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ACUTE KIDNEY INJURY CAUSED BY SNAKE ENVENOMATION IN JAMMU REGION: A PROSPECTIVE OBSERVATIONAL STUDY OF CLINICAL PROFILE IN A TERTIARY CARE CENTRE

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ABSTRACT

Snake envenomation is a common medical emergency and an occupational hazard, more so in tropical India, where farming is a major source of employment. The Jammu region of the Jammu and Kashmir state, which is located in the sub-Himalayan range, is extremely rich in poisonous snakes. Most of the patients are victims of Russell's viper or Echis carinatus bites, which cause acute kidney injury. Acute kidney injury following snake envenomation is associated with prolonged hospital stay, increased healthcare costs and high mortality especially in critically ill patients. As there were no prospective observational studies from the Jammu region, the present study was undertaken to know the incidence of acute kidney injury in patients with snake envenomation and to describe the clinical profile of snake bite patients and ascertain the correlation between various clinical factors and the subsequent development of kidney injury. 55.6% of the patients with snake envenomation developed acute kidney injury as per Acute Kidney Injury Network (AKIN) criteria.

Keywords: snake envenomation, clinical profile, acute kidney injury

INTRODUCTION

Snake bite is a common medical emergency and an occupational hazard, more so in tropical India, where farming is a major source of employment. Over 2,000 species of snakes are known worldwide, of which around 400 are poisonous and belong to the families Elapidae, Viperidae, Hydrophidae and Colubridae [1]. The highest prevalence is in rural area and the maximum number of cases have been reported in the monsoon season. The concept of the "Big 4" snakes of medical importance in India includes the Indian cobra (*Naja naja*), the common krait (*Bungarus caeruleus*), the Russell's viper (*Daboia russelii*) and the saw-scaled viper (*Echis carinatus*) [2]. India accounts for about 30,000 deaths per year due to snake bite [3]. The Jammu region of the Jammu and Kashmir state, which is located in the sub-Himalayan range, is extremely rich in poisonous snakes [4]. Acute kidney injury (AKI) is mainly observed following bites by the snakes which belong to the viperidae group and it is seen less with sea snake bites and the bites of snakes of the Colubridae group. Most of the Indians are victims of Russell's viper or *Echis carinatus* bites, which cause AKI [5]. Acute renal failure complicates the course in 5 to 30% of victims of severe viper poisoning. The viper venom induces several clinical abnormalities that favor the development of acute renal failure. These alterations include a varying degree of bleeding, hypotension, circulatory collrapse, intravascular hemolysis, and disseminated intravascular coagulation with or without microangiopathy. A direct cytotoxic action of snake venom on the kidney is also suspected. In sea snake poisoning, myonecrosis and myoglobinuria appear to play the predominant pathogenetic role [6]. Although there are a number of studies on acute kidney injury in snake bite victims from India, there is paucity of prospective studies on the risk factors in the development and outcome of AKI in India [7]. Some authors have postulated that the renal

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abnormality correlates well with late onset of treatment and that early ASV administration prevents renal damage. A detailed clinical study correlating the development of complications with timing of ASV administration was needed [8]. The present study, therefore, was undertaken to assess the risk factors and the prognostic factors of acute kidney injury caused by snake envenomation in the Jammu region.

Table I: Demographic characteristics of patients with snake envenomation

Demographic characteristic	Patients with snake envenoma-tion
Number	112
Male : Female	76 (67.9%): 36 (32.1%)
Age (years)	33.22 ± 12.14
Rural : Urban	103 (92.0%): 9 (8.0%)
Definite bite : Suspicious	56 (50%): 56 (50%)
Lower limbs : Upper limbs	90 (80.4): 22 (19.6%)
Fang marks	75 (67%)
Tourniquet	67 (59.8%)
Traditional treatment	57 (50.9%)
Local swelling	66 (58.9%)
20 min WBCT (Non-clotting)	79 (70.5%)
Hemorrhagic manifestations	54 (48.2%)
Incision marks	37 (33%)
Bite to ASV administration time (hours)	8.16 ± 2 (CI 1.38)
Reduced urine output	56 (50%)
Ptosis	35 (31.3%)
Respiratory involvement	26 (23.2%)
Development of AKI	62 (55.4%)

METHODOLOGY

The present study was conducted as a prospective, observational study. The patients enrolled in the study were those patients admitted in Government Medical College, Jammu (tertiary care centre). The methodology included clinical history taking, physical examination and laboratory evaluation. Snake bite patients were identified from their history of snake bite, definite or suspicious, presence of bite marks or other clinical features consistent with snake bite. The physical examination will include general physical examination, systemic examination and local examination (local bleed, local swelling, fang marks, tourniquet, etc). The laboratory investigations included all the routine investigations including 20 minute whole blood clotting time (WBCT).

Inclusion criteria

1. Definitive history of snake bite.
2. Suspicion of snake bite but the clinical picture is consistent with snake bite, as presence of fang marks or cellulitis or coagulopathy or neuroparalysis.
3. Presence of acute kidney injury (defined by AKIN) as an abrupt (within 48 hours) absolute increase in the serum creatinine concentration of ≥ 0.3 mg/dL from baseline value measured after admission to the hospital or elsewhere after snake bite, before referral to the hospital, or a percentage increase in the serum creatinine concentration of ≥ 50 percent above baseline, or oliguria of less than 0.5 mL/kg per hour for more than six hours.

Exclusion criteria

1. Patients with pre-existent renal disease (serum creatinine >1.5 mg/dL prior to snake bite or ultrasonography of abdomen suggestive of bilateral small kidneys/loss of corticomedullary differentiation / obstructive nephropathy/other renal pathology).
2. Diagnosed cases of hypertension/ diabetes mellitus.
3. Exposure to nephrotoxic drugs.

Assessment of severity of acute kidney injury will be done by RIFLE criteria:

1. Risk: serum creatinine increased 1.5 times or urine production of less than 0.5 ml/kg/hr for 6 hours.
2. Injury: doubling of serum creatinine or urine production less than .5ml/kg/hr for 12 hours.
3. Failure: rise of creatinine more than 4mg/dl or urine production below 0.3ml/kg/hr for 24 hours loss.
4. Loss: persistent AKI or complete of kidney function for more than four weeks.
5. End-stage renal disease: need for renal replacement therapy for more than three months.

After taking consent, all patients underwent a careful observation and evaluation. The study

protocol was reviewed and approved by the Institutional Ethics Committee. Written Informed consent was obtained from subjects over 18 years of age and from parents/guardians for subjects less than 18 years of age.

Statistical analysis

All the analysis was performed by using Microsoft Office Excel software and a commercially available portable IBM software "Statistical Package for the Social Sciences (SPSS)" Statistics version 19 on personal computer. Chi-square test (Pearson) was used to calculate p-value for the strength of association of various clinical parameters with acute kidney inj ury (AKI).

RESULTS AND OBSERVATION

During the study period, a total of 112 normotensive, nondiabetic patients above 18 years of age without previous history of renal disease or exposure to nephrotoxic drugs were admitted with snake envenomation in Government Medical College, Jammu.

DISCUSSION

Snake bite is a major public health problem in tropical and subtropical countries. Global mortality from snake bites is around 40,000 annually [9]. Of these, approximately 25% (10,000) deaths occur in India [6].

Sex: The analysis of the data revealed that 36(32.1%) were females and 76(67.9%) were males and a male: female ratio of 2.1:1. More males were victims of snakebite may be due to the fact that males were more involved in outdoor work and in fields as compared to females and thus at greater risk of exposure to the snakebite. **Nisar *et al.* (2009)** in their study of 65 patients found that 38.5% were females and 61.5% were males and a male: female ratio of 1.6:1 [10].

Age: The mean age of the patients admitted with snake envenomation was 33.22 years (SD ±12.14), the minimum age was 18 years and maximum age was 75 years. **Sharma *et al.* (2005)** in their study in a North Indian hospital had similarly reported a mean age of 31.2 years [11].

Age distribution: The majority of the patients (86.6%) were in the age group of 18-45 years of age. **Logaraj *et al.* (2013)** in his study on epidemiology of snakebite in a Medical College Hospital in Tamil Nadu had reported that majority (87.7%) of the victims were in the age group of 15-59 years [12].

Residence: 103 (92%) were from rural areas and 9 (8%) were from urban areas. **Kalantri *et al.* (2006)** reported that 84% patients with snake envenomations were from rural areas [13].

Table II: Demographic characteristics of snakebite patients with AKI and without AKI

Demographic Characters	Snakebite patients with AKI	Snakebite patients without AKI
Number	62 (55.4%)	50 (54.7%)
Male : Female	40(64.5%): 22(35.5%)	36(72%): 14 (28%)
Rural : Urban	57 (91.9%): 5 (8.1%)	46 (92.0%): 4 (8.0%)
Fang marks	45 (72.6%)	30 (60.0%)
Traditional treatment	39 (68.4%)	18 (31.6%)
Tourniquet	42 (67.7%)	25 (50%)
Local swelling	49 (79%)	17 (34%)
20 WBCT (Non-clotting)	59 (95.2%)	20 (40%)
Hemorrhagic manifestations	37 (59.7%)	17 (34%)
Incision marks	26 (41.9%)	11 (22%)
Bite to ASV administration time >6 hours	49 (79.0%)	26 (52.0%)
Reduced urine output	46 (74.2%)	10 (20%)
Ptosis	8 (12.9%)	27 (54.0%)
Respiratory involvement	5 (8.1%)	21 (42%)

Site of bite: 90 (80.4%) patients had a bite over lower limbs and 22 (19.6%) had bite over upper limbs. Out of 112 patients, 46 (41.1%) suffered a bite over right lower limb, 44 (39.3%) suffered a bite over left lower limb, 11 (9.8%) patients suffered a bite over left upper limb and 11 (9.8%) suffered a bite over right upper limb. **Saravu *et al.* (2012)** in their study had similarly observed that most of the snake bites were on the lower limb (77.63%), upper limbs were bitten in 21.95% of their victims [14].

History of bite (definite/suspicious): 56 (50%) had a definite history of snake bite, while the remainder 50% were admitted with history of suspicious of snake bite and associated systemic envenomations or local swelling. **Jarwani (2013)** in

his study on demographic, epidemiologic and clinical profile of snake bite cases in Ahmedabad, Gujarat had reported bite marks in 64% of the patients [15].

Fang marks: The fang marks were seen in 75 (67%) patients and were absent in 37 (33%) patients.

Tourniquet application: Out of 112 patients, a tourniquet was applied to the affected limb by 67 (59.8%) patients. **Logaraj (2011)** reported in his study the habit of tying a knot proximal to the site of bite in 39.6% of the patients [12].

Incision marks: Incision marks were seen over the site of bite in 37 (33%) patients.

Local swelling: Local swelling was seen in 66 (58.9%) patients. **Paul and Dasgupta (2012)** in their study found local swelling in 57.3% patients [16].

Coagulopathy: It was measured as 20 minute whole blood clotting time. It was present in 33 (29.5%) patients. **Davis *et al.* (2012)** had reported laboratory evidence of coagulopathy in 58.9% patients [17].

Haemorrhagic manifestations: Bleeding manifestations were seen in 54 (48.2%) patients. **Davis *et al* (2012)** in their study on mortality predictors of snake bite envenomations in southern India reported clinically evident bleeding manifestations in 40% of the patients [17].

Bite to needle time for ASV administration: The average for bite to needle time for ASV administration was 8.16 (SD ±2, CI 1.38) hours. **Metri (2013)** observed that "bite to needle time" was significantly more in the patients who developed AKI as compared to that in those who were in non-AKI group [18].

Acute kidney injury (AKI): In the present study, out of 112 patients, 50 (44.64%) patients did not develop AKI, it was present in 62 (55.35%) patients as per RIFLE criteria. **Paul and Dasgupta (2012)** in their study had found AKI in 43.27% of the patients [17]. The increased incidence of AKI in our study is probably due to increased "bite to needle" time due to delay on the part of the patients to report to the hospital as most of the patients were from rural areas. Moreover, the present study involved the admitted patients with evidence of envenomation following snake bite and not all the patients with snake bite, thereby, accounting for higher incidence of AKI.

Severity of AKI (RIFLE criteria): In the present study, out of 62(55.35%) patients with AKI, 9 (8%) patients had stage 1 AKI, 4 (3.6%) patients had stage 2 AKI, 46 (41.1%) patients had stage 3 AKI, 2 (1.8%) patients had stage 4 AKI and 1 (0.9%) had stage 5 AKI.

In the present study, it was found that there was significant positive association (p=.000) of AKI with 20 minutes WBCT, traditional treatment (p=0.003), reduced urine output (p=.000), hemorrhagic syndrome (p=.007), local swelling (p=0.000) and bite to ASV administration time>6 hours (p=0.004). However, there was no significant positive association of AKI for fang marks (p=0.15), tourniquet (p=0.057), sex (p=0.39) and place of residence (p=0.99). In the present study, there was significant negative association of AKI with ptosis (p=0.000) and respiratory involvement (p=0.000). **Athappan *et al*. (2008)** showed in their study that presence of bleeding manifestations were identified as independent predictors of poor outcome in snakebite patients [19]. Bleeding manifestations are the manifestation of coagulopathy which was demonstrated in our study as 20 minutes WBCT >20 minutes. **Paul and Dasgupta (2012)** reported that snakebite patients with neurological signs and symptoms were negatively correlated with AKI development [16].

The limitations of this study are that patients with age less than 18 years regional lymphadenitis, cellulites, hypotension, disseminated intravascular coagulation could not be included as predictors in our study, were not included and offending snake species or genus could not be identified.

CONCLUSION

From the results, we can conclude that development of AKI can be predicted early by presence of WBCT>20 min, traditional treatment, hemorrhagic manifestations, local swelling and bite to ASV administration time >6 hours. Dose and timely administration of the ASV is very important as bite to ASV administration time>6 hours was significantly associated with subsequent development of AKI. ASV should be made available and be administered to patients with envenomations in the periphery based hospital facilities as the majority of the bites occur in rural areas. The people in the rural areas need to be made aware that they should not delay the institution of ASV therapy as it puts them on a higher risk of developing AKI. The patients should report to the nearest medical facility immediately instead of the traditional healer. The haemorrhagic manifestations should be treated with blood and blood products in a pursuit to reduce the risk of development of AKI.

REFERENCES

1. Al-Homrany M. Acute renal failure following snake bites: a case report and review of the literature. *Saudi J Kidney Dis Transpl.* 1996; 7: 309-12.

2. Simpson ID and Norris RL. Snakes of medical importance in India: is the concept of the "Big 4" still relevant and useful? *Wilderness Environ Med.* 2007; 18(1): 2-9.

3. Warrell DA. WHO/SEARO Guidelines for the clinical management of snakebite in the Southeast Asian Region. *SE Asian J Trop Med Pub Hlth.* 1999; 30: 1-85.

4. Bhat RN. Viperine snake bite poisoning in Jammu. *J Indian Med Assoc.* 1974; 63: 383-92.

5. Albright RC Jr. Acute renal failure: a practical update. *Mayo Clin Proc.* 2001; 76(1): 67-74.

6. Chugh KS. Snake-bite-induced acute renal failure in India. *Kidney Int*. 1989; 35(3): 891-907.

7. Harshavardhan L and Lokesh AJ. A study on the acute kidney injury in snake bite victims in a tertiary care centre. *J Clin Diagn Res.* 2013; 7(5): 853-6.

8. Narvencar K. Correlation between timing of ASV administration and complications in snake bites. *J Assoc Phys India.* 2006; 54: 717-9.

9. Sanford JP. Snake bites. In: *Cecil Textbook of Medicine*, 20th edition (Bennett JC, Plum F, editors) 1966; 2: 1951-3.

10. Nisar A. Presentation and complications of snakebite in a tertiary care hospital. *J Coll Phys Surg Pak.* 2009; 19(5): 304-7.

11. Sharma N. Snake envenomation in a north Indian hospital. *Emerg Med J.* 2005; 22: 118-20.

12. Logaraj M. Epidemiology of snakebite reported in a Medical College Hospital in Tamil Nadu. *Int J Med Public Health.* 2011 (October-December).

13. Kalantri S, Singh A, Joshi R, *et al*. Clinical predictors of in-hospital mortality in patients with snake bite: A retrospective study from a rural hospital in central India. *Trop Med Int Health.* 2006; 11: 22-30.

14. Saravu K, Somavarapu V, Shastry AB, *et al*. Clinical profile, species-specific severity grading and outcome determinants of snake envenomation: an Indian tertiary care hospital-based prospective study. *Indian J Crit Care Med.* 2012; 16(4): 127-132.

15. Jarwani B. Demographic, epidemiologic and clinical profile of snake bite cases, presented to Emergency Medicine Department, Ahmedabad, Gujarat. *J Emerg Trauma Shock.* 2013; 6(3): 199-202.

16. Paul JP and Dasgupta R. Early prediction of AKI in snakebite patient at the time of hospital admission. *N Am J Med Sci.* 2012 (June); 4(5).

17. Davis S. Mortality predictors of snake bite envenomation in southern India – a ten-year retrospective audit of 533 patients. *J Med Toxicol.* 2012; 8(2): 118-23.

18. Metri SS. A study on the acute kidney injury in snake bite victims in a tertiary care centre. *J Clin Diagn Res.* 2013; 7(5): 853-6.

19. Athappan G, Balaji MV, Navaneethan U, *et al.* Acute renal failure in snake envenomation: A large prospective study. *Saudi J Kidney Dis Transpl.* 2008; 19: 404-10.