e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2025; 17(12); 862-869

Original Research Article

Clinical Profile, Toxicity Patterns, Bite-to-Needle Time, and Anti-Snake Venom Adverse Reactions in Snake Envenomation at a Tertiary Care Centre

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Received: 01-09-2025 / Revised: 15-10-2025 / Accepted: 21-11-2025
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Conflict of interest: Nil

Abstract

Background: Snakebite envenomation remains a major yet under-recognised cause of preventable morbidity and mortality in rural India, where delayed access to anti-snake venom and limited critical-care resources adversely influence patient outcomes.

Objectives: To assess the clinical profile and toxicity of snake envenomation; determine its prognosis with reference to bite to needle time; and to document the adverse effects of anti-snake venom therapy.

Methods: This was a single-centre, hospital-based descriptive study conducted in the Department of Emergency Medicine and Intensive Care Unit of Rajah Muthiah Medical College and Hospital, Chidambaram, Tamil Nadu, over one year (April 2018–April 2019). Consecutive patients aged ≥12 years with confirmed snake envenomation were enrolled.

Results: Among 43 snake envenomation cases, most were middle-aged (37.2% aged 41–50 years; 23.2% aged 31–40 years), predominantly female (58.1%) and entirely from rural areas. Bites mainly involved the lower limbs (right 55.8%, left 30.2%), occurred mostly in daytime (77.0%), and were frequently due to unidentified species (48.8%); Russell's viper accounted for 27.9%. Hemotoxic envenomation predominated (79.1%). Cellulitis was very common (86.0%), with acute kidney injury in 14.0% and neuroparalysis in 16.3%; 18.6% required mechanical ventilation. Over half received >8 vials of ASV (55.8%). ASV reactions were frequent, chiefly urticaria (30.2%) and anaphylactic shock (9.3%). Overall outcome was favourable: 86.0% were discharged, 9.3% referred and 4.7% died. Early ASV (<5 h) was associated with no deaths and no DIC, whereas both deaths and all DIC occurred when ASV was delayed >5 h (p=0.042, p=0.037).

Conclusion: Early hospital presentation and timely administration of anti-snake venom significantly improved outcomes in this rural cohort of snake envenomation patients, underscoring the need to strengthen community awareness, referral pathways, and emergency care capacity to reduce snakebite-related morbidity and mortality.

Keywords: Snakebite envenomation, Anti-snake venom, Bite-to-needle time, Hemotoxicity, Neurotoxicity, Rural India.

Introduction

Snakebite envenomation is a major yet neglected public health problem in many tropical and subtropical regions, disproportionately affecting poor rural communities in low- and middle-income countries.[1] Recognising this, the World Health Organization (WHO) has classified snakebite envenoming as a category A neglected tropical disease and launched a global strategy aiming to halve snakebite-related deaths and disabilities by 2030.[2] India bears the largest share of this burden; estimates from the Million Death Study suggest that approximately 1.2 million people died of snakebite between 2000 and 2019, averaging nearly 58,000 deaths annually, with most fatalities occurring in rural areas and among adults in their productive years.[3] Clinically significant envenomation in the Indian subcontinent is predominantly due to the so-called 'Big Four'

snakes—Russell's viper, saw-scaled viper, Indian cobra and common krait—which together account for the majority of severe hemotoxic and neurotoxic syndromes.[4] Viperine bites, especially those from Russell's viper, are strongly associated with local tissue damage, coagulopathy and acute kidney injury, and constitute a leading cause of snakebite-related renal failure in India.[5-7] Elapid bites (cobra and krait) primarily produce neuroparalysis with bulbar and respiratory involvement, often requiring ventilatory support and intensive care.[8] These distinct toxin profiles translate into heterogeneous clinical presentations and outcomes that can vary by geography, species distribution and local health-system capacity.[9,10] Timely administration of anti-snake venom (ASV) is the cornerstone of treatment and is repeatedly shown to improve survival and reduce complications when given early after the bite.[11] Longer bite-to-needle times have been linked to higher rates of systemic envenomation, increased ASV requirements, prolonged hospital stay and greater risk of morbidity and mortality, particularly in viperine bites. However, ASV is an equine-derived immunoglobulin preparation and is itself associated with acute adverse reactions, ranging from mild urticaria and vomiting to severe anaphylaxis and, less commonly, serum sickness; reported rates of early reactions in South Asian cohorts vary widely from about 20% to over 60%.[12,13]

In India, most snakebites occur in rural agricultural settings with delayed access to definitive care, and region-specific data from emergency and critical care services are crucial for planning context-appropriate interventions. There remains a need to better characterise the clinical profile and toxicity patterns of envenomation, evaluate the prognostic impact of bite-to-needle time, and describe the spectrum of ASV-related adverse events in real-world rural hospital settings. Against this background, the objectives of the present study were to assess the clinical profile and toxicity of snake envenomation; determine its prognosis with reference to bite to needle time; and to document the adverse effects of anti-snake venom therapy.

Materials and Methods

This was a single centre, hospital-based, descriptive study conducted in the conducted in the Department of Emergency Medicine and the Intensive Care Unit of Rajah Muthiah Medical College and Hospital, Chidambaram, Cuddalore district, Tamil Nadu, India over a period of one year between April 2018 and April 2019. The study was approved by the Institutional Human Ethics Committee (IHEC) with reference number IHEC/0334/2017 dated 20/02/2018. The participants (and their attenders/primary caregivers) were given the Participant Information Sheet (PIS) in their native language, and its contents were verbally explained to ensure their understanding and satisfaction. Enrolment into the study proceeded upon receipt of written informed consent. The study included patients 12 years of age and above, of both gender, presenting to the Department of Emergency Medicine or admitted in the ICU. However, patients with non-venomous snake bites were excluded.

The sample size was calculated using EnMaster sample size software, based on a single proportion. Redewad et al.[14] reported that the proportion of cellulitis among patients with snake-bite envenomation was 90.6%. Taking this as the prior estimate and assuming an expected proportion of cellulitis of 0.90 in the present study, with an absolute precision of 10% (d = 0.09) and a 95% confidence level (Z = 1.96), the required sample size was calculated using $n = Z^2p(1-p)/d^2$. Substituting these values, the minimum required sample size was rounded off to 43 patients. We used nonprobability sampling technique – convenience sampling/complete enumeration to enrol patients. Data were collected using a structured questionnaire. Snake bite and, where possible, species identification was confirmed based on a reliable history from the patient, eyewitnesses, or attendants, along with the presence of fang marks and local or systemic signs of envenomation. Demographic and event-related variables, including age, gender, time and site of bite, bite-to-needle time, type of snake, and pre-hospital management (first aid or traditional treatment), were systematically recorded. Clinical features such as local swelling, bleeding, ptosis, respiratory distress, hypotension, prior ASV treatment before referral, and the total dose of antivenom administered were documented. Complications, including cellulitis, acute kidney injury (AKI), disseminated intravascular coagulation (DIC), cardiotoxicity, and need for mechanical ventilation, were also noted. In vasculotoxic bites, the 20-minute whole-blood clotting time (20-minute WBCT) was performed as a key screening test for early detection of coagulopathy. Additional investigations—complete blood count, random blood sugar, coagulation profile (PT/INR), renal function tests, serum electrolytes, urine analysis, and electrocardiogram—were carried out and documented, with liver function tests, echocardiography, and other special investigations obtained when clinically indicated. ASV was administered to patients who demonstrated evidence of systemic envenomation, such as clinically significant coagulation abnormalities or systemic neurotoxic features (e.g., ptosis, respiratory muscle weakness), and initial as well as repeat doses were given according to the conventional institutional protocol. The total dose

of ASV and any adverse reactions to ASV were recorded. Each patient was followed prospectively from the time of hospitalization until discharge or death.

Statistical analysis: Data were entered in a spreadsheet and analysed using Statistical Package for the Social Sciences (SPSS) software (version 27.0; IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean and standard deviation, while categorical variables were expressed as frequencies and percentages. The primary exposure of interest—bite-to-needle time (<5 hours vs >5 hours)—was examined for its association with patient outcomes and major complications using the Chi-square test or Fisher's exact test. All tests were two-tailed, and a p-value <0.05 was considered statistically significant.

Results

Among the 43 patients, most were middle-aged adults, with 37.2% aged 41–50 years and 23.2% aged 31–40 years, while only 11.6% were older than 50 years. Females slightly outnumbered males (58.1% vs. 41.9%). All cases were from rural areas (100%). The lower limbs were the predominant site of bite, particularly the right lower limb (55.8%), followed by the left lower limb (30.2%), whereas upper-limb bites were less frequent (11.7%). Most bites occurred during daytime (77.0% between 07:01–19:00). The offending snake was unidentified in nearly half of the cases (48.8%), while Russell's viper accounted for 27.9%, and cobra and krait bites each for 9.3%. Hemotoxic envenomation was the most common toxicity pattern (79.1%), with neurotoxic (14.0%) and combined (7.0%) manifestations less frequent.

Among the 43 patients, cellulitis was the most frequent complication, observed in 86.0%, while acute kidney injury occurred in 14.0% and bleeding manifestations in 9.3%. Neurotoxic features included ptosis in 18.6% and neuroparalysis in 16.3%, whereas hypotension was seen in 7.0%. Serious systemic complications such as cardiotoxicity and disseminated intravascular coagulation (DIC) were each noted in 4.7% of cases. Mechanical ventilation was required in 18.6% of patients, indicating significant respiratory compromise in a subset. The bite-to-needle time was less than 5 hours in 67.4% and more than 5 hours in 32.6% of cases. More than half of the patients (55.8%) required higher doses of antivenom (>8 vials), while 44.2% received ≤8 vials. Following ASV administration, adverse reactions were relatively common, with urticaria being the most frequent, occurring in 30.2% of patients. More severe hypersensitivity manifestations included angioedema in 9.3%, bronchospasm in 7.0%, and anaphylactic shock in 9.3%, while vomiting was reported in 4.7%. Despite these reactions and the underlying envenomation, the overall outcome was favourable in the majority; 86.0% of patients were successfully discharged. A small proportion (9.3%) required referral to higher centres for further management, and mortality was recorded in 4.7% of cases. When outcomes were stratified by bite-to-needle time, patients who received ASV within 5 hours showed more favourable results. Among those treated early, 25 of 29 (67.6%) were discharged, 4 (13.8%) were referred, and none died, whereas in those with a delay >5 hours, 12 of 14 (32.4%) were discharged, none were referred, and both recorded deaths (2/14; 100%) occurred in this group ($p = 0.042$). DIC was also significantly associated with delayed treatment, being absent in all patients with bite-to-needle time <5 hours but present in 2 patients in the >5-hour group ($p = 0.037$). In contrast, there were no statistically significant differences between early and delayed treatment groups with respect to ASV dose requirements (<8 vs >8 vials; $p = 0.152$), cellulitis ($p = 0.965$), acute kidney injury ($p = 0.965$), cardiotoxicity ($p = 0.314$), or need for mechanical ventilation ($p = 0.741$).

Table 1: Baseline demographic profile and bite characteristics of snake envenomation cases (N = 43)

		Frequency (N = 43) n	Percentage %
Age (years)	12 to 20	3	7.0
	21 to 30	9	20.9
	31 to 40	10	23.2
	41 to 50	16	37.2
	51 to 60	3	7.0
	>60	2	4.6
Gender	Male	18	41.9
	Female	25	58.1
Residence	Rural	43	100.0
	Urban	0	0.0
Site of bite	Unknown	1	2.3
	Right upper limb	3	7.0
	Left upper limb	2	4.7
	Right lower limb	24	55.8

	Left lower limb	13	30.2
Time of bite	7:01 to 19:00	33	77.0
	19:01 to 7:00	10	23.0
Type of snake	Unknown	21	48.8
	Russell's Viper	12	27.9
	Saw Scaled Viper	2	4.7
	Krait	4	9.3
	Cobra	4	9.3
Type of toxicity	Hemotoxic	34	79.1
	Neurotoxic	6	14.0
	Combined	3	7.0

Table 2: Clinical manifestations, complications, and treatment characteristics among snake envenomation cases (N = 43)

		Frequency (N = 43) n	Percentage %
Clinical findings/complications	Bleeding manifestations	4	9.3
	Ptosis	8	18.6
	Neuroparalysis	7	16.3
	Hypotension	3	7.0
	Cellulitis	37	86.0
	Acute kidney injury	6	14.0
	Cardiotoxicity	2	4.7
	DIC	2	4.7
Need for mechanical ventilation	Absent	35	81.4
	Present	8	18.6
Bite to needle time (hours)	< 5	29	67.4
	> 5	14	32.6
Dose of ASV	< 8 vials	19	44.2
	> 8 vials	24	55.8

Table 3: Adverse reactions to anti-snake venom and outcomes among snake envenomation cases (N = 43)

		Frequency (N = 43) n	Percentage %
After ASV – adverse effects	Urticaria	13	30.2
	Angioedema	4	9.3
	Vomiting	2	4.7
	Bronchospasm	3	7.0
	Anaphylactic shock	4	9.3
Patient outcomes	Discharge	37	86.0
	Referral	4	9.3
	Death	2	4.7

Table 4: Association of bite-to-needle time with outcomes, complications, and treatment characteristics among snake envenomation cases (N = 43)

		Bite to needle time (hours)		P value
		< 5 (N = 29)	> 5 (N = 14)	
		n (%)	n (%)	
Patient outcome	Discharge	25 (67.6)	12 (32.4)	0.042*
	Referred	4 (100.0)	0 (0.0)	
	Dead	0 (0.0)	2 (100.0)	
Dose of ASV	< 8 vials	15 (51.7)	4 (28.6)	0.152
	> 8 vials	14 (48.3)	10 (71.4)	
Hypotension	Present	1 (33.3)	28 (70.0)	0.191
	Absent	2 (66.7)	12 (30.0)	
Cellulitis	Absent	4 (13.8)	2 (14.3)	0.965
	Present	25 (86.2)	12 (85.7)	
Acute kidney injury	Absent	25 (86.2)	12 (85.7)	0.965
	Present	4 (13.8)	2 (14.3)	
DIC	Absent	29 (70.7)	12 (29.3)	0.037*

	Present	0 (0.0)	2 (100.0)	
Cardiotoxicity	Absent	27 (93.1)	14 (100.0)	0.314
	Present	2 (6.9)	0 (0.0)	
Mechanical ventilation	Absent	24 (82.8)	11 (78.6)	0.741
	Present	5 (17.2)	3 (21.4)	
*Statistically significant at p<0.05				

Discussion

Snake envenomation in India remains an important public health problem, particularly in rural populations, and accounts for a substantial proportion of the estimated 81,000–138,000 annual global snakebite deaths.[3] Recent modelling from the Million Death Study suggests that India alone recorded about 1.2 million snakebite deaths between 2000 and 2019, averaging 58,000 deaths per year, with most fatalities occurring in rural areas and among adults aged 30–69 years.[15] The age distribution in the present cohort, where the majority of victims were middle-aged adults (31–50 years), mirrors these national patterns and reinforces the view that snakebite is largely an occupational and environmental hazard affecting working-age rural populations.[16, 17] In contrast to many Indian series that report a male preponderance—often attributed to greater outdoor and agricultural exposure among men—several recent reports from tea estates and agrarian settings have documented a substantial or even majority female burden, especially among women working barefoot in fields or plantations.[18] The slight female predominance in our study may therefore reflect local patterns of rural labour and domestic activities that bring women into close contact with snake habitats, underlining the need for gender-sensitive community education and protective measures. Rural residence in 100% of our cases is consistent with national data showing that most snakebite deaths in India occur in low-income rural communities with limited access to timely medical care.[15]

The predominance of lower-limb bites, particularly on the right lower limb in our cohort, aligns with multiple Indian clinico-epidemiological studies where 70–80% of bites involve the feet or legs during walking, farming, or outdoor activities.[11] Daytime predominance of bites in this series differs from some reports that describe a bimodal or nocturnal peak, especially for krait bites occurring at night when victims sleep on the floor, but daytime exposures have been increasingly recognized in agricultural and monsoon-related contexts.[19] These observations emphasize that preventive interventions should not be restricted to night-time precautions, but must also address footwear, field practices, and environmental modification during working hours. Nearly half of the offending snakes in our study were unidentified, which is a frequent challenge in Indian practice, as victims often do not see or retain the snake and photographs or reliable descriptions are rarely available.[20, 21] Nonetheless, the identified species profile—Russell's viper, cobra, krait, and saw-scaled viper—corresponds to the 'Big Four' snakes responsible for the majority of serious envenomations in the Indian subcontinent.[4] The predominance of hemotoxic manifestations (79.1%) in our series is concordant with the high burden of viperine envenomation reported from many parts of India, where Russell's viper is the leading cause of hemotoxic snakebite, often associated with coagulopathy, local tissue necrosis, and systemic complications.[22] The very high frequency of cellulitis (86.0%) in our cohort is in keeping with the recognized spectrum of local tissue injury in viper bites, where pain, swelling, blistering, and secondary infection are common and may predispose to compartment syndrome or chronic morbidity.[23-25] Several Indian studies of viperine envenomation have highlighted cellulitis, acute kidney injury, and coagulopathy as the dominant complications, with reported AKI rates around 10–20%, figures that are remarkably similar to the 14.0% incidence of AKI observed in our study.[26, 27] AKI in this setting is typically multifactorial, resulting from direct nephrotoxicity, intravascular hemolysis or rhabdomyolysis, hypotension, and renal microthrombi leading to acute tubular necrosis.[27] Early recognition and aggressive supportive care—including volume resuscitation and timely renal replacement therapy—are critical to improving renal outcomes.

Neurotoxic features such as ptosis and neuroparalysis in our patients reflect contributions from elapid bites (cobra and krait), which commonly produce descending paralysis and respiratory failure.[22] The requirement for mechanical ventilation in 18.6% of cases is broadly comparable to rates reported in intensive-care–based series of neurotoxic envenomation, where 10–30% of patients need ventilatory support depending on delay to ASV and severity at presentation.[28] The relatively low occurrence of cardiotoxicity and DIC (each 4.7%) is nonetheless clinically significant, as both complications carry a high risk of mortality if unrecognized, and have been described particularly in severe viperine envenoming.[26]

Our findings regarding ASV usage and reactions are also consistent with existing literature. National guidelines recommend an initial dose of 8–10 vials

of polyvalent ASV for significant envenomation, with further dosing guided by clinical and laboratory response, particularly in hemotoxic and neurotoxic syndromes.[29, 30] That over half of our patients required more than 8 vials suggests a high venom load or delayed presentation in a substantial proportion of cases and is similar to other Indian tertiary-care studies of moderate to severe envenomation.[11] Adverse reactions to ASV occurred in a sizeable fraction of our cohort, with urticaria (30.2%) being most common and anaphylactic shock seen in 9.3%. This pattern mirrors data from South Asian and Indian studies where overall ASV reaction rates range from about 20% to over 50%, with urticaria and rash as leading manifestations and moderate-to-severe anaphylaxis reported in 10–15% of recipients.[13, 31, 32] These observations reinforce the need for careful monitoring, readiness to treat anaphylaxis with intramuscular adrenaline, and consideration of pre-medication strategies as recommended in several interventional studies.[33] Despite the burden of complications and ASV reactions, the overall outcomes in our series were favourable, with 86.0% of patients discharged and a mortality rate of 4.7%. Comparable Indian hospital-based studies report mortality figures in the range of 3–10%, with higher rates generally linked to delayed presentation, inadequate ASV, or lack of intensive care facilities.[16, 34] Our results therefore suggest that timely administration of ASV and access to critical care support can achieve survival outcomes broadly in line with, or better than, reported national experience.

The present study had several limitations that warrant consideration. First, it was a single-centre, hospital-based descriptive study with a relatively small sample size (N = 43), which may limit the precision of estimates and the generalisability of findings to other regions or healthcare settings. The use of non-probability convenience sampling and inclusion of only patients presenting to the emergency department or ICU may have introduced selection bias, potentially under-representing milder cases managed at peripheral centres or not seeking care. Species identification was uncertain in nearly half of the cases, restricting species-specific inferences regarding clinical profiles and outcomes. Bite-to-needle time and some exposure variables were based on patient or attendant recall, which is susceptible to recall bias. As an observational design without multivariable adjustment, the study could not fully control for confounding factors such as baseline comorbidities, severity of envenomation at presentation, or pre-hospital interventions. Finally, follow-up was limited to the in-hospital course, and long-term renal, functional, or quality-of-life outcomes could not be assessed.

Conclusion

In conclusion, this hospital-based study from rural Tamil Nadu highlights that snake envenomation predominantly affects middle-aged adults from agrarian backgrounds, with lower-limb viperine bites and hemotoxic manifestations forming the major clinical pattern. Cellulitis and acute kidney injury emerged as the most frequent complications, and a substantial proportion of patients required higher ASV doses and critical care support. Although ASV-related adverse reactions, including anaphylaxis, were relatively common, most were effectively managed, and the overall in-hospital outcome was favourable, with a low mortality rate. Crucially, a shorter bite-to-needle time (<5 hours) was associated with the absence of DIC and zero mortality, whereas all deaths occurred among those receiving delayed ASV. These findings underscore the pivotal importance of early hospital presentation and timely administration of ASV, along with vigilant monitoring for complications and drug reactions, and support strengthening community awareness, prompt referral pathways, and capacity building of rural health facilities to reduce snakebite-related morbidity and mortality.

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