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INCIDENCE OF ACUTE KIDNEY INJURY IN VENOMOUS SNAKE BITE PATIENTS

General Medicine

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ABSTRACT

Introduction Snake bite envenomation is a significant public health issue, particularly in rural and forested regions of India. This study aims to investigate the incidence of Acute Kidney Injury (AKI) in patients with venomous snake bites, identify early predictors of AKI, and evaluate the in-hospital outcomes of AKI. **Objective** To study the incidence of Acute Kidney Injury in Venomous Snake Bite patients. **Methods** A prospective observational study was conducted at Bokaro General Hospital, India, from June 2018 to May 2020. The study involved 90 confirmed venomous snakebite patients. Clinical data, laboratory investigations, and outcomes were recorded. AKI was defined using the Kidney Disease: Improving Global Outcome (KDIGO) criteria. **Results** The study revealed a mean age of 44.49 years among patients. Symptoms such as reduced urine output, vomiting, hematuria at presentation, and hematuria a day after admission were significantly associated with poor outcomes ($p<0.05$). Symptoms including fang mark, signs of inflammation, bleeding from the bite site, and neurotoxicity-related symptoms did not show significant associations. Patients with poor outcomes had a significantly higher need for dialysis and ventilatory support ($p<0.00001$). Among the cases, 72.22% experienced AKI, with varying stages of severity (Stage I: 44.44%, Stage II: 7.78%, Stage III: 20.00%). AKI was strongly associated with symptoms such as hematuria at presentation, hematuria a day after admission, bleeding from the bite site, and neurotoxicity-related symptoms ($p<0.00001$). **Conclusion** This study highlights significant associations between certain symptoms and outcomes in venomous snakebite patients. Recognizing symptoms like reduced urine output, vomiting, and hematuria can help predict poor outcomes. Patients with poor outcomes often require dialysis and ventilatory support. AKI is prevalent among venomous snakebite patients and is strongly associated with specific symptoms. Early identification and appropriate interventions are crucial for improving patient outcomes in cases of snake bite envenomation.

KEYWORDS

INTRODUCTION

Snake bite envenomation has been recognized by humans since ancient times. It is most prevalent in temperate and tropical regions where manual agriculture sustains populations. In India, a significant number of snake bites occur when individuals are working barefoot in fields or walking at night. Globally, approximately 5 million people are estimated to be bitten by snakes each year, resulting in around 125,000 deaths and 400,000 cases of permanent disability or disfigurement. Snake bites have a mortality rate equivalent to one-fifth of malaria-related deaths worldwide and half of those attributed to HIV/AIDS in India.(1) The global annual mortality from snake bites is estimated at approximately 94,000, with India alone accounting for around 15,000 deaths per year.(2)

Envenoming by venomous snakes is a common occupational hazard, particularly affecting farmers and individuals residing in rural and forest areas. The practice of walking barefoot in these regions contributes to a higher incidence of snake bites.

It is a leading cause of premature death in rural India.(3) Snakebite represents a significant public health problem in India, with an estimated annual incidence of snake bites ranging from 66 to 163 per 100,000 population, morbidity ranging from 1.4 to 68 per 100,000 population, mortality ranging from 1.1 to 2.4 per 100,000 population, and a case fatality rate of 1.7 to 20%.(4)

India has the highest number of snakebites and related mortality worldwide.(5) Jharkhand, known as the "land of forests," is particularly affected, with high snakebite-related deaths (4.9 per 100,000 population).(6)

The "Big 4" snakes of medical importance in India are the Indian cobra (Naja naja), the common krait (Bungarus caeruleus), the Russell's viper (Daboia russelii), and the saw-scaled viper (Echis carinatus).(7) Among the 216 snake species in India, only 54 are venomous, and these four species are commonly encountered as causes of snakebite poisoning.(8)

Viperidae causes hemorrhagic syndromes, Elapidae causes neuromuscular paralysis leading to respiratory failure, and the effects of envenomation are observed in the nervous system, kidneys, heart, blood coagulation, vascular endothelium, and the site of the bite.(9,10.11)

Although acute renal failure can result from bites by all venomous snakes, a significant proportion of cases are caused by viper bites. The incidence of renal failure varies with the distribution of viperine snakes in different geographic regions.(12) Kidney-related complications are commonly observed in patients with poisonous snake bites. Acute tubular necrosis usually underlies renal failure, and it is often reversible. However, if bilateral cortical necrosis occurs, the prognosis for renal recovery becomes more grim.(13)

Acute kidney injury (AKI) is typically determined by an increase in serum creatinine concentration. AKI is defined as a rise in serum creatinine of at least 0.3 mg/dL within 48 hours or at least 50% higher than baseline within 1 week, or a reduction in urine output to less than 0.5 mL/kg per hour for longer than 6 hours.(14)

This study aimed to determine the incidence of AKI in patients with venomous snake bites, identify early predictors of AKI, and evaluate the in-hospital outcomes of AKI in the study population.

OBJECTIVE

To study the incidence of Acute Kidney Injury in Venomous Snake Bite patients.

MATERIAL AND METHODS

A prospective observational study was conducted at Bokaro General Hospital, a tertiary care center and teaching institute in Bokaro district, Jharkhand, India. The study was carried out in the wards, casualty, and critical care unit of the Department of General Medicine. Bokaro General Hospital is a 910-bedded multispecialty hospital operated by the central government of India (SAIL).

This study followed a prospective, observational cross-sectional design and was conducted over a period of two years, from June 2018 to May 2020. The study population consisted of 90 confirmed venomous snakebite patients who met the study criteria (inclusion and exclusion). The patients were selected from the wards, casualty, and critical care unit under the Department of General Medicine at Bokaro General Hospital.

The sample size was calculated using the Cochran formula, which indicated a minimum sample size of 80. However, to account for a margin of error, the sample size was increased to 90. Purposive/ convenience sampling was used to select eligible patients who provided written informed consent to participate in the study. The first

90 patients who met the criteria and agreed to participate were included in the study and interviewed.

The study procedure involved obtaining approval from the institutional ethical and scientific committee and obtaining valid informed consent from the patients. A detailed history and clinical examination were conducted for each enrolled patient. Data was collected using a pre-designed, pretested, and structured questionnaire through interviews with the study subjects or their caretakers. Hematological and biochemical investigations were performed.

AKI was defined according to the Kidney Disease: Improving Global Outcome (KDIGO) criteria, based on changes in serum creatinine levels and urine output. The staging of AKI was determined using the KDIGO 2012 criteria, which classified AKI into three stages based on serum creatinine levels and urine output.

Ethical approval was obtained, and data collection was carried out according to the approved protocols. Data was recorded in case record forms and entered into Microsoft Excel 2013.

Statistical analysis was conducted using SPSS Software version 20, including descriptive statistics, unpaired t-tests, chi-square tests, and Fisher's exact tests.

RESULTS

Maximum 26(28.89%) patients were in each age groups of 41–50 and 51-60 years, followed by 18(20%) in 18-30 years, 14(15.56%) in 31-40 years and 6(6.67%) in >60 years age group. Mean age of the patients was ± 44.49 years.

Table No. 1: Age distribution of patients studied

Age group (years)	Number of patients	%
18-30 years	18	20.00
31-40 years	14	15.56
41-50 years	26	28.89
51-60 years	26	28.89
>60 years	6	6.67
Total	90	100.00

Table 2: Association of Clinical features (Signs/Symptoms) with Outcome

Symptoms	Outcome		P value (chi square test)
	Good (n=74)	Poor (n=16)	
Reduced urine output	30(40.54%)	13(81.25%)	0.00311
Vomiting	29(39.19%)	11(68.75%)	0.0309
Hematuria at presentation	27(36.49%)	11(68.75%)	0.01782
Hematuria a day after admission	31(41.89%)	11(68.75%)	0.0489
Hemotoxicity Signs			
Fang mark	66(89.19%)	16(100%)	0.1682
Signs of inflammation	70(94.59%)	16(100%)	0.3414
Bleeding from bite site	50(67.57%)	12(75%)	0.5603
Cellulitis	16(21.62%)	11(68.75%)	0.00019
Peripheral pulses not felt	4(5.41%)	6(37.5%)	0.0002
Neurotoxicity			
Ptosis	17(22.97%)	3(18.75%)	0.7125
Diplopia	15(20.27%)	3(18.75%)	0.8903
Muscle weakness	15(20.27%)	3(18.75%)	0.8903
Loss of consciousness	8(10.81%)	3(18.75%)	0.3793
Respiratory paralysis	6(8.11%)	3(18.75%)	0.1982

The analysis of symptoms and outcomes in venomous snakebite patients showed significant associations between certain symptoms and poor outcomes. The symptoms of reduced urine output, vomiting, hematuria at presentation, and hematuria a day after admission were found to be significantly associated with poor outcomes ($p<0.05$).

However, symptoms such as fang mark, signs of inflammation, bleeding from the bite site, and neurotoxicity-related symptoms did not show significant associations with outcomes. Notably, symptoms like cellulitis and absence of peripheral pulses were strongly associated with poor outcomes ($p<0.001$).

Table No 3: Need for dialysis and ventilatory support

Parameters	Outcome		P value (chi square test)
	Good (n=74)	Poor (n=16)	
Dialysis			
Needed	18(24.32%)	13(81.25%)	0.00001
Not needed	56(75.68%)	3(18.75%)	
Ventilatory support			
Yes	7(9.46%)	10(81.82%)	<<0.00001
No	67(90.54%)	6(18.18%)	

In our study of 90 cases, 29 cases needed **dialysis** as supportive treatment. Among 74 good outcome cases 18(24.32%) required dialysis and among 16 poor outcome cases 13(81.25%) needed it. Dialysis was not needed in 56(75.68%) good outcome and 3(18.75%) bad outcome cases **(p value 0.00001**).

7(9.46%) Among 74 good outcome cases and 10(81.82%) among 16 poor outcome needed ventilatory support. 67(90.54%) among 74 and 6(18.18%) among 16 good and poor outcome cases respectively did not required ventilatory support **(p value<<0.00001)**

Table No. 4: Stages of AKI with number of patients

AKI	Number of patients	%
Absent	25	27.78
Present	65	72.22
Stage I	40	44.44
Stage II	07	7.78
Stage III	18	20.00
Total	90	100.00

In our study which included 90 venomous snake bite patients, AKI was present in 65(72.22%) cases. Out of 65 AKI patients 40(44.44%) were in Stage I, 7(7.78%) were in Stage II and 18(20.00%) were in stage III.

Table No.5: Association of Clinical Features with AKI

Symptoms	AKI		P value (chi square test)
	Present (n=65)	Absent (n=25)	
Vomiting	26(40%)	14(56%)	0.1712
Hematuria at presentation	38(58.46%)	0(0%)	<<0.00001
Hematuria a day after admission	42(64.62%)	0(0%)	<<0.00001
Hemotoxicity Signs			
Fang mark	64(98.46%)	18(72%)	0.000077
Signs of inflammation	65(100.00%)	21(84%)	0.00097
Bleeding from bite site	62(95.38%)	3(12%)	<<0.00001
Cellulitis	27(41.54%)	0(0%)	0.00011
Peripheral pulses not felt	9(13.85%)	1(4%)	0.1830
Neurotoxicity			
Ptosis	3(4.62%)	17(68%)	<<0.00001
Diplopia	2(3.08%)	16(64%)	<<0.00001
Muscle weakness	3(4.62%)	15(60%)	<<0.00001
Loss of consciousness	2(3.08%)	9(36%)	0.000019
Respiratory paralysis	1(1.54%)	8(32%)	0.000015

DISCUSSION

In our study the overall mean age of presentation was 44.49±12.23 years. Maximum 26(28.89%) patients were in both the age groups of 41–50 and 51-60 years. 58 patients were in the combined age group of 18 to 50. This was comparable with studies done by **Patil TB et al**[70], **Paul J et al**[73], **Arul P et al**[76], and **Panchalwar VS et al**[77].

In our study of 90 cases, several clinical manifestations were observed. Reduced urine output was present in 43 (47.78%) patients, while vomiting was reported by 40 (44.44%) patients. Hematuria at admission was observed in 38 (42.22%) cases, and 42 (46.67%) patients had hematuria 24 hours after admission. Neurotoxicity signs were identified in 20 patients, with ptosis being the most common (20, 22.22%), followed by diplopia and muscle weakness (18, 20% each). Unconsciousness was observed in 10 (11.11%) study subjects, and 9 (10%) exhibited signs of respiratory paralysis. At least one sign of hemotoxicity was present in 71 (78.89%) patients. Local examination revealed signs of inflammation in 86 (95.56%) cases, fang marks in 82 (91.11%) cases, bleeding from the bite site in 62 (68.89%) cases, and absence of peripheral pulses in 10 (11.11%) patients. Additionally, cellulitis at the bite site developed in 29 (32.22%) patients.

A study conducted by Mukherjee et al. (15) reported similar findings to our study, with comparable percentages of patients presenting with hematuria (29.5%) and nausea/vomiting (55.73%). However, the prevalence of ptosis (44.26%) in their study was higher than in our study. Respiratory paralysis was observed in 18.03% of their cases, which was similar to our findings.

Another study by Pasha et al. (16) showed comparable results to our study in terms of patient presentations, with hematuria (40%) and decreased urine output (50%) being similar. However, the prevalence of nausea and vomiting (26%) in their study closely matched our findings. They also found similarities in signs such as ptosis (10%) and fang marks (66%) compared to our study. The percentage of bleeding manifestations (40%) in their study was also close to our findings. However, they did not observe signs such as diplopia and muscle weakness, which were not seen in our study either.

In our study, reduced urine output was observed in 30 (40.54%) out of 74 patients with a good outcome and in 13 (81.25%) out of 16 patients with a poor outcome. The results showed a significant association with a p-value of 0.00311. Poor outcome cases were significantly associated with vomiting (39.19%, p-value 0.0309), hematuria at presentation (36.49%, p-value 0.01782), and hematuria a day after admission (41.89%, p-value 0.0489). Fang marks were seen in 66 (89.19%) out of 74 patients with a good outcome and in all 16 (100%) patients with a poor outcome, but the association was not statistically significant (p-value 0.1682). Signs of inflammation were observed in 70 (94.59%) patients with a good outcome and in all 16 (100%) patients with a poor outcome, without a statistically significant association (p-value 0.3414). Bleeding from the bite site was present in 50 (67.57%) patients with a good outcome and in 12 (75%) patients with a poor outcome, with no significant association (p-value 0.5603). However, cellulitis was observed in 16 (21.62%) patients with a good outcome and in 11 (68.75%) patients with a poor outcome, showing a significant association (p-value 0.00019). Peripheral pulses were not felt in 4 (5.41%) patients with a good outcome and in 6 (37.5%) patients with a poor outcome, indicating a significant association (p-value 0.0002). Neurotoxicity signs did not show a statistically significant association with the outcome.

In a study conducted by Arul et al. (76), they observed that reduced urine output was seen in 24 (55.8%) cases with a good outcome, which was slightly higher than our study. In cases with a poor outcome, 6 (85.7%) patients exhibited reduced urine output, which was comparable to our findings. Vomiting was observed in 15 (34.19%) cases with a good outcome and in 4 (57.1%) cases with a poor outcome, which closely matched our study. Hematuria was seen in 5 (11.6%) cases with a good outcome and in 2 (28.6%) cases with a poor outcome, which was lower compared to our study. The prevalence of fang marks was consistent with our study, with 66 (89.19%) out of 74 patients with a good outcome and all 16 (100%) patients with a poor outcome exhibiting fang marks (p-value 0.1682). Signs of inflammation were found in 42 (97.7%) cases with a good outcome and 7 (100%) cases with a poor outcome, showing similar results to our study. However, the occurrence of bleeding from the bite site was lower in their study, with 15 (34.9%) cases in the good outcome group and 1 (14.3%) case in the poor outcome group, compared to our findings.

In our study, out of 90 cases, 29 (34%) patients required dialysis, and 23 (25%) patients needed ventilatory support. Among the good outcome cases, 18 (24.32%) out of 74 patients required dialysis, while among the poor outcome cases, 13 (81.25%) out of 16 patients needed dialysis. Dialysis was not necessary for 56 (75.68%) patients with a good outcome and only 3 (18.75%) patients with a poor outcome (p-value 0.00001). Ventilatory support was needed by 7 (9.46%) out of 74 patients with a good outcome and 10 (81.82%) out of 16 patients with a poor outcome. In contrast, 67 (90.54%) out of 74 patients with a good outcome and 6 (18.18%) out of 16 patients with a poor outcome did not require ventilatory support (p-value <<0.00001). Both dialysis and ventilatory support were significantly associated with a poor outcome.
In a study by Athappan et al. (18), 159 (13.5%) patients developed acute kidney injury (AKI), and among them, 72 (45.3%) required dialysis, which is comparable to our study findings. In their study, 36 out of the 72 dialyzed patients expired, while no deaths occurred in the non-dialyzed group.

CONCLUSION

In conclusion, the analysis of the study data revealed significant associations between certain symptoms and outcomes in venomous snakebite patients. Symptoms such as reduced urine output, vomiting, hematuria at presentation, and hematuria a day after admission were significantly associated with poor outcomes ($p<0.05$). Other symptoms, including fang mark, signs of inflammation, bleeding from the bite site, and neurotoxicity-related symptoms, also showed significant associations with poor outcomes. Moreover, the need for dialysis and ventilatory support was significantly higher in patients with poor outcomes ($p<0.00001$). Among the cases studied, 72.22% had acute kidney injury (AKI), with varying stages of severity. AKI was strongly associated with symptoms such as hematuria at presentation, hematuria a day after admission, bleeding from the bite site, and neurotoxicity-related symptoms ($p<0.00001$). These findings highlight the importance of recognizing these symptoms and promptly providing appropriate interventions to improve patient outcomes.

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