Section: Pathology

Original Research Article

HAEMATOLOGICAL PARAMETERS IN SNAKEBITE ENVENOMATION: ASSOCIATION WITH CLINICAL SEVERITY AND SOCIODEMOGRAPHIC FACTORS - A CROSS-SECTIONAL STUDY

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Received *: 10/05/2026*
Received in revised form *: 28/06/2026*
Accepted *: 13/07/2026*

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DOI: 10.70034/ijmedph.2026.3.340

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2026; 16 (3); 2131-2136

ABSTRACT

Background: In Rural India, Snakebite is a major public health challenge. Its associated haematological derangements can predict clinical severity if identified early. This study explored sociodemographic influences & simultaneously assessed haematological parameters in patients with snakebite envenomation and examined their associations with clinical severity.

Materials and Methods: This retrospective, record-based cross-sectional study included 225 patients aged ≥ 18 years who presented with snakebite to the emergency department of a tertiary care hospital in Gadag, India, between 1st January 2023 and 31st December 2023, selected from 312 eligible records by convenience sampling. A pre-structured questionnaire was used to collect sociodemographic, clinical, and haematological data which was further analysed using frequency, proportion, mean, standard deviation & one-way ANOVA.

Results: Mean age was 37.84 ± 13.60 years, and most patients were from rural areas (77.8%) and male (61.3%). Total leukocyte counts, Platelet counts, RDW-SD, Serum Creatinine, Serum Potassium were significantly associated with envenomation severity ($p < 0.05$). Patients with moderate/severe envenomation had lower platelet counts, and higher total leukocyte counts, RDW-SD, Serum Creatinine, Serum Potassium than those with mild outcomes.

Conclusion: The study concluded the association between various haematological parameters like Total leukocyte counts, Platelet counts, RDW-SD, Serum Creatinine & Serum Potassium with the severity of snake envenomation.

Keywords: Snakebite; Haematological parameters; Clinical Outcome.

INTRODUCTION

Envenomation with a snakebite is a significant public health matter, especially in the context of rural and agricultural locations of developing countries, where mortality rates and incidence remain disproportionately high and alarming.[1,2] In India the snakebite cases contribute to a major cause of morbidity and mortality, National Health Profile 2019 data on snakebites reported 164,031 snakebite cases and as many as 885 deaths in 2018.[3] 6,595 snakebite cases which included 19 deaths were reported in Karnataka in 2023 according to a news article.[4] The Karnataka state government classified snakebite cases and deaths to be a 'notifiable disease' in order to keep an exact track of the number of such cases in the state, according to an official notification dated February 12, 2024.[5] While most of the snakes found in Karnataka and generally in India are non-poisonous, a certain percentage of the total accounts for venomous species with nearly 300 different species the major ones being the Daboia russelii, Naja naja, Bungarus caeruleus and echis carinatus also known as the saw scaled viper.[6] These snakes

inhabit in a vast array of environments across the map from forested areas and grasslands to agricultural zones.

Snake venoms are a mixture of highly complex compounds with a lot of components with majority of them being in the form of peptides and proteins, the venoms are majorly categorised based on the biochemical activity as neurotoxic which typically interfere with neuromuscular transmission and could lead to paralysis, hemotoxic venoms can cause coagulation abnormalities and cytotoxic usually cause tissue damage.[7] Snake venom also changes with the species and geographical location. So, the species found in Karnataka could have varied composition as we move from one place to the other.[7] All this can contribute to substantial mortality and morbidity therefore understanding the haematological alterations associated with snakebite and its impact on clinical outcome is of paramount importance to enhance patient care and management of outcomes. Some of the commonly used parameters in hospital settings include 20-minute whole blood clotting, complete blood count, coagulation profile, inflammatory markers, serum electrolyte concentrations and creatinine and blood glucose levels.[8] There have also been various studies involving different ratios like the platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio which could also provide valuable clinical insights into the disease course.[4]

Rapid primary assessment using various clinical and laboratory methods are an essential initial course of the management of snakebite envenomation, timely administrations of appropriate antivenom and providing supportive care can mitigate the risk of complications that could be life threatening including coagulopathy, neurotoxicity and also organ dysfunction.[8] In this cross-sectional study with the objective to assess the haematological profile of snakebite patients and recognise its associations with clinical outcomes and sociodemographic factors, we sought to generate findings that could guide the clinical management of snakebite envenomation in similar healthcare settings.

Objectives of the study: This study was aimed to assess the haematological parameters in patients presenting with snakebite envenomation, determine their association with clinical outcomes, and to evaluate their relationship with sociodemographic factors.

MATERIALS AND METHODS

Study Design and Setting: This retrospective, record-based cross-sectional study was conducted among patients aged 18 years or older who presented with a history of snakebite to the emergency department of Gadag Institute of Medical Sciences, a tertiary care hospital in Gadag, Karnataka, India. Institutional Ethical Committee clearance and permissions from the concerned authorities were obtained (14/03/2024; approval no. 61/24) of Gadag Institute of Medical Sciences. Gadag. Full Confidentiality of the data was maintained throughout the study.

Participants

The study population consisted of all patients aged 18 years or older who presented to the emergency department with a history of snakebite and were included in the study if they met the following criteria

1. Admitted to the emergency department with a history of snakebite from 1st January 2023 to 31st December 2023.
2. Had a previous and recent history of snakebite exposure and exhibited related local or systemic findings.
3. Underwent comprehensive laboratory testing, including complete blood count, biochemical, and coagulation studies.

Patients with inconclusive clinical history, laboratory test results, or if they had underlying medical conditions that could potentially cause bleeding diathesis or affect leukocyte and platelet morphology and counts were excluded.

According to the records maintained, 312 patients attended the emergency department with a history of snakebite from 1st January 2023 to 31st December 2023 at a tertiary care hospital in Gadag, India. Out of 312 cases, 225 cases were included in the study after meeting the inclusion and the exclusion criteria. Names of the patients were coded and their identification was hidden throughout the study, analysis and manuscript writing.

A standardized predetermined and pre-structured questionnaire was used to collect data from the records consisting of age, resident area, marital status, education, occupation, socioeconomic status, place, duration, site & time from the snakebite till the admission into the hospital, antivenom doses administered, vitals like systolic blood pressure (using a mechanical inflatable sphygmomanometer and stethoscope), heart rate, SpO2 levels (measured using a portable pulse oximeter), Haematological parameters like haemoglobin concentration, lymphocyte count, platelet count, PDW, PDWLR (platelet distribution width to lymphocyte ratio), RDW-SD, MPV, RBC count, Biochemical parameters like serum sodium, potassium, creatinine, and chloride levels and Coagulation profile included PT-INR.

Extent of Envenomation and Severity: The severity of envenomation was graded based on a severity scale and guidelines. We utilized a 4-grade classification system to assess the severity of snakebite envenomation.[9] This grading system provides a framework for healthcare providers to understand the degree of venom-induced damage namely:

Table 1: Severity Level

Grade	Severity Level	Defining Clinical/Laboratory Features
0	No Envenomation	The bite site may exhibit minor symptoms like soreness without any other signs of harm, similar to a small bruise.
1	Minimal Envenomation	Mild swelling around the bite and normal laboratory findings.
2	Moderate to Serious Envenomation	Noticeable swelling, pain, and potential systemic effects such as clotting abnormalities or low platelet counts (increased PT and PT-international normalized ratio [INR] and/or thrombocytopenia).
3	Severe Envenomation	Advanced/rapidly progressive swelling, intense pain, and critical features like tissue necrosis, and organ dysfunction including compartment syndrome and death.

We assessed the severity based on the patients' symptoms, laboratory test results, and their condition upon arrival and during the course of treatment and retrospectively graded them on the severity scale. For statistical analysis, Grades 0 and 1 were combined into a "none/minimal" group, while Grades 2 and 3 were grouped as "moderate/severe". This categorization helps us to understand the distribution of envenomation severity among the study population.

Statistical Analysis: Data was coded and entered in Microsoft excel sheet. Descriptive statistics was analysed by frequency, proportions, mean and standard deviation. Association between multiple laboratory and clinical variables to the severity rating scale was calculated using chi-square test & ANOVA by SPSS statistical software trial (version 16). Two-sided 'p' value of ≤0.05 was considered as statistically significant.

Statistics: With the method of universal sampling which is a type of convenience sampling, a total of 312 case records were selected and a thorough data extraction was done which included various test reports. The data was consolidated and was appropriately analysed and grouped accordingly.

Out of 312 cases, 225 cases were included in the final analysis after using inclusion and the exclusion criteria.

The data was recorded in MS Excel and digitally analysed using statistical software - SPSSV16 (trial version) and the results were obtained.

For Descriptive- frequency, proportion, mean and SD were used. For analytical statistics, univariate ANOVA- analysis of variance was done. P value ≤0.05 will be considered statistically significant.

RESULTS

Table 2: Patient Demographics

Demographics		Number	(%)
SEX	MALE	138	61.33
	FEMALE	87	38.66
PLACE	URBAN	50	22.2
	RURAL	175	77.8
BG Prasad class	1	17	7.6
	2	41	18.2
	3	110	48.9
	4	56	24.9
	5	1	0.4
AGE	<15yrs	0	0
	15-24yrs	42	18.6
	25-34yrs	52	23.1
	35-44yrs	65	28.9
	45-54yrs	30	13.3
	55-64yrs	26	11.6
	65-74yrs	10	4.4

Of the major demographic factors, the average number of patients belonged to 2.92 ± (0.86) of BG Prasad economic and social classification which is the standard classification system used in India.[10] According to modified BG Prasad classification, class 2 had per capita income of 4174-8348 rupees and class 3 had an income of 2505-4173 rupees.[10]

Victims mostly belonged to the cohort of 25-34yrs (23.1%) and 35-44 yrs (28.9%) which consists of young adults and people of working age group. A higher number of males consisting as much as two thirds of the study subjects were recorded. Rural areas reported relatively higher number of cases than urban locations.

Table 3: Clinical Parameters

Descriptive Statistics			
	N	Mean	Std. Deviation
Age(years)	225	37.84	13.607
Vitals			
Systolic blood pressure(mmHg)	225	125.57	15.574

Pulse (beats/minute)	225	84.49	10.12
Blood glucose(mg/dL)	225	127.1	39.398
Spo2 (%)	225	97.04	2.266
Hematologic parameters			
Haemoglobin (g/dL)	225	13.119	1.7604
Total leukocyte count (x10	225	10399.72	3981.923
Platelet count (105x L-1)	225	2.7715	2.33534
RBC count (millions/cumm)	225	4.8899	2.89867
PCV (%)	225	39.461	5.4284
RDW-CV (%)	225	15.22	10.8323
RDW-SD (fL)	225	44.4651	5.30891
lymphocyte count (103x L-1)	225	2.732	0.7102
MPV (fL)	225	11.026	9.0829
PDW (fL)	225	16.185	0.4811
PT-INR	225	1.3381	0.33376
Creatinine(mg/dL)	225	0.9167	0.49507
Biochemistry panel			
Sodium (mEq/L)	225	139.617	4.512
Potassium (mEq/L)	225	4.334	0.7458
Chloride (mEq/L)	225	107.605	7.6996
Other parameters			
ASV*(vials)	225	5.96	7.812
Hospital stays duration (days)	225	1.43	0.81
Hours lapsed since snakebite(hours)	225	4.1	5.788
*ASV-anti snake venom,			

The study included 225 patients after applying inclusion and exclusion criteria. The mean age and (standard deviation) of the study sample was 37.84 ± (13.60) years.

We found that majority of bites were on the lower limb, including the hip till the toes. This was followed by upper limbs which consisted of 32.9% of the total bite locations.

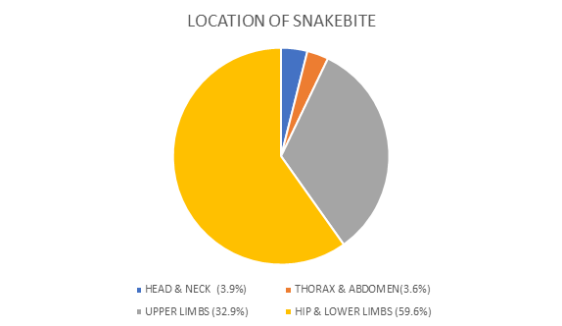

Figure 1: Location of Snakebite.

Table 4: ANOVA of Clinical Parameters

ANOVA Table							
Variable * Severity			**Sum of Squares**	**df**	**Mean Square**	**F**	**Sig.**
Pulse * severity	Between Groups	(Combined)	354.519	3	118.173	1.156	0.327
	Within Groups		22587.7	221	102.207		
	Total		22942.22	224			
Spo2 * severity	Between Groups	(Combined)	10.972	3	3.657	0.71	0.547
	Within Groups		1138.744	221	5.153		
	Total		1149.716	224			
Hb * severity	Between Groups	(Combined)	12.294	3	4.098	1.328	0.266
	Within Groups		681.888	221	3.085		
	Total		694.182	224			
Total leukocyte count * severity	Between Groups	(Combined)	1.22E+09	3	4.07E+08	38.662	0.001
	Within Groups		2.33E+09	221	10539575		
	Total		3.55E+09	224			
Platelet count * severity	Between Groups	(Combined)	60.514	3	20.171	3.839	0.01
	Within Groups		1161.136	221	5.254		
	Total		1221.65	224			
RDW-SD * severity	Between Groups	(Combined)	353.35	3	117.783	4.367	0.005
	Within Groups		5959.994	221	26.968		
	Total		6313.344	224			
PDW * severity	Between Groups	(Combined)	0.612	3	0.204	0.88	0.452
	Within Groups		51.229	221	0.232		
	Total		51.842	224			
PT-INR * severity	Between Groups	(Combined)	0.412	3	0.137	1.237	0.297
	Within Groups		24.54	221	0.111		
	Total		24.952	224			
Creatinine * severity	Between Groups	(Combined)	10.785	3	3.595	18.009	0.001
	Within Groups		44.116	221	0.2		
	Total		54.902	224			

Potassium * severity	Between Groups	(Combined)	5.156	3	1.719	3.18	0.025
	Within Groups		119.427	221	0.54		
	Total		124.583	224			

To determine the relationship between categorical predictor variables ANOVA (univariate analysis of variance) was used. This study compared the effects of multiple laboratory and clinical variables to the severity rating scale. We found significant relationship between several lab parameters and clinical severity of snakebite, including:

1. Total leukocyte counts with the severity of envenomation (F (3, 221) = [38.662], p = 0.001)
2. Platelet count with the severity of envenomation (F (3, 221) = [3.839], p = 0.01)
3. RDW-SD with the severity of envenomation (F (3, 221) = [4.367], p = 0.005)
4. Serum Creatinine with the severity of envenomation (F (3, 221) = [18.009], p = 0.001)
5. Serum Potassium with the severity of envenomation (F (3, 221) = [3.18], p = 0.025).

Patients with moderate/severe envenomation had mean lymphocyte counts of 1.71 ± 0.07 (× 10^3/L), platelet counts of 1.39± 0.714 (x10^5/µL), RDW-SD % of 45.10 ± 5.34, serum creatinine of 1.51 ± 0.81 mg/dL and serum potassium of 4.033 ± 0.70 mEq/L.

DISCUSSION

This cross-sectional study examined the association between various haematological parameters and the clinical severity of snake envenomation in patients presenting to the emergency department of a tertiary care teaching hospital. The severity of the snakebite was assessed using a standardized severity scale classification which has 4 grades of envenomation.[9] A demographic containing males, from rural areas, from 24 to 44 years of age and class 3 of socio-economic BG Prasad scale were found as the majority subset of people who were affected by snakebites. A similar study conducted in southern India found similar population demographics to have majorly affected by snakebites.[10,11]

The key findings from our study are significant for association of lymphocyte count, platelet count, RDW-SD, serum creatinine, and serum potassium with the severity of envenomation.

We also explored demographic and population characteristics of the victims of snakebite. Socioeconomic status was also explored using a standardised classification system used in India.[10] In this manner a broader sociodemographic profile was constructed to contextualise envenomation patterns.

Elevated total counts, including reactive polymorphic lymphocytosis, typically reflect an immune response to infection or inflammation.[12] Systemic inflammation causes multi-organ dysfunction, and also involves the renal system. Inflammatory damage to kidneys can lead to elevated serum creatinine levels as found in this study which could indicate acute kidney injury and its vast signs and symptoms. We found a mean serum creatinine of 0.91 mg/dl in our study and a statistically significant association (one-way ANOVA, $p<0.05$) which associated it with serious clinical course. A prior study about mortality risk prediction scores for viper envenomation in India found that - acute kidney injury defined as creatinine >3 mg/dl to be a significant in-hospital mortality predictor through their univariable analysis.[13] Management of such cases includes monitoring of vitals, administering anti snake venom, monitor fluid input and output and managing fluid overload, electrolyte disturbances, and acid-base imbalances.[14]

We found RDW-SD to be significant in patients with moderate to serious envenomation. Increased RDW values have been correlated with increased inflammation and sepsis.[15] A prior study shows that RDW rises with advancing age, independent of pathology.[16] Given the demographic of our study population which mainly consists of relatively older people having a serious outcome, it could explain the higher RDW values.

Potassium is a vital electrolyte in our body and its homeostasis is maintained within a narrow range of 3.5-4.5 mEq/L. Any gross derailment in its values can lead to life threatening consequences and complications. Research has shown that a higher serum potassium level increased all-cause mortality in patients with AKI (acute kidney injury).[17] Conversely, in a similar study Rangareddy et al. reported significant hypokalemia in their cohort study based in Karnataka, which they attributed to increased urinary excretion or intracellular shifting of potassium, which indicates the bidirectional nature of serum potassium variations in snakebite cases.[18]

The relatively large sample size from a single tertiary care hospital strengthens the representativeness of the findings for comparable rural settings around. With the burden of increasing cases, proper reporting systems and channels need to be established. Community level awareness programmes and structured reporting systems are required along with clinical investment. Geographical hotspots should be highlighted and established and more resources should be made available in such areas. Treatment options including anti snake venoms should be thoroughly researched and alternative treatment modalities should also be explored.[19]

Haematological parameters and clinical evaluations still hold paramount importance as quick, accessible and reliable entities when evaluating snake bites.

Limitations: The primary limitation of this single-centre study is the fact that the snake species responsible for the snakebite could not be identified. laboratory findings may be influenced by specific local and regional snake species and their venom characteristics, possibly limiting generalizability. Some parameters like D-dimer levels and Fibrinogen levels were not routinely measured. Additionally, the

retrospective grouping of sample population into cohorts based on severity could have introduced some observer bias. This may have exaggerated the potential statistical power and could have caused bias. The results of this study and its statistical inference cannot be generalised for external validity. A multicentre study using prospective grouping of study sample for a longer study duration could possibly tackle these limitations.

CONCLUSION

This study identifies significant associations between various haematological parameters and the clinical severity of snakebite envenomation in an endemic rural and suburban setting. Multiple parameters help aid the diagnosis, treatment and post treatment clinical course of a patient. Snakebite envenomation requires a multi-speciality approach. Lab parameters act as a cornerstone in management of snakebite envenomation.

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