



Original Article

## The Incidence and Clinical Profile of Acute Kidney Injury in Venomous Snake Bite

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### ABSTRACT

**Objective:** The objective of the study was to find out how many times acute kidney injury happened in patients with snake venom bites who presented to the hospital and their characteristics.

**Methods:** This was a prospective descriptive study that was conducted at the District Hospital in Tumkur, in the Department of General Medicine over an 18-month period (2022-2024). A total of 96 patients (aged 18 years or older) who had been bitten by a snake and had a clinical diagnosis of envenomation were included in the study. Data collection was performed using a standard data form including demographic information, clinical signs/symptoms, and laboratory results. Acute Kidney Injury (AKI) was defined according to RIFLE criteria. Statistical analysis was done using SPSS version 27.0. A p-value  $\leq 0.05$  was considered significant statistically.

**Results:** Majority of the patients were male (men 70.8%) and rural (rural 74%). Most of the reported snake bites were outdoors (90.6%) with Vipers being the commonest snake bite (54.2%). The majority of patients who developed AKI after snake bite was due to delay in administration of Anti snake venom ( $p < 0.05$ ), Oliguria ( $p < 0.001$ ) and deranged Coagulation Profile (INR  $> 1.1$ ) ( $p < 0.001$ ). Poorer outcome was seen in patients who sought traditional remedies prior to visiting the hospital.

**Conclusion:** AKI is a common complication due to venomous snakebite. Early identification of the clinical signs; such as oliguria and administration of anti-snake venom and prompt medical intervention; will help to reduce the incidence of AKI and improve patient outcomes.

**Keywords:** Snakebite, Acute kidney injury, Envenomation, Anti-snake venom, Rural health, Coagulopathy.

### INTRODUCTION

Snakebite envenoming is a major public health concern globally, with over 5 million reported cases every year, responsible for approximately 100,000 deaths worldwide (1–3). The problem mainly lies in neglected populations, particularly in tropical and subtropical regions. It is estimated that snakebites in India result in approximately 60,000–100,000 deaths each year. This reflects several key issues regarding access to timely medical care, public awareness of risks associated with snake bites, and a reliance on traditional healing practices and methods of treatment (2,4–6). Despite the advances and availability of modern healthcare, the majority of people affected by snakebites in India live in rural areas (most often as farmers) and therefore have limited access to adequate medical care (2,4–6). There are approximately 50 different species of snakes in India that are classified as venomous; among these are four of the most dangerous snakes which are commonly referred to as the “big four”: the Indian cobra (*Naja naja*), common krait (*Bungarus caeruleus*), Russell's viper (*Daboia russelii*), and the saw-scaled viper (*Echis carinatus*). These “big four” snakes cause the most clinically significant envenomation's found within India (1,3,7). The toxic effects of venom vary by species of snake; there are neurotoxic, hemotoxic, and myotoxic toxins, which can cause varying degrees of excruciating pain, destruction of local tissues, and sometimes lead to life-threatening systemic complications (4,7–9).

Acute kidney injury (AKI), one of the most severe and life-threatening systemic complications from venomous snakebites, is frequently seen with viper envenomations due to their hemotoxic and vascular toxic effects that cause endothelial injury,

coagulopathy, and renal ischemia. Incidence rates of AKI after snakebite vary greatly (7–30%) and depend on disease severity and availability of medical care (4,8–10). AKI also substantially increases morbidity and mortality, as renal replacement therapy and extended hospitalization are often needed following snakebite (10–12). Pathophysiology of AKI as it relates to snakes is multifactorial, however, some major factors include nephrotoxicity due to venom components (e.g., phospholipase A2 and metalloproteinases), which cause tubular necrosis and endothelial damage; systemic effects (e.g., hypotension, hemolysis intravascular, rhabdomyolysis, and disseminated intravascular coagulation) that result in decreased renal perfusion and ischemic injury (7–11,13–15). AKI due to snakebites is commonly associated with acute tubular necrosis and, in severe cases, cortical necrosis, both of which have been shown to result in poor renal outcomes (8,13).

The clinical manifestations associated with snake bite induced acute kidney injury (AKI) may include oliguria or anuria (reduced to absent urine output), haematuria (blood in urine), proteinuria (urinary excretion of protein), and a rise in serum creatinine levels. These clinical manifestations may appear within hours to days after the time of envenomation and frequently accompany additional clinical signs such as hypotension (low blood pressure), bleeding tendencies, or shock (22,24). Therefore, early identification of these clinical manifestations is crucial as timely intervention with anti-snake venom (ASV) and supportive care can greatly improve the clinical outcome of a patient. The burden of AKI from snake bites is further compounded in developing countries by delays in accessing appropriate health care services. Many patients seek traditional remedies for treating the bite, or they access the health care system late, both resulting in worse clinical outcomes (21,23,25). In resource-limited settings there are inadequate health care infrastructure and shortages of trained personnel, as well as limited access to ASV. All of these factors contribute to increased morbidity and mortality associated with snakebite induced AKI. A scoping review conducted by Mehta et al., demonstrated that human resource shortages in the health care system significantly affect the timely management of acute health conditions, including snakebite envenomation (18).

Acute kidney injury (AKI) is an important cause of morbidity and mortality in many types of clinical situations, including those with infectious and toxic causes. Increased risk of death and long-term complications associated with AKI demonstrates the need for prompt recognition and management (13). AKI has been shown to be a significant predictor of mortality specifically in critically ill patients reported by Anvar et al., which highlights the clinical significance of AKI in acute care (19). Similar mechanisms of systemic inflammatory response and multiple organ dysfunction also contribute to adverse outcomes after snakebite. At the population level, broader determinant factors (i.e., environmental exposures, occupational hazards and lifestyles) are important considerations in their relationship to the incidence and outcome of snakebite (2,18,20,26). Cross-sectional research evidence indicates importance in identifying specific risk factors and clinical patterns associated with poor outcomes in the development of focused intervention strategies, as well as improvements in healthcare delivery (27,28). For these reasons, the understanding of AKI incidence and clinical characteristics in patients who are bitten by snakes is essential to identifying effective management strategies to reduce the overall disease burden, particularly in rural and resource-scarce areas of the world.

### **Aim of the Study**

The present study aimed to evaluate the incidence and clinical profile of acute kidney injury (AKI) in patients presenting with venomous snakebite.

### **Objective**

To determine the incidence and evaluate the clinical profile of acute kidney injury in patients presenting with venomous snakebite.

### **METHODOLOGY**

This study's design is observational, descriptive, and prospective in nature; the location of the study is the District Hospital in Tumakuru, Karnataka, India, where the study will take place over the course of 18 months, beginning in the year 2022. There were adults who had a documented history of being bitten by a snake, and who exhibited either local or systemic effects (symptoms), which were considered to be medically indicative of having suffered a snakebite. A preliminary examination of the medical records of 96 patients allowed the researchers to establish that these patients met the established inclusion/exclusion criteria to be considered for participation in the study. The sample size for this study was based upon the following equation:

$$n = Z^2 p (1 - p) / d^2$$

Where:

$$p \text{ (prevalence of AKI)} = 0.47$$

$$d \text{ (precision)} = 0.10$$

$$Z = 1.96 \text{ (upon which there is a 95\% likelihood of finding an accurate confidence interval)}$$

The total number of patients required for the study was 96 patients.

### **Inclusion Criteria**

The study consisted of patients who had an established medical record history of a prior snake bite and subsequent snake bite symptoms within the last 12 months. Eligible patients had one or more symptoms related to the snake bite after 6-24 hours of initial presentation. As part of this research study, they also had to give permission (consent) to participate.

### Exclusion Criteria

- People who have previously been diagnosed with chronic kidney disease or have suffered from a snake bite in the past
- People with certain other health issues (for example: having diabetes or having high blood pressure)
- People taking medications known to cause side effects related to the kidneys
- People under 18 years old

### Data Collection

Eligible patients were admitted and assessed using structured forms for data collection: history of bite (time, type of snake if known, location) and local and systemic effects of envenomation; laboratory values measured included complete blood count, serum creatinine, blood urea nitrogen (BUN), INR, and 24-hour urine collection for renal function. Patients were monitored throughout hospitalization for urine output and other clinical criteria.

### Definition of Outcome (AKI)

Acute Kidney Injury is an acute and sudden loss of renal function that arises from multiple causes and occurs across all population subgroups. The most frequently used definitions of Acute Kidney Injury are based on the RIFLE Classification System. This classification system incorporates criteria of increased serum creatinine, reduced GFR (glomerular filtration rate), and decrease in urine output. All patients were followed for three days during hospitalization and then reassessed one week after hospital discharge for late onset AKI (acute kidney injury) to determine whether late-onset acute kidney injury (AKI) occurred.

### Management Protocol

Complete standard management for a snakebite event as dictated by institutional protocol, including initiation of ASV (antivenin) therapy and supportive measures, as well as monitoring for complications that could occur as a result of the snakebite. Acute kidney injury was managed with appropriate medical management and initiation of renal replacement therapy (if indicated)..

### Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS version 27.0 and GraphPad Prism version 5. Quantitative data were reported as a mean  $\pm$  standard deviation, while categorical data was presented as frequency and percentage. Categorical variables were analyzed using the chi-square test for comparison of the variables. Independent t-tests and paired t-tests were utilized for comparing variables that were continuous. A positive p value of 0.05 or less was considered statistically significant.

### Ethical Considerations

Approval for ethical research was granted by The Institutional Ethics Committee at Sri Siddhartha Medical College before beginning this study. The participants all submitted their informed consent in writing before being allowed to join the experiment.

## RESULTS

**Table 1: Baseline Characteristics of Study Population**

Variable	Category	Frequency (n)	Percentage (%)
Age (years)	21–30	15	15.6
	31–40	21	21.9
	41–50	25	26.0
	51–60	25	26.0
	61–70	8	8.3
	$\geq 71$	2	2.1
Sex	Male	68	70.8
	Female	28	29.2
Residence	Rural	71	74.0
	Urban	25	26.0

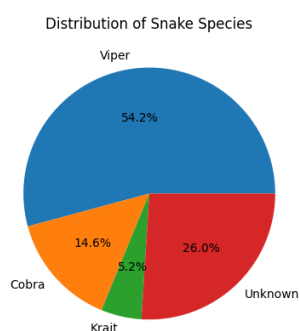
Table 1 shows the initial demographic information for the research sample of 96 people. Almost all of the participants were aged between 41 and 50 years or 51 and 60 years (26%) which were each equal proportions of all of the patients. 21.9% were aged 31 to 40 years, 15.6% were aged 21 to 30 years and the remaining patients were aged 60 years or older. Males made up the largest gender group at (70.8%) of all patients while females comprised (29.4%) of total sample. Most respondents reported they lived in rural (74%) compared to urban communities; 26% were from urban communities. The age, sex and residential status of all respondents were statistically different ( $p < 0.001$ ); those living in rural areas were at the highest risk for snakebites compared to females.

**Table 2: Clinical Profile of Snakebite**

Variable	Category	Frequency (n)	Percentage (%)
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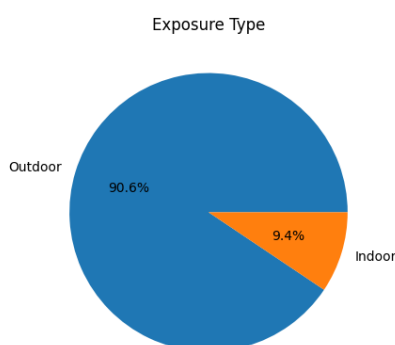
Site of Bite	Lower limb	60	62.5
	Upper limb	35	36.5
	Head	1	1.0
Type of Snake	Viper	52	54.2
	Cobra	14	14.6
	Krait	5	5.2
	Unknown	25	26.0
Exposure	Outdoor	87	90.6
	Indoor	9	9.4
Local Signs	Cellulitis + bleeding	50	52.1
	Bite mark only	28	29.7
	Others	18	18.2

The clinical characteristics of snakebites in study participants are summarized in Table 2. Generally, snakebites occurred mainly in the lower extremities (62.5%), followed by the upper extremities (36.5%), and very rarely occurred in the scalp. The majority of etiological exposures occurred outdoors (90.6%) and illustrate an occupational risk for agricultural and outdoor work. Viper bites represent the most widely documented type of snakebite (54.2%), followed by unknown (26.0%), cobra (14.6%) and krait (5.2%) bites. Local manifestation of snakebite exposure with the most commonly documented observation is the presence of cellulitis associated with bleeding at the site of the bite (52.1%). Isolated bite marks were the next most common local manifestation (29.7%). Statistically significant distribution of these clinical parameters were observed ( $p < 0.001$ ), indicating the predominance of hemotoxic envenomation and the occurrence of venomous snakebites associated with outdoor exposure.



**Figure 1: Distribution of Snake Species**

The distribution of snake species that contribute to snakebite envenomation is presented in figure 1 for the study population. Viper snake bites made up the largest percentage of the total number of snakebite cases with over half of the total (54.2%) being caused by viper species. Unknown species were next (26%), while the number of cobra and krait snake bites was much less frequent. This shows that viper snakes are very common causes of snake envenomation in the study setting, and this is important because viper snakebites are strongly associated with hemotoxicity and complications such as acute kidney injury.



**Figure 2: Exposure Type (indoor/outdoor)**

The demonstrated breakdown of snakebite threats in reference to where they occurred is illustrated in Figure 2. From this distribution, it can be seen that the overwhelming majority (90.6%) of cases occurred outdoors, while 9.4% of cases

occurred indoors. These results indicate that there is a very high correlation between being exposed to snakes while working outside, in particular through agricultural or rural based employment; and risk of being bitten. The results also highlight the necessity for prevention efforts aimed towards at-risk populations.

**Table 3: Laboratory Parameters**

Parameter	Mean ± SD
Age (years)	45.6 ± 13.1
Platelet count	263,583 ± 59,708
Blood urea (Day 1)	34.6 ± 17.4
Blood urea (Day 2)	33.5 ± 16.7
Blood urea (Day 3)	33.5 ± 31.5

**INR Distribution**

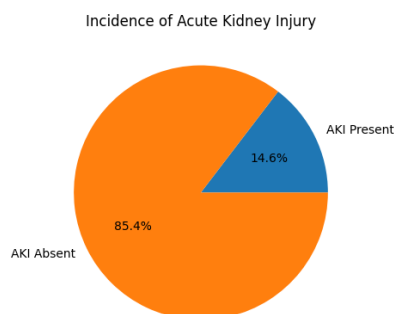
INR	Frequency	Percentage (%)	p-value
≤1.1	17	17.7	<0.001
>1.1	79	82.3	

Study Participant Laboratory Profile is described in Table 3. Average age, 45.6 ± 13.1 years; average platelet count, 263,583 ± 59,708 cells/mm<sup>3</sup>. Blood urea levels were consistent over three days: Day 1, 34.6 ± 17.4mg/dL; Day 2, 33.5 ± 16.7mg/dL; Day 3, 33.5 ± 31.5mg/dL. There was a statistically significant (p<0.001) difference between group means based on the number of subjects with deranged coagulation profiles (INR > 1.1) (82.3% deranged) and those with normal INR values (17.7% normal). This indicates that there was evidence of systemic envenomation by venom as well as hemotoxicity and disruption of coagulation pathways.

**Table 4: Incidence and Factors Associated with AKI**

Variable	Category	AKI (%)	No AKI (%)	p-value
AKI incidence	Present	14.6	—	<0.001
	Absent	85.4	—	
Traditional treatment	Yes	Higher	Lower	<0.05
	No	Lower	Higher	
Urine output	Low	Strong association	—	<0.001
INR	>1.1	Strong association	—	<0.001
Time to ASV	Delayed	Higher AKI	—	<0.05

The rate of acute renal failure (AKI) and associated risk factors are contained within Table 4. Of 96 individuals with confirmed cases of snakebite injury, 14 (14.6 percent) were diagnosed as having developed AKI subsequent to receiving anti-snake venom while the remaining 82 (85.4 percent) were classified without AKI (no AKI) according to standard definitions. In our study cohort, AKI was positively associated with an array of clinical and laboratory findings including delayed administration of anti-snake venom (P <0.05), or lack of urine output (i.e. oliguria) (P <0.001; strong predictor of AKI-early clinical indicator) and a deranged work-up indicating an abnormal coagulation profile (i.e. INRs [international normalized ratio] > 1.1; P <0.001). Additionally, those individuals who initially sought traditional modalities demonstrated worse prognosis than those who accessed medical providers in a timely manner. Our data demonstrate the modifiable and clinical risk factors associated with AKI.



**Figure 3: Incidence of Acute Kidney Injury**

The results of the study show an acute kidney injury (AKI) incidence rate following snakebite, as seen in the distribution of the two groups of patients with and without AKI. The group that developed AKI represented 14.6% of the total number

of patients, while 85.4% of patients were able to maintain normal renal function. This figure serves to further illustrate the AKI incidence rate reported in this study as well as the impact and significance of AKI as a prominent complication of snakebite envenomation.

## DISCUSSION

Envenomation resulting from snake bites continues to be a significant public health problem in many countries, especially in rural areas where people have more chance to be around snakes and little or no access to medical care for long period of time (1-3). The purpose of this investigation was to assess the occurrence and clinical characteristics of Acute Kidney Injury (AKI) in individuals who suffered from a bite from a venomous snake and identify important factors that relate to the development of AKI. The average age of the patients included in this analysis was 45.6 years old. Most of the individuals were 41–60 years old, which is similar to previous studies that were conducted by Naqvi R et al. (12) and Choudhary HR et al. (26) that reported that the majority of people over 40 years of age were diagnosed with AKI from snake bite due to greater-than-average participation in outdoor recreation and working outdoors. Furthermore, there were many more males (70.8%) than females enrolled in this study, and there is evidence to suggest that males are at increased risk of developing AKI due to more exposure while working in agriculture (11) and other outdoor occupations (16).

In this study, a sizeable portion (74%) of the sample population were from a rural environment, which is consistent with what has been previously reported by Harshavardhan L and colleagues (17) and Pandian G and others (27), who claim that snakebite primarily affects people living in a rural setting (i.e., the rural community) because that is where the greatest percentage of reported snakebites occur (90.6%). This correlates with Pal M and others' (21) findings showing that agriculture (placing snakebite victims in newly-created hazard areas) and field work (exposing agricultural workers to snakes) are two primary risk factors for being bitten by a snake. In terms of the variety of snakes that were involved in the bites documented in this study, viper to snakebites (54.2%) were the most prevalent. This finding has also been substantiated in earlier studies i.e., Harshavardhan L, (17). In addition, findings to date (i.e., Harshavardhan L, (17) study have shown that systemic complications (i.e., AKI) from viper venom are quite common. The increased prevalence of cellulitis and open bleeding in the present study is also indicative of the hemotoxic nature of viper venom as is supported by previous studies (10).

In our study, we found a 14.6% incidence of acute kidney injury compared to Albuquerque et al. (14) finding of 15.2% and Harshavardhan et al. (17) finding of 14.6%. However, higher rates of acute kidney injury have been reported by Dharod et al. (10) and Panchalwar (24), which may be due to severity of envenomation, delayed treatment, and access to care. Anvar et al. (19) discuss the importance of early identification and intervention of acute kidney injury as a major contributor to morbidity/mortality in patients with various acute illnesses. In this study, a significant association was found between the development of AKI and the delay in administration of antivenom ( $p < 0.05$ ), supporting previous studies from Paul et al. (22) and Harshavardhan (17) who identified delayed start of antivenom therapy as a major predictor of poor outcomes. When antivenom therapy is initiated promptly, it decreases the amount of free venom in circulation and decreases the systemic effects of venom, subsequently preventing injury to the kidneys.

The association between oliguria and acute kidney injury (AKI) was strong ( $p < 0.001$ ) as demonstrated by Naqvi R et al. (12) and Aye KP et al. (16) who reported that decreased urinary output was the largest clinical finding in AKI patients. Also found was that coagulation parameters (e.g., INR > 1.1) were highly significant for their association with AKI ( $p < 0.001$ ), as noted by the authors of this paper, demonstrating the role that hemotoxic venoms play in causing renal injury through mechanisms such as disseminated intravascular coagulation and microvascular thrombosis (10,24). Further, one other significant finding related to traditional treatment methods was the greater likelihood of poor outcomes in patients who had initially used traditional forms of therapy, most likely due to delays in accessing definitive medical care. There is evidence in the literature by Mehta V et al. (18) that the limitations and delays in accessing healthcare systems are major contributors to poor outcomes in developing nations, particularly by limiting timely access to the appropriate resources required for effective management.

Several factors cause acute kidney injury (AKI) due to snakebite envenoming which include direct effects on the kidney (nephrotoxicity), tissue breakdown (hemolysis), muscular breakdown (rhabdomyolysis), low blood pressure (hypotension), or bleeding disorders (coagulopathy). Siva Kumar DK et al. (25) and Sitprija V (7) conclude that the major causes of renal damage after snakebite are those due to pigment-induced nephropathy and due to ischemic injury. The findings from this study can help to explain why the current research shows a strong correlation between coagulopathy and AKI after snakebite. Additionally, there are some more global/national determinants (many within the community and home environment) that also contribute to the burden of AKI from snakebite. Examples of these factors include the impact of the environment/habitat, nature of the work environment/occupation and lifestyle of each individual. Further, evidence from many cross-sectional studies, such as Aljulifi MZ et al. (20), suggest that understanding the risk factors associated with developing AKI from snakebite envenoming will be useful in guiding clinical practice and public health interventions.

## CONCLUSION

Snakebites from venomous species caused by humans continue to pose a serious public health risk, especially among those who work outdoors in rural areas. Among the patients 14.6% were diagnosed with acute renal failure which significantly correlated with factors such as delayed administration of snake antivenom therapy, decreased urine output, and out-of-

range parameters on laboratory tests for clotting. In addition, data from this study should encourage readers to recognize the importance of early diagnosis and treatment for preventing renal failure and decreasing morbidity after snakebites. Another important finding was the negative outcome associated with struggling to reach health services for treatment, which commonly included resorting to the use of traditional remedies before seeking medical care. These findings will help provide a clearer picture of the issue and will help with the establishment of better infrastructure to deliver healthcare services, increase community education, and ensure the prompt delivery of snake antivenom therapies.

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