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# "EARLY PREDICTORS OF ACUTE KIDNEY INJURY FOLLOWING SNAKE BITE"

Medicine

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## ABSTRACT

**Background :** Acute renal failure is an important cause of morbidity and mortality in snake bite patients, especially in tropical countries like India.

**Aims :** 1) To find out early predictors of acute kidney injury in snakebite patients at the time of hospital admission. 2) To find out incidence of acute kidney injury in snakebite patients.

**Materials and Methodology :** It is a hospital based prospective observational study done in 100 consecutive patients, with history of poisonous snakebite, admitted to Coimbatore Medical College Hospital, Coimbatore, South India. Relevant history, physical findings and investigations were recorded and analyses done.

**Results :** Incidence of acute kidney injury was 29%. Acute kidney injury was independently associated with local swelling, bleeding from bite site, 20min whole blood clotting test (20 min WBCT) and oliguria.

**Conclusion :** These early predictors are essential for clinical management and early referral and hence decrease the morbidity and mortality.

## KEYWORDS

Acute kidney injury, early predictors of acute kidney injury, snakebite, 20min whole blood clotting test

## INTRODUCTION

Snake envenomation is a serious medical crisis, wherein the spectrum of injury can vary from local tissue damage to involvement of almost all vital organs of the body. Clinico - toxicologically, nature of snake envenomation is categorized into hemotoxic, neurotoxic, and myotoxic syndromes. Most snakebites are harmless and are caused by non-poisonous species. Nonetheless, of the 3,000 different species of snakes, about 450 are found to be dangerous for humans worldwide, 52 snakes are poisonous out of 216 Indian snakes. Major poisonous species are Russell's viper, krait, cobra and saw scaled viper.[1]

World health organization (WHO) has recognized snakebite as neglected public health problem. According to the WHO report, the global annual incidence of envenoming and resulting deaths ranges from a minimum of 421,000 to a maximum of 1,841,000 and 20,000 to 94,000, respectively. Also, it is mentioned that the greatest number of snakebites occur in sub-Saharan Africa and South Asia. India has the highest incidence of snakebite-resulted mortality, ranging from 13,000 to 50,000 cases annually.[2]

Attributes for such a high mortality worldwide, due to snakebite are traditional treatments, poor health services, difficulties with rapid access to health centres and scarcity of anti-snake venoms (ASV). Furthermore, wrong/erroneous identification of the snake species also leads to inappropriate/inadequate treatment and outcomes.[3]

In vasculotoxic snake bite, mortality is mainly due to renal failure. In Russell's viper snakebite, the incidence of renal failure is 13–32%. Disseminated intravascular coagulation (DIC) can develop in viper bites. It causes various bleeding manifestations. Early identification and treatment can decrease the incidence of renal failure.[2] Blistering and even gangrene can occur in Viper bites. Oliguria can develop as rapidly as 24 h to 2–3 days after the snake bite. Jaundice and hemoglobinuria can occur due to intravascular hemolysis.[4]

The incidence of snake bite in Coimbatore and its surroundings is high. Hence, this study is undertaken to find out the incidence and early predictors of acute kidney injury following snakebite.

## METHODOLOGY

It is a hospital-based prospective observational study in 100 consecutive patients, with history of poisonous snakebite, admitted to Coimbatore Medical College Hospital, Coimbatore, tertiary referral centre in South India during September 2014 to August 2015. A written informed consent was obtained from each subject included in the study. Ethical approval for the study was obtained from the hospital ethics committee before the commencement of the study.

It is the hospital policy to admit all snakebite patients for observation. Snakebite and species identification was confirmed by a reliable history from patients, patient's relatives, specimen brought, presence of fang marks and signs of local and systemic envenomation. All patients were interviewed using a standardized questionnaire to maintain a record of patient's history relevant to snakebite envenomation.

Patients with history of suspected snakebite, wherein patients or attenders have seen the offending snake or having definite fang marks or with features of local or systemic envenomation were included in the study.

Patients with history of suspected snakebite, wherein patient or attenders have not seen the snake, with no fang marks or features of envenomation were excluded. Also, known cases of hypertension, diabetes mellitus, renal diseases and bleeding disorders were excluded.

Bite to needle time was calculated as time from snake bite to the time when the patient received anti-snake venom. Neurotoxicity was defined as documented ptosis, external ophthalmoplegia, weakness of neck or bulbar muscles, use of neostigmine or ventilatory support. Acute kidney injury(AKI ) was defined as an abrupt (within 48 hours) absolute increase in the serum creatinine concentration of $\geq$ 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). Creatinine clearance (Glomerular Filtration Rate) <60 mL/min/1.73m2 in the first 72 hours after snakebite was defined as Acute renal failure (ARF).[7]

Subjects satisfying the inclusion criteria were observed for local swelling at the site of bite, bleeding from the bite sites and black or brown urine. Bite to needle time, twenty minutes whole blood clotting test, total amount of anti-snake venom serum given, presence of neurological signs and history of diabetes and hypertension were noted.

Multivariate linear regression analysis with 95% confidence interval (CI) was done for statistical analysis. Data are expressed in mean ± SE (Standard Error). p value <0.05 was taken as statistically significant. All these analysis were performed using a commercially available software Statistical Package for the Social Sciences (SPSS) on personal computer.

## OBSERVATION & RESULTS

Only in 3% of cases, snakes were identified. Incidence of Acute Kidney Injury (AKI) was found to be 29%. In our study, mean age group of AKI was 41.5 ± 14.6 years and median age was 40 years. Incidence of AKI was 59% in males and 41% in females. It was found to be 94% in rural population and 6% in urban population. In our study, it was found that 42.6% of patients with AKI had local swelling (p-0.000, highly significant). 57.6% of patients with AKI had bleeding from bite site (p-0.000, highly significant) and 25% of the patients with AKI had neurotoxicity (p>0.05, not significant).

None of the patients with AKI had brown or black coloured urine. 74.2 % of patients with AKI had whole blood clotting time more than 20min (p-0.000, highly significant). 50% of patients had Urine RBC (p>0.05, not significant). AKI developed in 60% patients with bite to needle time less than or equal to 2 hours and 37% with interval more than 2 hours (p>0.05, not significant). All patients with Acute kidney Injury had oliguria (p-0.000, highly significant). 80.6% of patients who received 20-30 vials of ASV developed AKI whereas patients who received less than 20 vials didnot develop AKI (p-0.000, highly significant).(Table 1, Table 2, Table 3)

**TABLE : 1**

| Age | Count | Percent | |
|---|---|---|---|
| <20 | 6 | 6.0 | |
| 20 – 29 | 14 | 14.0 | |
| 30 – 39 | 29 | 29.0 | |
| 40 – 49 | 23 | 23.0 | |
| 50 – 59 | 13 | 13.0 | |
| 60 – 69 | 12 | 12.0 | |
| >=70 | 3 | 3.0 | |
| Mean ± SD | 41.5 ± 14.6 | | |
| Median | 40 | | |
| **Sex** | **Count** | **Percent** | |
| Male | 59 | 59.0 | |
| Female | 41 | 41.0 | |
| **Locale** | **Count** | **Percent** | |
| Urban | 6 | 6.0 | |
| Rural | 94 | 94.0 | |
| **Snake identified** | **Count** | **Percent** | |
| Yes | 3 | 3.0 | |
| No | 97 | 97.0 | |
| **AKI** | **Count** | **Percent** | **95 % CI** |
| No | 71 | 71.0 | 18.3 – 39.7 |
| Yes | 29 | 29.0 | |

**TABLE : 2**

| Local swelling | AKI | | | | $X^2$ | P |
|---|---|---|---|---|---|---|
| | No | | Yes | | | |
| | Count | Percent | Count | Percent | | |
| Yes | 39 | 57.4 | 29 | 42.6 | 19.22** | 0.000 |
| No | 32 | 100.0 | 0 | 0.0 | | |
| **: - Significant at 0.01 level | | | | | | |
| **Bleeding from bite site** | **AKI** | | | | **Odds** | |
| | **No** | | **Yes** | | | |
| | **Count** | **Percent** | **Count** | **Percent** | | |
| Yes | 14 | 42.4 | 19 | 57.6 | 7.73 (2.95 – 20.26) | |
| No | 57 | 85.1 | 10 | 14.9 | 1 | |
| $X^2$ = 19.53**, p = 0.000 | | | | | | |
| **Neurotoxicity** | **AKI** | | | | **Odds** | |
| | **No** | | **Yes** | | | |
| | **Count** | **Percent** | **Count** | **Percent** | | |
| Yes | 3 | 75.0 | 1 | 25.0 | 1 | |
| No | 68 | 70.8 | 28 | 29.2 | 1.24 (0.12 – 12.39) | |
| $X^2$ = 0.03, p = 0.857 | | | | | | |
| **Brown urine** | **AKI** | | | | | |
| | **No** | | Yes | | | |
| | **Count** | **Percent** | **Count** | **Percent** | | |
| **Yes** | 0 | 0.0 | 0 | 0.0 | | |
| **No** | 71 | 71.0 | 29 | 29.0 | | |

**TABLE : 3**

| WBCT> 20 MIN | AKI | | | | Odds |
|---|---|---|---|---|---|
| | No | | Yes | | |
| | Count | Percent | Count | Percent | |
| Yes | 8 | 25.8 | 23 | 74.2 | 30.19 (9.45 – 96.41) |
| No | 63 | 91.3 | 6 | 8.7 | 1 |
| 2 = 44.57**, p = 0.000 | | | | | |
| **Urine RBC** | **AKI** | | | | **Odds** |
| | **No** | | **Yes** | | |
| | **Count** | **Percent** | **Count** | **Percent** | |
| Yes | 1 | 50.0 | 1 | 50.0 | 2.50 (0.15 – 41.37) |
| No | 70 | 71.4 | 28 | 28.6 | 1 |
| 2 = 0.44, p = 0.509 | | | | | |
| **Interval between bite & ASV** | **AKI** | | | | **Odds** |
| | **No** | | **Yes** | | |
| | **Count** | **Percent** | **Count** | **Percent** | |
| <=2 Hours | 6 | 40.0 | 9 | 60.0 | 2.55 (0.79 – 8.23) |
| >2 Hours | 34 | 63.0 | 20 | 37.0 | 1 |
| 2 = 2.54, p = 0.111 | | | | | |
| **Urine output** | **AKI** | | | | **$X^2$** | **P** |
| | **No** | | **Yes** | | | |
| | **Count** | **Percent** | **Count** | **Percent** | | |
| Adequate | 71 | 100.0 | 0 | 0.0 | 100** | 0.000 |
| Oliguria | 0 | 0.0 | 29 | 100.0 | | |
| **: - Significant at 0.01 level | | | | | | |
| **Total ASV given** | **AKI** | | | | **$X^2$** | **P** |
| | **No** | | **No** | | | |
| | **Count** | **Count** | **Percent** | **Count** | | |
| <20 | 33 | 100.0 | 0 | 0.0 | 45.86** | 0.000 |
| 20 – 30 | 7 | 19.4 | 29 | 80.6 | | |
| **: - Significant at 0.01 level | | | | | | |

## DISCUSSION

This study was conducted to find out early predictors of acute kidney injury in snakebite patients at the time of hospital admission and to find out incidence of acute kidney injury in snakebite patients. The present study was a hospital based prospective observational study done in 100 consecutive patients, with history of poisonous snakebite, admitted to Coimbatore Medical College Hospital, Coimbatore, tertiary referral centre in South India during September 2014 to August 2015.

Incidence of Acute kidney injury(AKI) varies from 17%, 20.48% to 30.96% in studies conducted by Ali *et al.*[3], Patil *et al.* [5] and Mrudul *et al.*[5] respectively and it was 29% in our study. In our study, mean age group of AKI was 41.5 ± 14.6 years and the median age was 40 years. It was 36.14 ± 14.64 years and 40.47 ± 1.19 years in studies conducted by Mrudul *et al.*[5] and Paul *et al.*[6] respectively. Athappan *et al.*[2] found that AKI patients were older than non-AKI patients 39.1 vs. 35.4 years.

AKI was found to be 59% in male and 41% in female in our study. It was found to be (70.11% ,29.89%), (68.40%,31.60%) and (63%,37%) in males and females in studies conducted by Mrudul *et al.*[5], Kulkarni *et al.*[7] and Bawaskar *et al.*[8] respectively. It was found that 94% rural and 6% urban population had AKI in our study. It was 63.22% in rural areas and 36.78% in urban areas in study by Mrudul *et al.*[5]. Urban to rural ratio was found to be 1:4.7 in study by Sharma *et al.*[9]. Kalantri *et al.*[10] found 84% incidence in rural population. Snakes were identified in 3% of cases only.

We found that 42.6% of patients with local swelling developed AKI. 57.30%, 92% and 100% of patients with AKI had cellulitis

in studies conducted by Paul *et al.*[6], Mrudul *et al.*[5] and Tushar *et al.*[5] respectively. It was found that 57.6% of patients with bleeding from bite site developed AKI. 22.8%, 47.95% and 82.76% patients had bleeding tendencies in studies conducted by Tushar *et al.*[5], Paul *et al.*[6] and Mrudul *et al.*[5] respectively. Sharma *et al.*[9] found out that 27 out of 52 viper bite cases with haemostatic abnormalities developed AKI. In our study, 25% of the patients with neurotoxicity developed AKI. 15.78% and 26.3% AKI patients had neurological signs in studies conducted by Paul *et al.*[6] and Tushar *et al.*[5] respectively.

None of the patients with AKI had brown or black coloured urine in our study. 52.04% had brown-coloured urine in study by Paul *et al.*[6]. Van holder *et al.*[11] demonstrated that urine colour was strongly related to renal failure. It was found that 50 % of patients with AKI had Urine RBC. Tushar *et al.*[5] found hematuria in 29.8% of cases. We found that 100% of patients with AKI had oliguria. Tushar *et al.*[5] found oliguria in 84.2% of cases. In our study, 74.2 % of patients with whole blood clotting time more than 20 minutes developed AKI whereas Paul and Dasgupta *et al.*[6] found that 54.45% patients developed AKI.

In our study, 60 % and 37% of patients with bite to needle time less than 2 hours and more than 2 hours respectively developed renal failure. Athappan *et al.*[2] found that, " Bite to needle time more than 2 hours was an independent risk factor for the development of AKI". Mean bite to needle time were 6.5 ±10.3 hours and 7.63 ± 9.26 hours in studies conducted by Kalantri *et al.*[10] and Athappan *et al.*[2] respectively. On the contrary, Danis *et al.*[12] observed that there was no association. Paul and Dasgupa *et al.*[6] found that mean bite to needle time was 85.36 ± 4.43 min. AKI developed in 80.6% of patients who received 20-30 vials of ASV whereas, none of the patients who received less than 20 vials developed AKI in our study. In our study, 29 out of 100 patients developed acute kidney injury. Dialysis was done in all cases of AKI.

The incidence is similar to previous studies. Local cellulitis was found in 42.6% indicating the vasculotoxic nature of envenomation. The common symptoms were local swelling ( 42.6%), bleeding from bite site (57.6%), neurotoxicity (25%), oliguria (100%) and hematuria (50%). Previous studies show similar results. Common laboratory finding was coagulopathy - whole blood clotting time more than 20 minutes (74.2%). The prevalence of coagulopathy (74.2%) is more when compared to that noted by Athappan *et al.*[2] (27.7%), whereas it is comparable to other studies (60-80%).

The morbidity and mortality can be reduced by intervention at various levels. It includes early transfer of the patient to a primary health care facility, where ASV should be given. The high risk patients should be identified and referred to higher centre as early as possible.

The strength of our study is that the present study is similar to that published in the literature. The limitations of our study is that it is conducted in a small population of patients admitted in Coimbatore Medical College Hospital. Snakes could be identified in only 3% of cases. Thus the bias in selecting population can be avoided by conducting the study at a large scale and at multiple centres.

## CONCLUSION

Snakebites are still a common medical emergency encountered, especially in rural areas. Timely treatment is the mainstay for reduction of morbidity and mortality. Recognition of predictor signs is essential for clinical management and early referral which could lead to a significant decrease in morbidity and mortality. Based on the present study, it was found out that in snake bite patients, local swelling, bleeding from bite site, whole blood clotting time more than 20 minutes and oliguria are early predictors of development of acute kidney injury. The study demonstrates that the incidence of Acute kidney injury is 29% in snakebite patients. Early adequate administration of snake anti-venom may reduce the development of Acute kidney injury. Further long term studies might help to assess predictors of renal failure in snake bite envenomation.

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