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Nephrology

Risk Factor Analysis for Acute Kidney Injury in Snake Bite: Retrospective Study from Western Rajasthan

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Abstract	**Original Research Article**

Background: Despite being extremely common medical problem in India, the pathogenic mechanism of snake-bite induced acute kidney injury (AKI) remains elusive. Analysis of the risk factors for snake-bite induced AKI may be helpful in AKI prevention and early treatment. **Methods:** The study included 201 snake-bite patients who were hospitalized to our hospital during period of January 2019 to March 2020. The patients were divided into AKI and non-AKI groups. The Chi-square test, Student's t-test were used for statistical analysis. **Results:** The mean age of patients was 40.5 ± 9.5 years. Of the 201 patients 40.8% cases, (n=82) suffered from AKI. While, 33.3% (n=67) case suffered from severe AKI and needed renal replacement therapy. There were statistically significant differences between the AKI and non-AKI groups with respect to older age, female gender, time interval from snake bite to antivenom therapy, creatine kinase, Lactate Dehydrogenase (LDH), hemoglobin level, and presence of diabetes. Occurrence of AKI was very significantly associated with mortality risk (P value 0.0001). **Conclusion:** Occurrence of AKI was linked to advanced age, female sex, markers of hemolysis and muscle injury, delay in anti-snake venom therapy, and diabetes.
Keywords: Acute kidney injury, hematotoxic snake bite, hemolysis, outcome AKI, risk factor, snake bite.

INTRODUCTION

Snake bites are considerable cause of mortality and morbidity in tropical countries, with approximately 125,000 deaths worldwide annually [1]. Snakebite is now recognized as a Neglected Tropical Disease (NTD) by the World Health Organization (WHO). An accurate measure of the global burden of snakebite envenoming remains elusive due to lack of data [2-6]. However, the available literature reports that the vast majority of snakebite induced deaths occur in Asia and Sub-Saharan Africa [3]. Mortality due to poisonous snakebites in India is the highest in the world, with around 35000-50000 deaths per annum [5-7]. The principle effects of envenomation is on the nervous system, kidneys, heart, lungs, liver, blood coagulation system, vascular endothelium and local effects at the site of bite [4].

Renal involvement is a common complication of snake envenomation, and the renal manifestations of snake bite consist of acute kidney injury (AKI), hematuria, and proteinuria [8]. The pathogenic mechanisms of snake-bite induced AKI have not been studied in detail. It is reported that snake-bite induced AKI was associated with disseminated intravascular coagulation (DIC), intravascular hemolysis, rhabdomyolysis, and direct effect of toxin on vascular endothelium [9]. Among all organ involvement, occurrence of AKI carries worst prognosis, in cases of snake-bite [10]. The purpose of this study was to review the demographic, clinical and laboratory findings in snakebite patients admitted to our institution, to analyze risk factors associated with development of AKI.

METHOD AND MATERIALS

This was a retrospective study, conducted at Dr SN medical college, Jodhpur, India. All adult (>18 years) cases of poisonous snake bite who attended our hospital, during period of January 2019 to March 2020, were included in analysis. Patients were included if they had a definite history of snake bite and developed features of envenomation. Patients with nonvenomous or so-called "dry" bite, defined by lack of signs or symptoms of envenomation after a period of observation, were excluded from analysis. Patients were also excluded if they had clinical or laboratory features suggestive of pre-existing chronic kidney disease (CKD). Study was approved by institutional ethics

committee, and since it was retrospective type of study hence patient consent was not taken.

Definition of AKI

Occurrence of AKI was diagnosed according to the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) guideline [11]. As per KDIGO guideline, AKI was considered when: (1) increase in the serum creatinine concentration of 0.3 mg/dL from the baseline, or (2) 1.5-fold rise in serum creatinine from baseline. We didn't use urine output criteria since urine output monitoring was not routinely done at our ward.

The patient's information, including gender, age, co-morbidities such as diabetes and hypertension, time interval from snake bite to antivenom therapy, hemoglobin, LDH, serum creatinine, and creatinine kinase, were extracted from case records. Patient data was then divided into 2 groups in regard to occurrence of AKI: AKI group and Non-AKI group. Available clinical and laboratory parameters were analyzed to find out risk factors, associated with development of AKI.

STATISTICAL ANALYSIS

Categorical variables are reported in the form of number (%), while continuous data are expressed as mean ± standard deviation. Chi-square test was used for dichotomous variables, while continuous data were analyzed using unpaired t test. A statistical value of $p < 0.05$ was considered significant. All the calculations were carried out using SPSS software version 16 (SPSS Inc., Chicago, IL, USA).

RESULTS

Data of 201 cases, who were admitted to our hospital during study period, was analyzed to assess risk factors associated with development of AKI. Most of patients were of younger age with mean age of 40.5±9.5 years. A total of 182 (90.5%) patients belonged to rural background. Male gender (n=142; 70.6%) predominated the study population. Both of these demographic data can be explained by the fact that snake bite in our country is mainly seen with farming activity. These 201 patients were then categorized into 2 categories; patients who developed or presented with AKI: "AKI group", and cases who did not have any evidence of renal involvement during hospital stay: "Non-AKI" group. The demographic, laboratory, and outcome parameters of AKI and Non-AKI groups were then compared to evaluate risk factors for occurrence of AKI (Table-1).

Table-1: Comparative analysis of demographic and laboratory parameters of "AKI" vs. "Non-AKI" groups

Parameter	AKI group (n= 82)	Non-AKI group (n=119)	P-value
Age (yrs)	41.9±10.3	39.5±8.9	0.07 (NS)
Male	49	93	**0.005**
Female	33	26	**0.005**
Advanced age (>60 yrs)	43	41	**0.01**
Diabetes	29	24	**0.01**
Hypertension	27	39	0.98 (NS)
Time interval* (hrs)	19.3±7.4	11.7±9.3	**0.0001**
MBP ** (mm Hg)	73.4±11.2	76.1±10.9	0.08 (NS)
Hemoglobin (gm/dl)	7.7±2.6	9.1±1.8	**0.001**
Platelet count (<1 Lacs)	21	32	0.83 (NS)
WBCT (minutes)	17.2±5.5	15.9±6.1	0.12 (NS)
Serum Bilirubin (mg/dl)	1.8±0.7	2.0±0.9	0.09 (NS)
SGPT (IU/L)	34.4±9.5	36.2±10.4	0.21 (NS)
LDH (IU/L)	1874.3±269	312±108.6	**0.0001**
Creatinine Kinase (IU/L)	1103±169.1	136.3±28.4	**0.0001**
Blood urea (mg/dl)	106.4±20.1	37.5±6.3	**0.0001**
Serum creatinine (mg/dl)	5.6±1.3	1.1±0.3	**0.0001**

*Time interval between snake bite and administration of anti-snake venom.
**Mean blood pressure at time of admission.
Abb: MBP; Mean blood pressure, WBCT; Whole blood clotting time, LDH; Lactate Dehydrogenase, NS; Not significant.

Of 201 cases, 82 (40.8%) patients developed AKI, while 67 (33.3% of total cases) required renal replacement therapy. A total of 23 (28.1%) of AKI died during course of illness, while 55 (67.1%) patients out of remaining 59 cases, fully recovered from AKI. Meanwhile, 4 cases had biopsy proven diffuse renal cortical necrosis and remained dialysis dependent at time of discharge. Mortality rate in Non-AKI group was 10.1% (n=12). Thus development of AKI was associated with statistically significant risk of mortality (P value=0.0001).

The AKI group had significantly higher proportion of female gender (P-value 0.005), and diabetes as co-morbidity (P-value 0.01) in comparison to Non-AKI group. Likewise, significantly more patients in AKI group (n=43) were older than 60 yrs than in Non-AKI group (n=41) [P-value 0.01]. Mean

values of creatinine kinase, blood urea, serum creatinine were higher in AKI group (P value 0.0001 for each variable). Delay in administration of anti-snake venom was extremely significantly associated with development of AKI (P-value 0.0001).

DISCUSSION

Snakebite is a common medical emergency and an occupational hazard in India. In the present study, the mean age of study population was 40.5±9.5 years. More than 70% cases were males, and belonged to rural areas. This may be related to snakes biting frequently in rural areas; the males were vulnerable to be attacked by poisonous snakes because they were the primary outworkers for their families. The results are in consistence with the other studies published from India (10, 12). The over-all mortality rate in present study was 17.4% (n=35). Similar findings are reported from various regions, across the India (6, 13-15). Mortality rate in Non-AKI group was 10.1% (n=12), while 23 cases (28.1%) of AKI died during course of illness. Thus development of AKI was associated with statistically significant risk of mortality (P value=0.0001).

The pathogenic mechanism of snake-bite induced AKI is unclear. Our study reported that development of AKI was significantly higher in female gender. This is a noval finding and has not been reported in literature [9]. Our explanation for this finding is that females are usually socially and medically neglected in less developed countries like India, and this may lead to delay seeking medical help. Another explanation could be that females have lesser body surface area and build-up so that same amount of venom should produce more toxic damage in females in comparison to males. However, further studies are needed to ascertain whether female sex is really susceptibility factor for AKI, or it was just a chance finding. Older age and presence of diabetes were other risk factors associated with occurrence of AKI in our study. Both these conditions are characterized as having angiosclerosis, poor renal reserve and compensatory ability, and microcirculation dysfunction, which might predispose to development of AKI [16].

In our study, increased time interval from snake bite to antivenom administration was extremely significant risk factor for snake-bite induced AKI. Some of the snake-bite patients initially received traditional treatment instead of going to the nearest hospital, which could potentially have delayed time to admission. Increased time interval from snake bite to antivenom therapy makes the snake venom circulate in bodies longer with resultant local tissue damage and hemolysis, which is associated with AKI. To further support this hypothesis, laboratory markers of muscle damage and hemolysis such as low hemoglobin, elevated LDH, creatinine kinase, were significantly raised in AKI group. The similar observations have been reported in previous studies [9].

There are certain limitations to present study. First, being a retrospective study, the cause and effect relationship could not be established. Second, the quantity of snake venom was not detected. Amount of venom injected, is one of the most important determinant of local tissue necrosis at bite site and other organ damage. Radio immunoassay and enzyme-linked immunosorbent assay can be used to detect the quantity of snake venom [17].

CONCLUSION

Advanced age (>60 years), female gender, presence of diabetes, increased time interval between bite and administration of anti-snake venom, low hemoglobin, elevated creatinine kinase, and LDH were risk factors for development of AKI in patients with poisonous snake-bite, in present study. Our research will be of benefit to the early treatment of snake-bite induced AKI and will improve the prognosis of snake-bite patients.

REFERENCES

1. Chippaux JP. Snake-bites: appraisal of the global situation. Bull World Health Organ. 1998; 76(5):515–524.
2. White J. Clinical Toxinology. Curr Infect Dis Rep, 2011;13:236-242.
3. Kasturiratne A, Wickremasinghe AR, de Silva N, Gunawardena NK, Pathmeswaran A, Premaratna R, et al. The Global Burden of Snakebite: A Literature Analysis and Modelling Based on Regional Estimates of Envenoming and Deaths. PLoS Med 2008; 5(11): e218.
4. Alirol E, Sharma SK, Bawaskar HS, Kuch U, Chappuis F. Snake bite in South Asia: a review. PLoS neglected tropical diseases. 2010 Jan;4(1):e603.
5. Mohapatra B, Warrell DA, Suraweera W, Bhatia P, Dhingra N, Jotkar RM, Rodriguez PS, Mishra K, Whitaker R, Jha P, Million Death Study Collaborators. Snakebite mortality in India: a nationally representative mortality survey. PLoS neglected tropical diseases. 2011 Apr;5(4).
6. Kirte RC, Wahab SN, Bhathkule PR. Record Based Study of Snakebite Cases Admitted at Shri Vasantro Naik government medical college and hospital, Yavatmal (Maharastra). Indian J Public Health 2006; 1:35-37.
7. Gaitonde BB, Bhattacharya S. An epidemiological survey of snake-bite Cases in India. Snake 1980; 12:129–133.
8. Sitprija V. Animal toxins and the kidney. Nature clin pract Nephrol, 2008; 4: 616–27.
9. Li W, Chen F, Wu S. The Related Risk Factors Analysis of Snake-Bite Induced Acute Kidney Injury. Med Sci Monit, 2016; 22: 2335-2339.

10. Menon JC, Joseph JK, Jose MP, Dhananjaya BL, Oommen OV. Clinical Profile and Laboratory Parameters in 1051 Victims of Snakebite from a Single Centre in Kerala, South India. JAPI 2016; 64: 22-29.

11. Kidney Disease Improving Global outcome (KDIGO). Acute kidney injury work group, KDIGO clinical practice guideline for AKI. Kidney Int, 2012;(Suppl. 2):1-138.

12. Kumar KG, Narayanan S, Udayabhaskaran V, Thulaseedharan NK. Clinical and epidemiologic profile and predictors of outcome of poisonous snake bites – an analysis of 1500 cases from a tertiary care center in Malabar, North Kerala, India. International Journal Gen Med, 2018;11:209-216.

13. Lal P, Dutta S, Rotti SB, Danabalan M, Kumar A. Epidemiological profile of snakebite cases admitted in JIPMER hospital. Indian J Community Med. 2001 Jan 1;26(1):36-8.

14. Kalantri S, Singh A, Joshi R, Malamba S, Ho C, Ezoua J, Morgan M. Clinical predictors of in-hospital mortality in patients with snake bite: a retrospective study from a rural hospital in central India. Tropical Medicine & International Health. 2006 Jan;11(1):22-30.

15. Inamdar IF, Aswar NR, Ubaidulla M, Dalvi SD. Snakebite: Admissions at a tertiary health care centre in Maharashtra, India. South African medical journal. 2010;100(7):456-8.

16. Mittal BV. Acute renal failure following poisonous snake bite. Journal Postgrad Med, 1994; 40: 123–126.

17. Theakston RDG. The application of immunoassay techniques, including enzyme-linked immunosorbent assay (ELISA), to snake venom research. Toxicon, 1983; 21: 341–352.