severity. The median sampling interval was 10 minutes (IQR, 9) in patients without laboratory-defined coagulopathy and 5 minutes (IQR, 5) in those with laboratory-

Table 3. Comparison of laboratory parameters according to the presence of laboratory-defined coagulopathy

	Laboratory-defined coagulopathy		p
	No	Yes	
CK (U/L)[1]	174; 87.4	147; 124.0	0.435
NLR[1]	3.38; 6.20	3.99; 7.69	0.423
PLR[1]	118.96; 69.42	109.20; 86.16	0.936
SII[1]	790.39; 855.25	976.40; 1531.33	0.471
Platelet count (/μL)[2]	268,333±92,692	229,308±62,741	0.199

[1]: Median; IQR, [2]: Mean ± SD, CK: Creatine kinase, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, SII: Systemic immune-inflammation index, IQR: Interquartile range, SD: Standard deviation

Table 4. Comparison of laboratory parameters according to envenomation severity

	Envenomation severity		p-value
	Grade 0-1	Grade 2-3	
Prothrombin time (PT), s[1]	14.95; 2.50	15.00; 2.80	0.223
Prothrombin activity (%)[1]	83.5; 16	83; 17	0.340
aPTT (s)[2]	29.83±8.11	28.58±4.01	0.569
INR[1]	1.12; 0.15	1.13; 0.17	0.340
CK (U/L) [1]	174; 57.3	146; 122	0.919
NLR[1]	2.81; 7.63	3.77; 5.74	0.372
PLR[2]	146.73±88.118	112.51±40.44	0.151
SII[1]	888.64; 1680.46	844.63; 903.31	0.808
Platelet count (/μL)[2]	288,666±63,754	228,789±86,188	0.035

[1]: Median; IQR, [2]: Mean ± SD, PT: Prothrombin time, aPTT: Activated partial thromboplastin time, INR: International normalized ratio, CK: Creatine kinase, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, SII: Systemic immune-inflammation index, IQR: Interquartile range, SD: Standard deviation

Table 5. ROC analysis of hematological and inflammatory indices for laboratory-defined coagulopathy and moderate-to-severe envenomation

	Parameter	Cut-off value	95% CI	p-value	AUC	Sensitivity (%)	Specificity (%)
Laboratory-defined coagulopathy	PLT (/μL)	≤252,000	0.489-0.879	0.065	0.684	69.2	72.2
	NLR	≥3.71	0.374-0.797	0.428	0.585	61.5	61.1
	PLR	≤112.26	0.269-0.714	0.940	0.491	53.8	61.1
	SII	≥969.67	0.359-0.795	0.490	0.577	53.8	66.7
Moderate-to-severe envenomation (Grade 2-3)	PLT (/μL)	≤262,500	0.505-0.880	**0.044**	0.693	63.2	75.0
	NLR	≥1.57	0.380-0.813	0.383	0.596	84.2	41.7
	PLR	≤146.5	0.359-0.808	0.467	0.583	84.2	41.7
	SII	≥445.504	0.301-0.752	0.819	0.526	78.9	41.7

ROC: Receiver operating characteristic, AUC: Area under the curve, CI: Confidence interval, PLT: Platelet count, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, SII: Systemic immune-inflammation index

defined coagulopathy (p=0.087). Corresponding values were 5 minutes (IQR, 8) for Grade 0-1 and 10 minutes (IQR, 7) for Grade 2-3 envenomation (p=0.099) (Table 6).

Discussion

The present study provides a comprehensive evaluation of pediatric snakebite by examining clinical characteristics together with routinely available laboratory parameters in relation to laboratory-defined coagulopathy and envenomation severity. The main findings were that laboratory-defined coagulopathy occurred frequently in this cohort, and that platelet count showed the highest observed discriminatory performance among the evaluated laboratory parameters. In contrast, NLR, PLR, and SII did not demonstrate statistically significant associations with either laboratory-defined coagulopathy or envenomation severity in this cohort.

Consistent with previous pediatric reports, most patients in our cohort were boys, a pattern generally attributed to increased outdoor activity and greater environmental exposure to snakes in rural settings (3,8).

Likewise, snakebite episodes occurred predominantly during the summer months, reflecting seasonal increases in both snake activity and human outdoor exposure (8,12).

The predominance of lower-extremity bites in our cohort also agrees with previous observations that accidental encounters most commonly occur while walking through snake habitats (6,13).

Our findings highlight the close relationship between venom-induced hematological abnormalities and clinical severity. Hemotoxic snake venoms are known to activate coagulation pathways while simultaneously promoting platelet consumption, resulting in coagulation disturbances that may progress to clinically significant bleeding and other systemic complications (4,5).

Consistent with these mechanisms, platelet counts were numerically lower among children with laboratory-

Table 6. Comparison of time to initial blood sampling according to laboratory-defined coagulopathy status and envenomation severity

	Laboratory-defined coagulopathy		
	Without laboratory-defined coagulopathy	**With laboratory-defined coagulopathy**	**p-value**
Time from hospital presentation to initial blood sampling (min)[1]	10; 9	5; 5	0.087
	Envenomation severity		p-value
	Grade 0-1	Grade 2-3	
Time from hospital presentation to initial blood sampling (min)[1]	5; 8	10; 7	0.099

[1]: Median; interquartile range

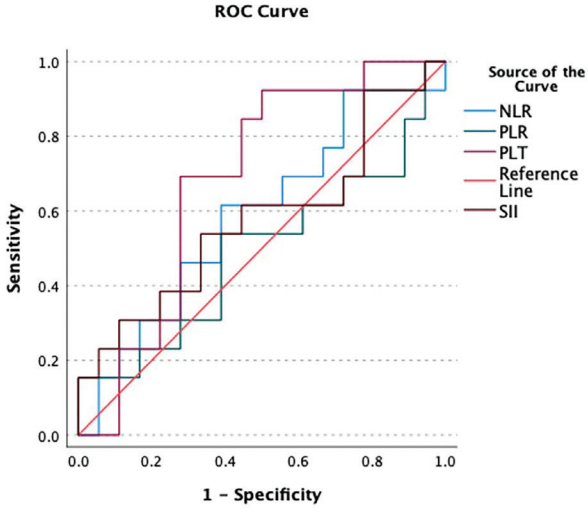


Figure 1. Comparison of ROC curves for PLT, NLR, PLR, and SII in discriminating laboratory-defined coagulopathy

ROC: Receiver operating characteristic, PLT: Platelet count, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, SII: Systemic immune-inflammation index

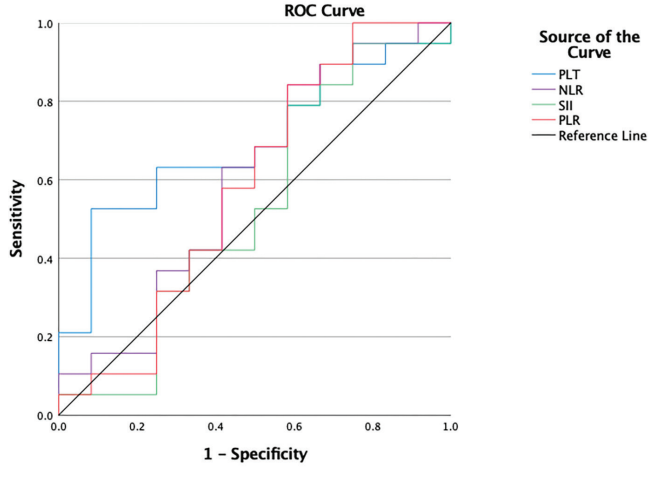


Figure 2. Comparison of ROC curves for PLT, NLR, PLR, and SII in discriminating moderate-to-severe envenomation (Grade 2-3)

ROC: Receiver operating characteristic, PLT: Platelet count, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, SII: Systemic immune-inflammation index

defined coagulopathy, although this difference was not statistically significant, whereas significantly lower platelet counts were observed in children with moderate-to-severe envenomation. Previous clinical studies have likewise identified thrombocytopenia as a marker associated with more severe envenomation and adverse clinical outcomes (6). However, mean platelet counts in both severity groups remained above the conventional threshold for thrombocytopenia. Therefore, the observed finding should be interpreted as a relative reduction in platelet count associated with greater envenomation severity rather than as thrombocytopenia. Within our cohort, platelet count demonstrated the highest observed discriminatory performance among the evaluated laboratory parameters; however, the ROC-derived threshold represents an exploratory, cohort-specific discriminatory value rather than a clinical threshold for thrombocytopenia.

In a pediatric series of 77 children from Türkiye, Ozay et al. (7) reported that platelet count was inversely correlated with both clinical severity grade and length of hospitalization, while a platelet count below 120,000/mm^3 was independently associated with serious complications. Similarly, Aktar and Tekin (14) found thrombocytopenia to be significantly more frequent in children with severe envenomation, although platelet-derived inflammatory indices did not differ significantly across severity groups. These findings support an association between declining platelet count and increasing clinical severity. Nevertheless, unlike the overt thrombocytopenia evaluated in those studies, the platelet counts in our cohort generally remained within the conventional reference range. Thus, the present findings suggest that even a relative reduction in platelet count may accompany greater envenomation severity, but they do not establish a clinically applicable threshold for predicting severe disease (7,14).

The frequency of laboratory-defined coagulopathy did not differ significantly between children with Grade 0-1 and Grade 2-3 envenomation. Therefore, although hematological abnormalities have been associated with increasing envenomation severity in previous studies (13), the present cohort did not demonstrate a statistically significant association between laboratory-defined coagulopathy and envenomation severity.

In contrast, the inflammatory cell-derived indices NLR, PLR, and SII did not demonstrate statistically significant associations with either laboratory-defined coagulopathy or envenomation severity in the present cohort. Similarly, none of these indices showed statistically significant discriminatory performance in ROC analyses for either outcome. However, given the small sample size, these non-significant findings should not be interpreted as evidence of an absence of biological or prognostic relevance. The limited sample size may have reduced the ability to detect small-to-moderate associations, and the possibility of type II error cannot be excluded.

Our findings regarding NLR and PLR are consistent with those of Aktar and Tekin (14), who found no significant differences in these indices among children with mild, moderate, and severe snakebite envenomation. In contrast, Aslan et al. (15) reported that admission NLR was positively correlated with length of hospital stay and tended to increase with advancing disease stage, although the difference across clinical stages was not statistically significant. This partial inconsistency may be explained by differences in sample size, outcome definitions, severity distribution, and timing of laboratory measurements. Moreover, Aslan et al. (15) evaluated serial NLR measurements, whereas the present study focused on laboratory parameters obtained from the initial blood sample. Taken together, the available evidence suggests that a single admission measurement of NLR or PLR may have limited value as a stand-alone marker of pediatric envenomation severity. Evidence regarding SII in pediatric snakebite remains particularly limited, and its prognostic role requires evaluation in larger cohorts using serial measurements (14,15).

A possible explanation for these findings is that NLR, PLR, and SII primarily reflect the host inflammatory response, whereas the early clinical manifestations of hemotoxic snakebite may be more directly influenced by venom-mediated effects on platelets and the coagulation cascade. Consequently, these inflammatory indices may have limited ability to reflect the severity of venom-induced coagulation abnormalities during the initial phase following envenomation.

Although NLR, PLR, and SII have demonstrated prognostic value in various inflammatory disorders, they did not demonstrate statistically significant associations or discriminatory performance for laboratory-defined coagulopathy or envenomation severity in the present cohort. Platelet count showed the highest observed discriminatory performance among the evaluated laboratory parameters; however, these findings should be interpreted cautiously given the small sample size and the absence of multivariable adjustment for potential confounders.

Study Limitations

This study provides region-specific evidence from an area where pediatric snakebite has been relatively underrepresented and evaluates routinely available hematological and inflammatory indices in relation to two clinically relevant outcomes: laboratory-defined coagulopathy and envenomation severity. To minimize incorporation bias, platelet count was excluded from the revised definition of laboratory-defined coagulopathy, patients were reclassified, and the analyses were repeated.

The findings should be interpreted in light of the retrospective, single-center design and small sample size, which limited statistical power, subgroup comparisons, and the reliability of multivariable adjustment. Consequently, residual confounding

cannot be excluded, and the ROC-derived cut-off values should be considered exploratory and sample-specific. The limited availability of fibrinogen and D-dimer measurements may have affected the classification of laboratory-defined coagulopathy, while the inability to identify snake species prevented species-specific analyses. Variations in the intervals between the bite, hospital presentation, and blood sampling may also have influenced the laboratory findings. In addition, changes in some analytical platforms during the study period and the inability to verify historical reagent-lot changes may have introduced measurement variability despite the use of institutional reference intervals. Larger multicenter pediatric studies are needed to validate these findings.

Conclusion

Laboratory-defined coagulopathy was frequent in this pediatric snakebite cohort but was not significantly associated with envenomation severity. Among the evaluated laboratory parameters, platelet count showed the highest observed discriminatory performance for envenomation severity, whereas NLR, PLR, and SII showed no statistically significant discriminatory performance for either laboratory-defined coagulopathy or envenomation severity. Given the small sample size, these findings should be interpreted as exploratory and require validation in larger pediatric cohorts.

Ethics

Ethics Committee Approval: The study was approved by the Hatay Mustafa Kemal University Non-Interventional Clinical Research Ethics Committee (meeting no: 04, decision no: 67; date: March 25, 2026).

Informed Consent: Informed consent was not obtained because this was a retrospective medical record review.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.Y.H., Concept: U.D., Design: U.D., Data Collection or Processing: O.F.Ç., A.Y.H., Analysis or Interpretation: O.F.Ç., A.Y.H., Literature Search: O.F.Ç., Writing: U.D.

Conflict of Interest: No conflict of interest was declared by the authors.

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