

Clinical profile of acute kidney injury in snake bite patient at tertiary care center

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Abstract

Background: Snake-bite is an environmental, occupational and climatic hazard in rural and urban areas. Acute kidney injury is an important complication of snake bite and major cause of mortality. **Aim:** To study the clinical profile of acute kidney injury following snake bite. **Material and Methods:** In this cross sectional observational study 106 patients of snake bite-induced AKI were included. Clinical history taking, physical examination, and laboratory evaluation was done. All patients received standard treatment including anti-snake venom. Outcome was measured. **Results:** Out of 106 cases, incidence of AKI was more common with viper snake bite 97 (91.5%) followed by cobra bite 9 (8.5%). Edema was seen in 36 (33.96%), along with respiratory distress 28 (26.41%), and hypotension 21 (19.81%). The earliest symptom was development of pain and swelling due to cellulitis. The other common symptoms were albuminuria (100%), oliguria 92 (86.79%). **Conclusion:** Acute kidney injury incidence was 29.04% among snake bite. Mortality in this study was lower than other similar studies; this may be due to aggressive and timely management of snake bite patients at study center.

Key Word: Snake bite, acute kidney injury, viper, albuminuria, cellulitis

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INTRODUCTION

Snake-bite is an environmental, occupational and climatic hazard in rural and urban areas, predominantly in countries like India. The World Health Organization (WHO) estimates that about 5 million snakebites occur each year, resulting in up to 2.7 million envenomings.¹ India accounts for the highest number of snakebites and related mortality globally. Snakebite mostly affects the underprivileged rural communities, mainly in Asia and Africa, socioeconomic status and farming add to increased snake-human interaction.² Acute kidney injury (AKI) is an important complication

of snake bite and major cause of mortality. An incidence of renal involvement with snakebite has been reported to be around 10-32%.³ Data regarding the actual number of Snake bite induced AKI and requiring HD and their complications are inadequate in our country. Renal damage can develop very early in cases of Russells Viper bite and even when the patient arrives at hospital soon after the bite, the damage may already have been done. Studies have shown that even when ASV is administered within 1-2 hours after the bite; it was incapable of preventing ARF.⁴ For better outcome, proper supportive management after antivenom administration is important. Most of the patients of acute tubular necrosis recover by few weeks, with the help of occasional need of hemodialysis, but who develops cortical necrosis requires renal replacement therapy on a long-term basis. This study was undertaken to study the clinical profile of acute kidney injury following snake bite.

MATERIAL AND METHODS

This cross sectional observational study was conducted on acute kidney injury in snake bite patients admitted at inpatient Department of Medicine in a tertiary care

teaching hospital. Institutional Ethics Committee approval was obtained prior to commencement of the study. Patients included in study were asked detailed clinical history and detailed physical examination was noted. Blood samples were collected for HB, TLC, Red blood cell count, bleeding and clotting time, urine microscopy, urine albumin, kidney function test, serum electrolyte, in all patients and whenever required Abdominal and Pelvic ultrasonography was done.

Inclusion criteria

- All patients who were more than 12 years.
- A definitive history of snake bite
- Clinical picture with bit emarks, cellulitis, coagulopathy, hematuria, nephropathy.
- Presence of an acute kidney injury as abrupt (within 48 hours) absolute increase in the serum creatinine concentration of ≥ 0.3 mg/dL from baseline value measured after admission or elsewhere after the snake bite, or a percentage increase in the serum creatinine concentration of $\geq 50\%$ above baseline, or oliguria of less than 0.5 mL/kg per hour for more than 6 hours, or serum creatinine more than 1.5 mg/dL or oliguria (urine output less than 400 mL/day).

Exclusion criteria

- Age less than 12 years
- Pre-existing renal disease.
- Diagnosed Case of hypertension.
- Patient on nephrotoxic drugs.
- Patient not willing to consent for the study.

The diagnosis and line of treatment were decided by the physician. No additional drugs or investigations were advised by us during the study period. Patients were classified as per outcome in the form of discharge (group A) and death (group B). Group A received first dose of anti-snake venom (ASV) <4hrs and Group B received first dose of ASV > 4hrs after snake bite.

Statistical analysis

The results were expressed in percentages. Statistical analysis was done by using Microsoft office Excel 2010 and SPSS for Windows version 17.0 (SPSS, Inc, Chicago).

RESULTS

Throughout the study duration of one and half year, about 365 patients were admitted with snake bite, among which 106 (29.04%) patients developed acute renal failure. Most of the victims i.e., 74 (69.81%) in our study were bitten outdoors; generally, in the field during the daytime. The most frequently bitten site was the lower extremity in 71 (66.98%) patients. Majority of

the snake bite victims were from the rural areas. The peak incidence in the snake bite cases occurred during the months of June to September. The average age of the patients was 37.70 years. Average age of male patients with acute kidney injury was 36.64 years (range 17-75 years) and that of the female patients was 40.55 years (range 16-78 years). Out of 106 study population majority of patients were males 70 (66.04%) and females were 36 (33.96%). Fang marks were seen in 99 (93.39%) of the cases, and in 6 cases, abrasion marks were present at the site of the bite. First aid measures were employed in a majority of the patients 91 (85.84%), while the other 15 victims did not receive any first aid treatment. Out of 106 cases, incidence of AKI was more common with Viper snake bite 97 (91.5%) followed by cobra bite 9 (8.5%).

Table 1: Clinical characteristics

Clinical characteristics	No. of patients	Percentage (%)
Albuminuria	106	100%
Oliguria	92	86.79%
Edema	36	33.96%
Hypotension	21	19.81%
Hematuria	22	20.750%
Respiratory distress	28	26.41%
Bleeding manifestations	26	24.52%

Almost all patients had developed local cellulitis. The earliest symptom was development of pain and swelling due to cellulitis. The other common symptoms were albuminuria (100%), oliguria 92 (86.79%), edema 36 (33.96%), hematuria 22 (20.750%) and bleeding manifestations in 26 (24.52%) patients.

Table 2: Symptomatology of envenomed patients

Symptomatology	No. of patients	Percentage
Progressive pain	106	100%
Local swelling	104	98.11%
Local ecchymosis	92	86.79%
Coagulopathy	74	69.81%
Bulla Tissue necrosis	76	71.69%
Paresthesia	15	14.15%
Vomiting and/or nausea	69	65.09%
Ptosis	08	7.54%

Edema was seen in 36 (33.96%), along with respiratory distress 28 (26.41%), and hypotension 21 (19.81%). Albuminuria was present in all (100%) patients and Coagulopathy was seen in 74 (69.81%). Complete recovery was associated with minimum delay in ASV administration. Laboratory investigations showed

anemia (Hb<10gm%) in 27 (25.47%); leucocytosis in 45 (42.45%); thrombocytopenia in 40 (37.73%); coagulopathy in 74 (69.81%); albuminuria 100%; hematuria in 22 (20.75%); hypokalemia in 22 (20.75%) and hyperkalemia in 13 (12.27%) patients. Increased blood urea was seen in 91 patients, and increased serum creatinine was seen in 106 cases.

Table 3: Comparison of timing of first dose of ASV with outcome in AKI patients

Outcome	First dose timing		
	4hrs	4-8hrs	>8 hrs
Recovered	58	37	7
Complications (Dialysis)	01	01	02
Mortality	0	01	0

On radiological investigations 106 (100%) patients had normal size kidneys, altered cortical echotexture, and a normal cortico-medullary differentiation. Amongst 106 patients, 4 (3.77%) patients received hemodialysis, 11 (10.37%) required inotropes for correction of shock, 16 (15.09%) received transfusion to correct anemia, and 6(5.66%) patients required ventilation.

Table 4: Comparison between Group A and B

Outcome	Group A	Group B	Total
Recovered	58	44	102
Complication	0	4	4

Group A= received first dose <4hrs and Group B= received first dose > 4hrs The comparison between group A (first dose within 4hrs) and group B (first dose after 4 hrs) shows delay in first dose administration has more complications, indicating its associated with poor outcome.

DISCUSSION

Snake bites are usually encountered on large scale in rural areas, especially related to farming occupation. Snakebites have the highest incidence in Asia and represent an important health problem. Clinically renal involvement is manifested by hematuria, pigmenturia, proteinuria, and renal failure. Nephropathy usually is associated with bites with hemotoxic or myotoxic snake venoms. Envenoming by snake bite can lead to a variety of clinical manifestation. Local tissue necrosis at the site of bite was evident in most of the patients in acute kidney injury. Antivenom have very little or no role in preventing local tissue necrosis. Locally edema and ecchymosis at the bite site develops rapidly due to cytolysis, hyaluronidase (spreading factor), and anticoagulant effects of the venom.⁵ Acute kidney injury is mainly evident after bites by the viperidae group, and

the colubridae group, but most of the time these cases are due to viper bites. The incidence of acute renal failure (ARF) following poisonous snakes ranges from 13% to 22% due to *Echis carinatus* or Russell's viper bite. The exact pathogenesis of ARF due to snake bite is not well-established. However, many factors contribute, viz, bleeding, hypotension, circulatory collapse, intravascular hemolysis, disseminated intravascular coagulation, microangiopathic hemolytic anemia, and direct nephrotoxicity of venom.⁶ Most of the victims were found to be men in working age group, mainly from rural population and majority of the snake bites happened during working hours in the field. As expected, the snake bites more commonly involving lower limbs and hence, footwear can reduce the snake bites. The present study was based on 106 cases of snakebite envenomation. Higher incidence in rural area may be due to life style which involves outdoor activities and occupational exposure as farmers or labors. Young male agricultural workers were the most common affected group in our study, an occupational hazard. It was observed the occurrence of most of the cases during the month of June to September, which is the monsoon season with agricultural activity in our study region, and also the time of increased activity of snakes as they come out of their shelters. Maharashtra state in western India is one of the most prevalent for viper snakes envenomation than other snakes. Distribution of various snake species in this geographic area is dependent on various environmental and climatic conditions viz. rainfall, altitude, vegetation, and abundance of preferred prey etc.⁷ Hemotoxic syndrome was the most common snakebite syndrome, due to the prevalence of viper snake species (hallmark for hemotoxic syndrome), followed by neurotoxic syndrome of cobra bites (hallmark for neurotoxic syndrome). Simultaneous neurotoxic and hemotoxic manifestations in patients were due to krait envenomation. These results are very similar to other reports from the state of Karnataka and other states in India, i.e. Punde DP et al; Adhisivam B et al.^{8,9} Severe local symptoms observed among viper envenomation were also in accordance with other studies such as Hayat AS et al; Chippaux JP et al.^{10,11} Pain and swelling at the bite site were the commonly encountered symptoms in the patients with viper envenomation. Cellulitis, acute injury, and coagulopathy were found to be the most common complications with viper envenomation in accordance with other studies of Hayat AS et al, Mahasandana S et al and Bandyopadhyay SK et al.^{10,12,13} Acute Renal failure was attributable to damage tubules by venom, hemoglobinuria, rhabdomyolysis, hypotension, and renal microthrombi

formation causing acute tubular necrosis. The rationale for the use of ASV is well defined; dose requirement in various envenomation situations differ widely and are related to the severity grade with the associated snake species. In our study, out of 365 patients of all snake bite patients during study period, 106 (29.04%) patients developed acute renal failure. This incidence is similar to the other previous studies from India; Chugh KS et al and Homrany MA et al.^{14,15} Only 19 (17.92%) of the snake bite victims could come to the hospital within one hour of the bite. All the venomous snake bite sufferers received the equine polyvalent Anti-Snake Venom (ASV). The average quantity of ASV was 23 vials (range 10-35) given for the viper bites. Most common snake type involved in development of renal failure was Vipers 97 (91.5%) followed by cobra 9 (8.5%). The incidence of AKI caused by these snakes varies from 5% to 29% depending on the species of snake and the severity of envenomation.^{14,16,17} Tubular necrosis is an important pathological correlate of AKI. Prolonged AKI with oliguria after snake bite is indicative of cortical necrosis or acute tubular necrosis associated with interstitial nephritis or extracapillary glomerulonephritis. The higher incidence may be due to delay in administration of ASV as there is a delay in taking the patient to hospital after snake bite, which may be related to social factors, and the long distances that the tribal and rural people have to travel before reaching a health facility. All of the patients had local cellulitis, indicating the vasculotoxic nature of envenomation. In viperine bites, the earliest symptom is development of pain and swelling due to cellulitis, which can spread over whole extremity, and can also lead to compartment syndrome threatening the viability of the limb or its part. This can have important consequences if it leads to loss of digits due to ischemia and gangrene. The other common symptoms were albuminuria (100%), oliguria 92 (86.79%), edema 36 (33.96%), which are consequences of renal failure in this patients.¹⁸ Out of 106 patients 22 (20.750%) patients had hematuria, and other bleeding manifestations were present in 26 (24.52%) patients. Similar figures have been reported previously also.¹⁹ Common findings on examination were edema 36 (33.96%), respiratory distress 28 (26.41%), and hypotension 21 (19.81%). The hypotension can be result of various factors like bleeding, disseminated intravascular coagulation, vascular endothelial damage by the toxins, which leads to plasma exudation. An early shock is probably explained by vasodilatation, and late shock is precipitated by massive GI hemorrhage or acute pituitary and adrenal insufficiency. Hypotension can be managed by early administration of ASV, timely

correction of coagulopathy by administration of fresh frozen plasma or platelet concentrates as needed, and optimization of intravascular volume by crystalloids. Albuminuria was present in all (100%) patients. This shows the toxin-induced breakdown of the renal filtration barrier. However, this finding is more useful in follow-up of these patients as persistent albuminuria can serve as a marker of residual renal dysfunction after recovery from acute renal failure.¹⁹ Furthermore, the comparison between the patients who survived and those who died showed a significant difference with regard to coagulopathy, uremic encephalopathy, and mode of dialysis, and no significant difference with regard to hyperkalemia and extensive cellulitis. Severity of renal involvement was found to be in direct relation the mean effective neutralizing dose of ASV, the time taken for normalization of coagulation abnormalities. Possibility of venom's direct toxicity on organ system is pointed by the direct proportionality between incidences of complication with venom neutralization time and delay in ASV administration. Hence, an early institution of ASV is beneficial in preventing complications.

CONCLUSION

Snake bite is an occupational hazard in rural India for farmers and workers. Snake bite is a lethal condition which may involve risk of mortality. Prompt treatment and management is desirable for a favorable outcome. Acute Kidney injury incidence was 29.04% among snake bite. Mortality in this study was lower than other similar studies; this may be due to aggressive and timely management of snake bite patients at study center.

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