



Original Research Article

Clinical profile and outcome of Aki in snake bite patients

Vivek C Ganiger¹, Avinash Itagi², Deba Prasad Kar³, Shiv Shankar Sharma^{4,*}¹Dept. of Nephrology, Karnataka Institute of Medical Sciences, Hubli, Karnataka, India²Dept. of Medicine, Karnataka Institute of Medical Sciences, Hubli, Karnataka, India³Dept. of Nephrology, Institute of Medical Sciences and SUM Hospital, Bhubaneswar, Odisha, India⁴Dept. of Medicine, Nephrology Sub Unit, Mahatma Gandhi Memorial Medical College, Indore, Madhya Pradesh, India

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ABSTRACT

Introduction: Snake bite is an important cause of Acute kidney injury (AKI), which contributes to 8%-45% of total AKI patients. There are number of published studies describing Acute Kidney Injury in Snake bite patients. However, there is a lack of recent data on AKI in Snake bite from India. The purpose of this study was to analyze the clinical profile and outcome AKI in Snake bite patients.

Materials and Methods: All AKI (Acute Kidney Injury) Patients due to snake bite were evaluated. Detail clinical profile of AKI patients including history and physical examination were studied. Complete blood count, renal function tests, Liver function tests, Urinalysis, Coagulation profile, total CPK, LDH, D-dimer were done in all patients. Patients with persistent renal dysfunction even after of 3 weeks are advised to undergo Contrast Enhanced Computed Tomography scan of KUB and/or renal biopsy. Demography, clinical profile, causes of AKI, course in the hospital, management aspects and outcome were studied in detail. Patients were followed up for 3 months to determine the recovery of renal function or progression to chronic kidney disease.

Results: Among Two hundred twenty-one AKI patients (221), twenty-three patients were found to have AKI due to snake bite, with an incidence of 10.4%. Acute tubular necrosis was noted in 69.6% of the patients followed by Acute interstitial nephritis in 13% and renal cortical necrosis in 8.6%. 56.5% (13) of the patients were dialysis dependent at time of admission. Among them, two patients were progressed to chronic kidney disease.

Conclusion: Oligoanuria was the main presenting complaint. Sepsis and Hypotension were present in more than 50% of the patients. The main reason for AKI in our patients was (ATN) Acute tubular necrosis. Mortality was observed in 8.7% of total AKI patients.

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1. Introduction

Snake bite is an important cause of morbidity and mortality in tropical countries like India. According to the estimation of WHO, about 5 million people are bitten each year by poisonous snakes which results in 2.5 million envenomation, 100000 deaths and 300000 amputations.¹ Asia and Sub-Saharan Africa contributes to the majority of snake bite induced death.² In India, mortality is estimated

between 35000-50000 per annum, and it is highest in the world.^{2,3} 500 species are considered to be venomous out of 2500 - 3000 species of snakes.⁴ There are 2 important groups (families) of venomous snakes in south-east Asia – Elapidae and Viperidae. Elapidae have short permanently erect fangs. This family includes the cobras, king cobra, kraits, coral snakes, and the sea snakes. Viperidae have long fangs, which are normally folded up against the upper jaw, but when the snake strikes, are erected. Russel's viper (*Daboia russelli*), Cobra (*Naja naja*), Common Krait (*Bungarus caeruleus*) and Saw scaled

* Corresponding author.

E-mail address: drshivssharma@gmail.com (S. S. Sharma).

viper (*Echis carinatus*) are medically important snakes of India, that occur throughout the country. About 5% to 29% of the patients will develop AKI following snake bite depending on the species of snake and the severity of envenomation.⁵⁻⁷ It takes few hours to as late as 4 days to develop AKI after snake bite. AKI generally lasts for 2 to 3 weeks. Main reason for AKI after snake bite is Acute tubular necrosis. Other reasons are which contribute to AKI are acute interstitial nephritis, cortical necrosis, glomerulonephritis and vasculitis. Haemorrhage is mainly caused by vasoactive mediators, cytokines and direct toxicity of venom. Hypotension, disseminated intravascular coagulation, intravascular haemolysis and rhabdomyolysis enhances renal ischemia which leads to AKI.⁸ The purpose of this study is to analyse the clinical profile and outcome of AKI in snake bite patients.

2. Material and Methods

All Snake bite AKI (Acute Kidney Injury) patients attending to the department of Nephrology and Medicine for a period 1 year were evaluated. Meticulous clinical examination was carried in all cases. They were evaluated further using appropriate laboratory investigations to determine the cause of AKI individually such as Urine examination, complete blood count with peripheral smear, random blood sugar, serum lactate dehydrogenase, coagulation parameters (Prothrombin time, Activated partial thrombin time), D-dimer, total CPK, renal function tests, liver function tests. Radiology examination (USG abdomen for Kidney size, margin, echogenicity, corticomedullary differentiation, associated lesions (hydronephrosis, calculus) was done in all cases. Contrast enhanced CT scan KUB and/or Kidney Biopsy in patients with prolonged AKI (oligoanuria of more than 3 weeks) to look for the cause and prognosis of AKI. Demography, clinical profile, causes and types AKI, course in the hospital and Management aspects were studied in detail. Patients were followed up for 3 months determine the recovery of renal function or progression to chronic kidney disease/End stage renal disease.

2.1. Study design

Cross sectional observational study.

2.2. Inclusion criteria

1. History of snake bite.
2. Clinical features suggestive of snake bite such as, presence of fang marks/cellulitis /coagulopathy or neuroparalysis.
3. AKI was defined according to KDIGO criteria (increase in serum creatinine by ≥ 0.3 mg/dL within 48 hours or increase in serum creatinine to ≥ 1.5 times baseline, which is known or presumed to have occurred within the past 7 days).

2.3. Exclusion criteria

Patients who had not given voluntary consent, Patients with underlying kidney disease /chronic kidney diseases.

2.4. Consent

Written informed consent was obtained from each enrolled patient prior to their induction into the study. A detail history, review of case sheets, physical examination and laboratory investigations were conducted for each patient. Patients have received treatment according to standard snake bite guidelines.

2.5. Statistical analysis

SPSS software was used for analysis of data and the results were recorded as mean, median and standard deviation.

3. Results

Two hundred and twenty-one patient were evaluated during the study period. Among them, 23 patients were diagnosed to have AKI due to snake bite with an incidence of 10.4% of total Acute kidney injury patients. AKI due to snake bite noted in 1 in 10 of total AKI patients. the age of AKI ranged between 23 to 75 years, with mean of 47 ± 3.4 years. Majority were males 15(65.2%) and remaining were females 8(34.8%) (Table 1). Oligoanuria was the main presenting complaint with complete anuria in 13 (56.5%) of the patients and remaining 8(34.8%) were oliguric. Cellulitis and oedema were the presenting complaints in 73.9% (seventeen) of the patients. Icterus was noted in 60.9% (14) of the patients. Sixteen (69.6%) patients were having hypotension at the time of admission. AKI patients had mean systolic blood pressure of 101 ± 2.82 mmHg, ranging from 66-160 mmHg and mean diastolic blood pressure of 64 ± 1.7 mmHg ranging from 40 to 88 mmHg. 12(52.2%) patients were febrile at admission. Eleven (47.6%) had hematuria at the of admission. Among 23 patients 69.6% (sixteen) had a sepsis and platelets were low in 13(56.5%) patients. 21.7% (5) patients had Gastro intestinal bleed and 17.4% (4) presented with seizures. Coagulation parameters was deranged and D-dimer were elevated in 47.8% (11) of the patients. Rhabdomyolysis was noted in 30.4% (7) patients and intravascular hemolysis in 34.8% (8) (Table 2). The mean serum urea was 124 ± 48 mg/dl, ranging from 45 – 221 mg/dl, while serum creatinine ranging from 1.9- 10.4 mg/dl, mean was 6.7 ± 3.1 . Levels of potassium were in the range of 3.4-8.5meq/L, mean was 5.9 ± 1.4 meq/L (Table 3). Of 23 patients, fifteen had normal renal function at the end of three weeks, were presumed to have acute tubular necrosis. Six had persistent renal dysfunction. Contrast enhanced CT scan was done in 1 patient which showed cortical necrosis. Five patients underwent renal biopsy, three had Acute

interstitial nephritis, one had severe acute tubular necrosis and patchy cortical necrosis was noted in another patient (Table 4). Fifteen (65.2%) patients received hemodialysis during hospital stay. Mortality was 8.7% (2 patients) (Table 5).

Table 1: Age & Gender distribution of study subjects

Gender	N(Percent)	AGE (Years) Mean (SD)
Male	15 (65.2)	48.6 (15)
Female	8 (34.8)	44.2 (19)
Total	23 (100)	47.1(16)

Table 2: Clinical features in Snake bite AKI patients

Features	No. of patients (%)
Oligoanuria	21(91.3)
Cellulitis	17(73.9)
Icterus	14(60.9)
Hypotension	16(69.6)
hematuria	11(47.6)
Gastro intestinal bleed	04(17.4)
DIC	11(47.8)
Rhabdomyolysis	07(30.4)
Intravascular hemolysis	08(34.80)
seizures	04(17.4)

Table 3: Severity of AKI in Snake bite patients. (n=23)

Parameters	Range	Mean
Serum urea(mg/dl)	45 – 221	124±48
Serum creatinine(mg/dl)	1.9- 10.4	6.7±3.1
Serum potassium(meq/L)	3.4-8.5	5.9±1.4

Table 4: Renal lesion in snake bite AKI patients (n=21)

Lesion	Number(percentage)
ATN	16(69.6%)
AIN	3(13)
Cortical Necrosis	2(8.6)

Table 5: Outcome in snake bite AKI patients

Outcome	Number(percentage)
Complete Recovery	19(82.6)
Progression to chronic kidney disease	2(8.7)
Death	2(8.7)

4. Discussion

Snake bite is an important cause AKI worldwide and in tropical countries especially like India. It is mainly an occupational hazard. Snake bite AKI and related

fatalities mainly seen in monsoon season in India^{9,10} and worldwide.¹¹ About 5% to 29% of the patients develop AKI following snake bite.⁵⁻⁷ In another study it was 8%-45% in adults, 46% in children.^{5-7,12} An incidence of 18.1% was noted from a study from India.¹³ In our current study incidence was 10.4% of total AKI patients. Thus, we have noted Snake bite AKI in one in ten of total AKI patients. Higher incidence snake bite AKI in developing countries, including India, is mainly related to visiting the traditional healer and tying of tourniquets which leads to higher incidence of cellulitis and sepsis.

Males are affected more often than the females, as they constitute the working majority who are actively engaged in farming and other outdoor activities. In our study we have noted AKI in 65.2% of the males and 34.8% in females. Our findings were concurrent with those of earlier studies.^{6,14}

In India, most of the snake bites are caused by Russell's viper or *Echis carinatus* bites.⁵ Snake venom consists of many proteins such as enzymes, polypeptide toxins and non-toxic proteins. Among them, Phospholipase A2 is the important one which damages the mitochondria, red blood corpuscles, white blood corpuscles and platelets. It will hamper the functioning of nerve endings, skeletal muscle, vascular endothelium, and other membranes. It produces presynaptic neurotoxic activity, opiate-like sedative effects which leads to the auto pharmacological release of histamine and anticoagulation. Viper bites are responsible for the most of the systemic symptoms such as: Coagulopathy; haemolysis; AKI; a generalized increase in capillary permeability; rhabdomyolysis; and neurotoxicity.^{8,15} Haemoglobinuria and myoglobinuria caused by intravascular haemolysis from rhabdomyolysis contribute to the development of AKI after snake bite. Bleeding, hypotension, (DIC)disseminated intravascular coagulation, intravascular haemolysis, and rhabdomyolysis enhances renal ischemia which leads to acute kidney injury. Enzymatic activities of snake venoms account for direct nephrotoxicity. Immunologic mechanism plays a minor role.⁸

In our study, mean duration of arrival at hospital was 3.3±2 days. It ranges from few hours to 8.8 days in other studies.^{7,16} In our study we have noted cellulitis was one of the important risk factors to the development of AKI. pain and swelling at the bitten part are the earliest symptoms which are seen in the patients of viper bite. Previous studies have noted cellulitis in 39%-98.7%.¹⁶⁻¹⁸ We have observed cellulitis in 73.9% of the patients, quite similar to other studies. Studies have reported Oligoanuria in 13 % to 100%^{5,16,17} and haematuria or black coloured urine in 24%-86%^{5,16} as compared to that of 91.3% and 47.8% respectively in our study. We have seen neurotoxicity in 17.4% of the patients as to compared to that of 3.2%- 100% in other studies.¹⁷⁻¹⁹ Intravascular haemolysis, rhabdomyolysis and thrombocytopenia were

noted in 34.8% and 30.4%, 56.5%, of the patients respectively. Other studies have quoted thrombocytopenia in 9.7% to 60%,^{5,16} intravascular haemolysis in 13.8%-54%^{5,16} and rhabdomyolysis in 68% to 100% of the patients.^{7,13} Rhabdomyolysis is an important cause of AKI in snake bite patients and is mainly caused by sea snakes. Russell's viper venom in certain geographical areas can cause both rhabdomyolysis and intravascular haemolysis. In our study, 2 patients had both haemoglobinuria and myoglobinuria. Viper venom has various procoagulant enzymes which is responsible for the activation of coagulation cascade leading to a state of disseminated intravascular coagulation which results in severe blood loss leading to hypotension and further adds to renal ischaemia. Disseminated Intravascular Coagulation (DIC) plays an important role in development of snake bite-induced cortical necrosis. It is characterized by the presence of microangiopathic hemolytic anaemia, thrombocytopenia and fibrin thrombi in renal microvasculature.^{5,17} In our study, DIC was observed in 47.8% patients as compared to 11.1%-43% of patients in other studies.^{5,16}

Acute tubular necrosis (ATN), acute interstitial nephritis (AIN), renal cortical necrosis (RCN) are the main lesions responsible for AKI in Snake bite patients, other rare lesions are glomerulonephritis and rarely papillary necrosis. ATN has been observed in 70%-80% of the patients who have developed AKI following snake bite.⁵ Biopsy done in earlier days of ATN shows tubular injury, intratubular casts, interstitial edema, interstitial nephritis and regenerating tubular epithelium in later days of ATN. We have observed ATN in 69.6% of the patients which is similar to the above study. AIN was noted in 13% of snake bite AKI patients. It is considered to be a rare cause but studies have shown AIN in 5.7%-11.9% of total AKI patients following snake bite.^{20,21} Kidney biopsy in these patients shows mainly lymphocytes with some degree of neutrophils, eosinophils and plasma cells. Renal cortical necrosis is an important cause of AKI with adverse outcomes. There is a necrosis of all renal elements of cortex (glomeruli, blood vessels and tubules) of both kidneys. Necrosis can be of total (complete) or subtotal (patchy).^{22,23} Russell's viper and *Echis carinatus* bites are responsible for most of the RCN cases.⁵ Significant decrease in renal arterial perfusion due to vascular spasm and microvascular injury contributes to the development of RCN. The striking features of this condition are a prolonged period of oligoanuria and failure of complete recovery of renal function. We have seen RCN in 2 patients (8.7%) of total AKI patients. Previous studies had shown RCN in 24% of total AKI patients caused by snake bite^{5,18} and none of the patients shown RCN in two studies.^{20,21}

We have observed that, 56.5% of the patients in our study were dialysis dependent at the time of admission. However, most of them (82.6%) were recovered and had normal renal function by the end of 3 weeks. Only two (8.7%) patients were having renal cortical necrosis and had persistent renal

dysfunction at the end of 3 months of follow up and progressed to chronic kidney disease. Previous study had observed persistent renal damage in the form of decreased renal function, proteinuria and/or hypertension.²⁴ We have observed mortality in 2(8.7%) patients. Both are above 65 years and admitted after 7 days of snake bite after receiving treatment from local native healers. Studies had shown mortality 6.3%-39.1% of total snake bite AKI patients^{5,7,16} and none in another study.¹⁹ Important reasons which contribute to increased mortality are delay in transport, lack of availability of ASV in peripheral hospitals and inadequate knowledge among medical practitioners regarding snake bite management and inappropriate first-aid measures such as incision, suction and herbal treatment.^{10,15,25}

5. Conclusion

Snake bite is an important cause of morbidity and mortality. Majority of the complications and deaths can be easily prevented by educating the local practitioners about appropriate first aid measures and rapid transport to the nearby hospital.

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7. Conflict of Interest

The authors declare they have no conflict of interest.

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Author biography

Vivek C Ganiger, Assistant Professor

Avinash Itagi, Assistant Professor

Deba Prasad Kar, Associate Professor

Shiv Shankar Sharma, Professor

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