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Incidence, Mechanisms, and Clinical Outcomes of Hyponatremia in Venomous Snakebite Envenomation: A Cross-Sectional Study from South India

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ABSTRACT

Background: Snakebite envenomation is a major neglected tropical disease associated with significant morbidity and mortality. Endocrine complications, particularly hyponatremia, remain understudied despite their potential for severe outcomes.
Aims and Objectives: To determine the incidence of hyponatremia in patients with venomous snakebites and to examine its association with snake type, clinical severity, and outcomes.
Materials and Methods: This observational cross-sectional study included 100 adult patients with confirmed venomous snakebites admitted to a tertiary care hospital in Coimbatore, India, from January 2024 to January 2025. Serum sodium levels were measured at admission and serially. Demographic, clinical, and laboratory data were analyzed using descriptive statistics, chi-square, and t-tests.
Results: Hyponatremia (serum Na^+ <135 mEq/L) occurred in 38% of patients. Viper bites showed significantly higher incidence (52.1%) than elapid bites (26.2%, p=0.014). Hyponatremic patients had longer hospital stays (7.8 vs. 4.9 days, p<0.001) and higher rates of acute kidney injury (36.8% vs. 12.9%, p=0.005).
Conclusion: Hyponatremia is common in venomous snakebites, especially viper envenomation, and is linked to worse clinical outcomes. Routine electrolyte monitoring and targeted management are recommended to improve prognosis.

Keywords: *Snake Bites; Hyponatremia; Envenomation; Viperidae; Pituitary Diseases; Electrolyte Imbalance.*

INTRODUCTION

Snakebite envenoming remains a critical yet neglected public health challenge, particularly in tropical and subtropical regions. The World Health Organization (WHO) has classified it as a Neglected Tropical Disease, highlighting its disproportionate impact on impoverished rural communities [1]. Globally, an estimated 81,000 to 138,000 deaths occur annually due to snakebites, with many more survivors experiencing long-term disabilities such as limb loss or permanent functional impairment [2]. These figures likely underestimate the true burden, as many fatalities occur before hospital arrival, and dry bites or delayed presentations complicate accurate reporting [3]. In developing countries, snakebites predominantly affect agricultural workers, pastoralists, fishermen, hunters, children aged 10–14 years, and residents of poorly constructed rural dwellings. Pregnant women face heightened risks, including antepartum hemorrhage and fetal loss following envenomation [4].

India bears nearly half of the global snakebite mortality, with unofficial estimates suggesting 45,900 to 50,900 deaths per year, the majority (approximately 97%) occurring in rural areas [5]. Official government data report far lower figures—for instance, 1,123 deaths in 2013 and 1,008 in 2014—underscoring significant gaps in surveillance and reporting systems [6]. High-burden states include West Bengal, Uttar Pradesh, Andhra Pradesh, Tamil Nadu, Bihar, and Maharashtra. Bites frequently occur during sleep (30%), play (30%), or field activities (28%), with rapid progression of complications limiting the window for effective intervention [7]. Key contributors to mortality include delayed transport to health facilities, scarcity of antivenom, inadequate infrastructure, reliance on traditional remedies, and poor referral pathways [8].

Venomous snakebites, primarily from vipers, cobras, and kraits, trigger both local and systemic effects. Local manifestations encompass swelling, blistering, and tissue necrosis, while systemic involvement may include neuromuscular paralysis, cardiovascular collapse, coagulopathy, and acute kidney injury [9]. Endocrine and metabolic derangements are increasingly recognized, including pituitary dysfunction, adrenal insufficiency, hypoglycemia, electrolyte imbalances (particularly hyponatremia and hypo- or hyperkalemia), and type 4 renal tubular acidosis [10]. Among these, hyponatremia stands out as a particularly dangerous complication capable of leading to seizures, cerebral edema, and fatal outcomes if unmanaged.

Despite growing awareness of snakebite complications, literature specifically addressing hyponatremia in envenomation remains limited. Mechanisms appear to differ by snake type: Russell's viper bites may induce pituitary engorgement via capillary leak syndrome, direct hormonal stimulation, vascular injury, or microthrombi formation, leading to hypopituitarism and subsequent hyponatremia. In neurotoxic krait bites, cerebral salt wasting mediated by brain natriuretic peptide release or sympathetic dysregulation has been proposed. However, clinical data on incidence, severity, timing, and prognostic implications of hyponatremia in Indian cohorts are scarce. This gap hinders optimal supportive care and risk stratification.

The present study was conducted to examine serum sodium levels in patients with envenomation due to venomous snakes and to elucidate how snake toxins influence sodium homeostasis, and to determine the frequency of hyponatremia in victims of venomous snakebites and its association with clinical outcomes.

MATERIALS AND METHODS

Study Setting: This observational cross-sectional study was conducted in the Department of General Medicine at Government Coimbatore Medical College and Hospital, Coimbatore, a tertiary care teaching hospital serving urban and rural populations in Tamil Nadu, India. The study period extended from January 2024 to January 2025, allowing for comprehensive recruitment across seasonal variations in snakebite incidence.

Study Participants: Study participants included adult patients (aged above 18 years) of either gender who presented with established venomous snakebites, confirmed by the presence of neurotoxic features (such as ptosis or respiratory paralysis) or hemotoxic features (such as cellulitis or bleeding manifestations). Patients with vomiting or diarrhea, active or chronic infections, use of diuretics known to cause hyponatremia, serious comorbidities including pulmonary, endocrine, hepatic, or renal disease, and individuals below 18 years of age were excluded to minimize confounding factors affecting serum sodium levels.

Sample Size and Sampling Technique: A sample size of 100 patients was determined based on the availability of eligible patient records meeting the inclusion and exclusion criteria during the study period. Consecutive sampling was employed to enroll all eligible patients presenting during the study duration until the target sample size was achieved.

Study Tools: Data collection was performed using a structured proforma that captured demographic details, clinical history (including time of bite, snake identification where possible, and first-aid measures), physical examination findings, laboratory parameters (particularly serial serum sodium levels), and outcome measures. Laboratory investigations included complete hemogram, renal function tests, coagulation profile (20-minute whole blood clotting time), and electrolytes. Serum sodium was measured using standard ion-selective electrode methods in the hospital's central laboratory.

Study Procedure: Patients presenting to the emergency department or medical wards with suspected snakebite were screened for eligibility. After obtaining written informed consent, detailed history and clinical examination were conducted. Blood samples for serum sodium estimation were collected at admission and as clinically indicated during the hospital stay. Envenomation severity was assessed based on local and systemic manifestations, and standard management protocols including antivenom administration were followed as per institutional guidelines. Patients were monitored for complications, including the development or worsening of hyponatremia, until discharge or clinical stabilization. All data were recorded anonymously in the study proforma.

Ethical Issues: The study protocol was approved by the Institutional Ethics Committee of Government Coimbatore Medical College and Hospital. Written informed consent was obtained from all participants (or their legally authorized representatives in cases of altered sensorium) after providing a detailed explanation of the study objectives, procedures, risks, and benefits in the local language. Confidentiality of patient data was strictly maintained, and the study adhered to the principles of the Declaration of Helsinki.

Statistical Analysis: Data were analyzed using SPSS version 27 statistical software. Descriptive statistics were expressed as means ± standard deviation for continuous variables and frequencies/percentages for categorical variables. The incidence of hyponatremia was calculated with 95% confidence intervals. Associations between hyponatremia and clinical variables (such as snake type, severity, and outcomes) were examined using Chi-square test or Fisher's exact test for categorical data and independent t-test or Mann-Whitney U test for continuous data, as appropriate. A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 100 patients with confirmed venomous snakebites were included in the analysis. The mean age of participants was 42.6 ± 12.8 years, with a slight male predominance (62%). Most bites occurred in rural areas during agricultural activities, consistent with known epidemiological patterns. Table 1 presents the baseline demographic and clinical characteristics of the study population. Viper bites (primarily Russell's viper) accounted for 48% of cases, followed by elapid bites (cobra and krait, 42%) and unidentified venomous bites (10%).

Table 1: Demographic and Clinical Characteristics of Patients with Venomous Snakebites (N = 100)

Variable	Frequency (%) or Mean ± SD
Age (years)	42.6 ± 12.8
Male	62 (62%)
Rural residence	78 (78%)
Time to hospital (hours)	6.4 ± 4.2
Snake type	
Viper (Russell's/Saw-scaled)	48 (48%)
Elapid (Cobra/Krait)	42 (42%)
Unidentified	10 (10%)
Local envenomation	65 (65%)
Systemic envenomation	82 (82%)

Note. Data are presented as mean ± SD or n (%).

Hyponatremia (serum sodium <135 mEq/L) was observed in 38 patients, yielding an incidence of 38%. Severe hyponatremia (<125 mEq/L) occurred in 12% of cases. Mean serum sodium at admission was 133.8 ± 7.2 mEq/L. Table 2 summarizes the distribution of serum sodium levels and the prevalence of hyponatremia.

Table 2: Serum Sodium Levels and Prevalence of Hyponatremia (N = 100)

Serum Sodium Category	Frequency (%)	Mean Sodium (mEq/L)
Normal (≥135 mEq/L)	62 (62%)	140.1 ± 3.4
Mild hyponatremia (130–134)	18 (18%)	132.4 ± 1.2
Moderate (125–129)	8 (8%)	127.5 ± 1.3
Severe (<125)	12 (12%)	118.9 ± 4.1
Overall hyponatremia (<135)	38 (38%)	126.7 ± 6.8

Note. Hyponatremia defined as serum Na^+ < 135 mEq/L.

Patients with viper bites showed a significantly higher incidence of hyponatremia (52.1%) compared to elapid bites (26.2%), with $\chi^2(2) = 8.47$, $p = 0.014$. Time to hospital arrival was longer in hyponatremic patients (mean 8.1 vs. 5.3 hours, $t(98) = 3.12$, $p = 0.002$). Table 3 displays the association between snake type and hyponatremia.

Table 3 Association Between Snake Type and Hyponatremia

Snake Type	Hyponatremia Present n (%)	Hyponatremia Absent n (%)	Total
Viper	25 (52.1%)	23 (47.9%)	48
Elapid	11 (26.2%)	31 (73.8%)	42
Unidentified	2 (20.0%)	8 (80.0%)	10
Total	**38**	**62**	**100**

Note. $\chi^2 = 8.47$, $p = 0.014$.

Hyponatremia was significantly associated with poorer outcomes, including prolonged hospital stay (mean 7.8 ± 3.1 vs. 4.9 ± 2.4 days, $t(98) = 5.21$, $p < 0.001$) and higher rates of complications such as acute kidney injury and neurological sequelae. Table 4 shows clinical outcomes stratified by hyponatremia status.

Table 4 Clinical Outcomes According to Hyponatremia Status

Outcome	Hyponatremia (n=38)	No Hyponatremia (n=62)	p-value
Hospital stay (days), mean ± SD	7.8 ± 3.1	4.9 ± 2.4	<0.001
Acute kidney injury, n (%)	14 (36.8%)	8 (12.9%)	0.005
Need for ASV >10 vials, n (%)	22 (57.9%)	19 (30.6%)	0.008
Mortality, n (%)	3 (7.9%)	1 (1.6%)	0.12

Note. p-values from independent t-test or χ^2/Fisher's exact test.

Electrolyte disturbances frequently co-occurred with hyponatremia. Hypokalemia was present in 42.1% of hyponatremic patients versus 12.9% in normonatremic patients ($\chi^2 = 11.36$, $p = 0.001$). Pituitary dysfunction markers (e.g., persistent hypotension responsive to steroids) were noted more frequently in the hyponatremic group. Table 5 presents associated laboratory abnormalities.

Table 5: Laboratory Abnormalities Associated with Hyponatremia

Parameter	Hyponatremia (n=38) Mean ± SD or n (%)	No Hyponatremia (n=62) Mean ± SD or n (%)	p-value
Serum potassium (mEq/L)	3.4 ± 0.7	4.1 ± 0.5	<0.001
Hypokalemia (<3.5), n (%)	16 (42.1%)	8 (12.9%)	0.001
Serum creatinine (mg/dL)	1.8 ± 0.9	1.2 ± 0.6	0.002
Abnormal 20-min WBCT, n (%)	24 (63.2%)	28 (45.2%)	0.08

Note. p-values from independent t-test or χ^2 test.

In summary, hyponatremia occurred in 38% of venomous snakebite victims and was significantly associated with viper envenomation, delayed presentation, prolonged hospitalization, and other electrolyte and renal complications. These findings emphasize the need for routine electrolyte monitoring and prompt correction in the management of snakebite envenomation.

DISCUSSION

The present study documented a 38% incidence of hyponatremia among 100 patients with confirmed venomous snakebites, highlighting this electrolyte disturbance as a frequent and clinically relevant complication in envenomation. Viper bites were associated with significantly higher rates of hyponatremia (52.1%) compared to elapid bites (26.2%), and hyponatremic patients experienced delayed hospital presentation, prolonged hospitalization, and increased rates of acute kidney injury and other complications. These findings align with the growing recognition of endocrine and metabolic derangements in snakebite envenoming and underscore the importance of systematic electrolyte monitoring [11, 12].

Our observed incidence of hyponatremia (38%) is consistent with limited prior reports from tropical regions. Earlier studies have reported rates ranging from 20% to 55% depending on the predominant snake species and timing of assessment [13]. The higher prevalence in viper envenomation corroborates mechanistic insights into Russell's viper venom effects on the pituitary gland. Capillary leak syndrome, direct hormonal stimulation, vascular injury, microthrombi, and hemorrhagic infarction of the pituitary can lead to acute or delayed hypopituitarism, manifesting prominently as hyponatremia due to cortisol and thyroid hormone deficiencies. The significantly longer time to hospital arrival in hyponatremic patients (8.1 vs. 5.3 hours) suggests that delayed antivenom administration may exacerbate vascular leakage and pituitary engorgement [14].

In contrast, the lower but still notable incidence in elapid (krait and cobra) bites supports the role of cerebral salt wasting (CSW) syndrome. Neurotoxic venom may trigger brain natriuretic peptide release or sympathetic dysregulation, resulting in natriuresis and volume depletion [15]. This mechanism was evident in our cohort through higher urinary sodium excretion (data not shown) in several neurotoxic cases. The co-occurrence of hypokalemia in 42.1% of hyponatremic patients further indicates multifactorial tubular dysfunction, possibly compounded by rhabdomyolysis and acute kidney injury, both more frequent in the hyponatremic group [16].

The association between hyponatremia and adverse clinical outcomes is particularly noteworthy. Hyponatremic patients required more antivenom vials and had nearly double the length of hospital stay. This may reflect greater envenomation severity or the additive morbidity of uncorrected hyponatremia, including cerebral edema, seizures, and prolonged recovery [17]. Although mortality was low overall (4%), the numerically higher rate in the hyponatremic subgroup (7.9% vs. 1.6%) aligns with reports linking severe hyponatremia to fatal arrhythmias and neurological deterioration in resource-limited settings.

Most previous studies focused on hematological or neurological complications, with endocrine manifestations remaining under-investigated. Our cross-sectional design captured real-world clinical practice, including seasonal and demographic patterns typical of South India [18]. The use of standardized laboratory methods and exclusion of major confounders (diuretics, pre-existing renal disease, gastrointestinal losses) strengthens the internal validity of the hyponatremia estimates. The study has a few limitations. First, the sample size of 100, while adequate for prevalence estimation, may have limited power to detect subtle associations or rare outcomes such as mortality. Second, snake species identification relied primarily on clinical features and patient history rather than ELISA-based venom detection, potentially leading to misclassification. Third, as a single-center study conducted in a tertiary hospital, the findings may not fully represent milder cases managed at peripheral facilities or those with rapid pre-hospital mortality. Serial hormone assays (cortisol, TSH, ACTH) were not performed routinely due to resource constraints, limiting definitive attribution of hyponatremia to hypopituitarism versus SIADH or CSW in individual cases.

Despite these limitations, the study has important clinical and public health implications. Routine measurement of serum electrolytes at admission and during the first 48–72 hours should be incorporated into snakebite management protocols, particularly for viper bites and delayed presentations. Early correction of hyponatremia with cautious fluid management and, where indicated, corticosteroid replacement may prevent complications. Training programs for primary care physicians in rural endemic areas should emphasize recognition of endocrine complications alongside conventional

hemotoxic and neurotoxic features. The development of region-specific antivenoms with improved neutralization of pituitary-toxic components warrants further research.

Future studies should adopt prospective designs with larger, multicenter cohorts and incorporate advanced diagnostics such as venom antigen detection, serial pituitary MRI in severe cases, and comprehensive hormonal profiling. Longitudinal follow-up would clarify whether pituitary insufficiency persists and requires hormone replacement therapy. Interventional trials evaluating prophylactic hydrocortisone in high-risk viper envenomation could be valuable. Integration of point-of-care electrolyte monitoring in emergency departments of district hospitals would facilitate timely intervention in resource-constrained settings.

In summary, hyponatremia represents a common, under-recognized, and prognostically significant complication of venomous snakebites. By elucidating its frequency, species-specific associations, and clinical correlates, this study contributes to a more holistic understanding of snakebite pathophysiology and supports the call for comprehensive, multidisciplinary management strategies aligned with WHO guidelines for neglected tropical diseases.

CONCLUSION

This study demonstrates that hyponatremia occurs in 38% of patients with venomous snakebites, with significantly higher rates following viper envenomation. It is associated with delayed presentation, prolonged hospitalization, and increased complications. Routine electrolyte monitoring and prompt correction are essential components of optimal snakebite care. Larger multicenter studies with hormonal profiling are needed to further characterize endocrine sequelae and improve outcomes in this vulnerable population.

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