

# A study on clinico-epidemiological profile and determination of clinical predictors of acute kidney injury following snake bite envenomation in a tertiary care hospital in Eastern India

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## Abstract

**Background:** Snake bite is a major public health issue in India causing significant morbidity and mortality. But, due to lack of awareness and unscientific treatment practices there is under-reporting of cases. In this study we wanted to know about epidemiological profile of snake bite patients and to assess the risk factors of acute kidney injury following poisonous snake bite.

**Materials and methods:** It was a prospective, observational, single institutional study among patients admitted with snake bite in general medicine ward of our institute between January 2020 to September 2021. After selection, proper history, detailed clinical examination and some laboratory examination like-Renal function test, coagulation profile was done. We assessed different clinical/laboratory parameters that were significantly associated with Acute kidney injury(AKI).

**Results:** Among total 100 patients, 56% of patients developed AKI. There was significantly higher incidences of swelling (98% vs 65%, p-value-0.001), bleeding (62.5% vs 6.8%, p-value-0.002) and cellulitis (75% vs 9%, p-value-0.004) in patients with AKI than patients without AKI. Significantly deranged coagulation profile in terms of raised bleeding time of >10 minutes (67% vs 0%, p-value-0.003), abnormal Prothrombin Time (PT), Activated partial Thromboplastin Time (APTT), Whole blood clotting time (WBCT) of >20 minutes, deranged INR (International normalized Ratio) >1.5 (3% vs 0%, p-value-0.003) was seen in AKI patients.

**Conclusion:** So, from our study multiple clinical parameters - Local signs like-swelling, bleeding from wound, cellulitis, coagulative parameters like-BT, PT, APTT, INR>1.5, clotting time, D-DIMER and low BP have emerged out to have significant association with AKI after snake bite.

**Key words:** Snake bite, Epidemiology, Acute kidney injury, clinical predictors

## 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.

India is estimated to have the highest snake bite mortality in the world. World Health Organization (WHO) estimates place the number of bites to be 81,000 per annum with 11,000 deaths<sup>[1]</sup>. Snakebite

is now recognized as a Neglected Tropical Disease by the World Health Organization (WHO). Such high incidences of snake bite in India are due to certain environmental, occupational factors. But the community is also not well informed about the occupational risks and simple measures which can prevent the bite.

Acute kidney injury is one the most common cause

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of death in snake bite patients, especially in vasculotoxic snake bite. Many lives can be saved if AKI cases are managed properly following snake bite. But, most of the fatalities are due to the victim not reaching the hospital in time where definite treatment can be administered. Due to lack of knowledge people continue to adopt harmful first aid practices such as tourniquets, cutting, and suction, etc worsening the outcome further. Moreover, Studies revealed that there are certain gaps in knowledge of primary care givers for treatment of snakebite<sup>[2]</sup>.

Because of the lack of awareness among people, most of the cases of snake bite remain unreported and so, the available data on the epidemiology of snakebite from the Indian subcontinent section is sparse. Only the cases of snakebite with severe envenomation reach the health care centers and got notified.

In this study we wanted to see the different clinical presentations and epidemiological profile of snake bite envenomation patients and to assess the risk factors and clinical predictors of acute kidney injury following poisonous snake bite. These results will give us an idea about the magnitude of acute kidney injury due to snake bite and help plan preventive measures to check this.

#### **Materials and Methods:**

It was a prospective, observational, single institutional study among patients admitted with snake bite in general medicine ward of our institute between January 2020 to September 2021.

#### **Inclusion Criteria:**

Patients who had a definitive history of snakebite or clinical picture consistent with snake bite like presence of fang marks or cellulitis or coagulopathy or Neuroparalysis were included in this study.

#### **Exclusion Criteria:**

1. Patients having acute or chronic kidney disease or USG suggestive of bilateral small kidneys or loss of corticomedullary differentiation.
2. Patients with acute kidney injury due to other causes (e.g. septicemia, drugs induced, post-surgical cases, obstetric causes, contrast induced, obstructive etiology etc).

#### **Study Technique:**

Patients who were included in the study using the above mentioned inclusion and exclusion criterias underwent a thorough clinical examination and their detailed history was taken.

Laboratory investigations including haemoglobin, total and differential leukocyte counts, platelet counts, red cell counts, bleeding and clotting time, coagulation

profile including Prothrombin time (PT), activated partial thromboplastin time (APTT) and international normalized ratio (INR), urine microscopy, urine protein, CRP, Serum Urea, Creatinine, liver function tests and serum electrolytes were done for all patients along with X-ray chest and ultrasonography of abdomen.

Patients who had Acute kidney Injury (AKI) were separated and their other clinical parameters were analysed for statistical correlation with AKI.

Acute kidney Injury, 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 to our hospital or else where after snakebite, before referral to our hospital or a percentage increase in the serum creatinine concentration of  $\geq 50\%$  above baseline, or oliguria ( $< 0.5$  ml/kg urine per hour for more than 6 hours). Presence of at least one or more indication of renal replacement therapy. All patients will be treated as per WHO standard protocol Ethical clearance was taken from institutional ethical committee.

There was no source of financial support for this study.

#### **Statistical Analysis:**

Statistical Analysis was conducted using IBM SPSS Statistics version 20.0 (SPSS Inc. Chicago, IL) and online Graph Pad Quick Calcs application. For normally distributed data, the mean values between the two arms were compared for test of significance using unpaired t test. Inter-arm mean differences were compared for test of significance using paired t test. For comparing proportions of different events in between the two arms Pearson's Chi-square test was applied as test of significance. p-value  $\leq 0.05$  was considered for statistically significant.

#### **Results:**

100 patients of snake bite were analysed and among them 56 patients had AKI. Different clinical parameters are compared between patients having AKI and not having AKI to find any correlation.

Most of the study population was male (61%) with a male : female ratio of 1.5:1. Majority of the patients were farmer (34%) by profession followed by manual laborer (26%) and most of the cases were from lower socio-economic class (48%).

**Table 1: Distribution of Epidemiological Characteristics of patients**

Variables		Number of Patients
Age (in years)	≤20	11
	21-30	27
	31-40	21
	41-50	20
	51-60	11
	>60	10
Total		100
Sex	Female	39
	Male	61
Total		100
Residence	Urban	32
	Rural	68
Total		100
Occupation	Service	07
	Business	18
	Labourer	26
	Farmer	34
	Housewife	15
Total		100
Socio-Economic Status	Upper	12
	Middle	40
	Lower	48
Total		100

Variables		Number of Patients		P-value	Significance
		AKI			
		Present	Absent		
Age (in years)	≤20	06	05	0.919	Not significant
	21-30	16	11		
	31-40	12	09		
	41-50	11	09		
	51-60	07	04		
	>60	04	06		
Sex	Female	26	13	0.086	Not Significant
	Male	30	31		

Bites were most commonly seen in the lower extremities (78%). Overall the most common site of bite was foot (35% of patients) followed by Leg (34%). 34% were poisonous bites at night and 66% were poisonous bites at day time. Patients who developed AKI had significantly higher incidences of swelling (98% vs 65%), bleeding (62.5% vs 6.8%) and cellulitis (75% vs 9%) than patients without AKI. Patients with AKI also had numerically higher incidences of blister formation and ulceration at local site but not statistically significant.

**Table 3: Distribution of characters of Bite site (Local changes)**

Variable		Number of Patients		P-value	Significance
		AKI			
		Present	Not Present		
Site of Bite	Abdomen	00	01	0.453	Not Significant
	Ankle	02	00		
	Forearm	01	00		
	Finger	08	06		
	Foot	19	16		
	Hand	05	01		
	Heel	01	01		
	Leg	16	18		
	Toe	04	01		
Swelling	Present	55	29	0.001	Significant
	Not present	01	15		
Bleeding from local site	Present	35	03	0.002	Significant
	Absent	21	41		
Cellulitis (>2 joints)	Present	42	04	0.004	Significant
	Absent	14	40		
Blister	Present	09	03	0.158	Not Significant
	Absent	47	41		
Ulceration	Present	49	43	0.061	Not Significant
	Absent	07	01		

Patients with AKI had incidences of Anuria (15% vs 0%), Oliguria(35% vs 0%) and Hematuria (28% vs 0%) significantly higher than patients without AKI. These patients had significantly higher serum urea (Mean 62.5 mg/dl) and creatinine (Mean 2.36 mg/dl) also.

**Table 4: Distribution of Renal Parameters Among Patients**

Variables		Number of Patients		P-Value	Significance
		AKI			
		Present	Absent		
Anuria	No	44	44	0.001	Significant
	Yes	12	0		
Oliguria	No	36	44	0.002	Significant
	Yes	20	00		
Hematuria	No	40	44	0.003	Significant
	Yes	16	00		
Serum Urea	Normal	10	35	0.002	Significant
	Abnormal	46	09		
Serum Creatinine	Normal	04	34	0.001	Significant
	Abnormal	52	10		

Among the 15 patients of low BP, 14 (93.3%) cases had developed AKI and 1(6.7%) case did not.

Patients with AKI had a significantly deranged coagulation profile in terms of raised bleeding time of >10 minutes (67% vs 0%), abnormal Prothrombin Time (PT), Activated partial Thromboplastin Time (APTT) and deranged INR(International normalized Ratio) >1.5 in 3% of patients in comparison to none in non-AKI patients. D-DIMER was also raised in AKI patients significantly (66% vs 0%). WBCT came more than 20 minutes for total 68 (68%) cases and among them AKI developed in 53 (77.9%) case, and in 15 (22.1%) case and AKI developed requiring hemodialysis in 32 (47%) cases and death occur in 5 (7%) cases.

**Table 5: Distribution of Blood Coagulation parameters**

Variables		Number of Patients		p-value	significance
		AKI			
		Present	Absent		
Platelet count	Abnormal	39	09	0.004	Significant
	Normal	17	35		
Bleeding Time (>10 minutes)	Yes	38	00	0.003	Significant
	No	18	44		
Clotting Time	Normal	37	44	0.003	Significant
	Abnormal	19	00		
PT	Normal	04	21	0.004	Significant
	Abnormal	52	23		
APTT	Normal	44	44	0.001	Significant
	Abnormal	12	00		
INR>1.5	No	37	44	0.003	Significant
	Yes	19	00		
WBCT>20 minutes	Yes	53	15	0.001	Significant
	No	03	29		
D-DIMER	Raised	37	00	0.001	Significant
	Not Raised	19	44		

Neurological symptoms like- paralysis (92% vs 81%, p-value 0.092) and Encephalopathy (12% vs 9%, p-value-0.065) of snake bite were comparable between AKI and non-AKI patients.

**Table 6: Distribution of Neurological Symptoms among patients**

Variables		AKI		p-value	significance
		Present	Absent		
Neuroparalysis	Present	52	36	0.092	Not Significant
	Not Present	04	08		
Encephalopathy	Present	07	04	0.065	Not Significant
	Not present	49	40		

Liver function test (LFT) parameters were abnormal in 65% of patients with AKI in comparison to 6% of patients without AKI and the difference was statistically significant (p-value 0.048).

Mean time from occurrence of snake bite and starting of treatment was almost double (4.12 vs 2.69 Hours) for patients with AKI. Almost 60% of patients with AKI underwent hemodialysis. Out of them 5(14%) patients died and around 86% patients discharged. Only one patient among those who did not need hemodialysis died.

**Table 7: Clinical outcome for Patients with AKI**

Variable		Outcome		P-value	Significance
		Death	Discharge		
AKI Having Hemodialysis	Yes	05	29	0.230	Not Significant
	No	01	21		

**Discussion:**

Purpose of this study was to determine those parameters which showed statistically significant association with the development of acute kidney injury that may help us to look those parameter abt cautiously and manage them vigorously.

This was a hospital based observational study of 100

snake bite patient, among them most were male 61 (61%) and presenting age mostly in the range of 21-40 years (48%) [TABLE 2]. Mean age of the population was 32±2.9 years. In a study by Sanjay Vikrant and Ajay Jaryal it has been seen that mean age of the patients was 42.2 ± 15.1 years<sup>[3]</sup>. Majority of the patients were farmer (34%) by profession followed by

manual laborer (26%). People associated with outside field work were mostly associated with the snake bite as they are most susceptible group and most of the cases were from lower socio-economic class (48%). [TABLE1] A higher proportion of males in our study may be attributed to the fact that men typically go daily in the fields, were more active at night, travel wider, while women for the most part, stay in and around houses and compounds.

This gender distribution is consistent with other studies. Kulkarni et al studied 633 cases, of which 433 (68.40%) were males while 200 (31.60%) were females<sup>[4]</sup>. Another study by Bawaskar et al showed the same results<sup>[5]</sup>.

Patients who developed AKI had significantly higher incidences of local signs like swelling (98% vs 65%, p-value 0.001), bleeding (62.5% vs 6.8%, p-value 0.002) and cellulitis (75% vs 9%, p-value 0.004) than patients without AKI. These may be due to higher amount of envenomation which caused local tissue damage leading to intense local reaction. [TABLE3]

Subsequently this venom caused AKI.

Renal parameters were all deranged in AKI cases. Serum urea, creatinine was significantly higher in these cases and there was also presence of anuria, oliguria. But, these findings are effect of AKI rather than cause. [TABLE 4]

In terms of coagulopathy, AKI patients showed significantly decreased platelet count, prolonged PT, APTT, INR>1.5, BT more than 10 minutes and increase in CT value and D-DIMER. Disseminated intravascular coagulation (DIC) had been one of the major contributors to death after snake bite in studies by Kularatne et al and Sujathan et al<sup>[6,7]</sup>.

The most important bedside test for bleeding tendency was WBCT and WBCT came more than 20 minutes for total 68 (68%) cases and among them AKI developed in 53 (77.9%) case, and in 15 (22.1%) case and AKI developed requiring hemodialysis in 32 (47%) cases and death occur in 5 (7%) cases.

Among AKI patients incidences of low BP was significantly high (93.3% vs 6.7%, p-value 0.002). In their study Dharod and Patil also showed that low BP was an important predictor of outcome for developing AKI<sup>[8]</sup>.

Mean bite to needle time was 4.12 hours for AKI patients than 2.7 hours of non-AKI patients which showed statistical significance (p-value<0.05). In a study by Dharod and Patil they showed bite to needle time as an important risk factor for developing AKI<sup>[8]</sup>. In a study by R.R. Singh and Uraiya showed increased time interval between bite to the administration of

ASV (bite to needle time) had a direct correlation with the development of AKI<sup>[9]</sup>. Tejendra S Chaudhari et al found that prolonged bite to needle time i.e., delayed arrival to hospital was associated with higher mortality rate<sup>[10,11]</sup>. This can be explained by the fact that incidence of complications is directly proportional to the duration of venom in the blood prior to its neutralization by AVS due to late arrival of patient at hospital causing multiple organ involvement and subsequent mortality<sup>[12]</sup>. This delay can be attributed to lack of awareness of hazards of snakebite, belief in traditional methods of treatment<sup>[13]</sup>.

So, from our study multiple clinical parameters emerged out to have significant association with AKI after snake bite. Local signs like swelling, bleeding from wound, cellulitis, coagulative parameters like BT, PT, APTT, INR>1.5, clotting time, D-DIMER and low blood pressure had significant association with AKI. Tejendra S Chaudhari and Patil also showed in their study that mortality in patients with snake bite can be predicted by simple variables like presence of bleeding tendencies, respiratory failure, and shock. These parameters can help the doctors at peripheral health centers to predict outcome, so that such high risk cases can be referred to higher centers for expertise management without wasting time<sup>[10]</sup>.

But, there were certain limitations also in this study—first, the sample size was small and duration was also short. Secondly, this was a single centered study, had it been multicentric the results would have been more corroborative to the results found in study involving larger population. The study population was not randomized so there might be some confounding and biasing factors behind our results.

### Conclusion:

Snake bite is a serious health issue in countries like India causing both suffering and loss of human life. Clinical parameters that have emerged as associated factors for development of acute kidney injury should be further studied by a large population based study to confirm the association and if it exists then to know the strength of association.

### Recommendations:

Widespread awareness regarding snake bite, its symptoms and requirement of prompt intervention should be spread among people, specifically in rural areas to prevent mortality. Installation of treatment facility, transport must be available for victims to prevent renal complications and death.

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