

## Original Article

# A Study of Laboratory Determinants and Clinico-pharmacological Correlates of Vasculotoxic Snake Bites in a Tertiary Care Hospital in West Bengal

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**Background :** Snake bite is an often neglected but lethal disease in a tropical country like India. There is a dearth of data regarding true magnitude of vasculotoxic Snake bite in a tertiary care facility catering a predominantly rural area relying heavily on agriculture. The objective of our study, therefore, was to identify the burden and determinants of outcome of a vasculotoxic Snake bite poisoning in this specific setting.

**Methodology :** A cross-sectional study was undertaken at Burdwan Medical College and Hospital, West Bengal over a period of 1 year which recruited 127 cases of Snake bite poisoning and their Epidemiological, Clinical, Biochemical and Haematological parameters were collected in a pre-designed case record form at admission. The data regarding time delay in admission, duration of hospital stay, pre-referral treatment and definitive anti-snake venom serum therapy were also collected.

**Results :** Commonest bites were vasculotoxic in nature (48.65%) and affects 31-40 years age group (33.85%) who typically presented with fang marks, local swelling, pain and bleeding from bite site mostly in the lower limbs. Mortality was 8 and complications developed in 27.56% patients, systemic hypotension and Acute Kidney Injury being the commonest duo. A bite-to-hospital delay of 2 to 6 hours is noted in majority (49.60%) and a 2/3rd mortality observed when admitted after 12 hours. The mean total count, ESR, CRP, LDH, CPK, Serum Urea and Creatinine were raised and statistically significant in patients with complications.

**Conclusion :** Renal function deterioration is one of the earliest signs of development of complications in vasculotoxic poisoning and decision delay, prompt institution of ASV are key determinants of improved prognosis

[J Indian Med Assoc 2023; 121(7): 24-8]

**Key words :** Snake bite, Vasculotoxic, Biochemical abnormality, Acute Kidney Injury, Toxicology.

In a developing economy like India, the poor reporting and under reporting of neglected health problems can have detrimental effect. Even WHO has perceived the importance of Snake bite as an area of serious concern and a neglected problem of tropical countries and working on a strong mandate to develop a comprehensive plan for effective Snake bite management<sup>1</sup>.

Researchers have revealed that over 8 lakhs of Indian population died due to Snake bite envenomation during 2001 to 2014 with age standardized snake bite

### Editor's Comment :

- Acute renal insult and hypotensive shock are common complications of vasculotoxic snake bite in rural agricultural terrains.
- Haematological and electro-renal parameters appear to be strong predictors of imminent development of renal complications in this scenario.
- Eliminating decision delay and rapid referral is key to prevent vasculotoxic deaths.

death rate at 4.8 per 1,00,000 population<sup>2</sup>. Even the Standard treatment guidelines of Government of India mentioned a serious lacuna that exists between the number of Snake bite deaths reported from direct survey and official data<sup>3</sup>. Even previous studies in West Bengal have pointed towards underreporting of Snake bite cases in rural areas due to inaccessibility<sup>4</sup>. Many studies focus on profiling of cases but miss out the clinical, biochemical and hematological correlation with outcomes.

Due to less availability of literature in this particular agrarian area, this study was a novice attempt on the part of the researchers with an objective to identify determinants of outcome with Clinical, Hematological, and Biochemical correlates in vasculotoxic Snake bite

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Received on : 18/09/2022

Accepted on : 16/12/2022

patients in a hospital setting which forms the novelty of the study.

### MATERIAL AND METHODS

The study was conducted at Department of Medicine, Burdwan Medical College and Hospital in Burdwan district, West Bengal from 01-09-2016 to 31-08-2017. The medical college is a tertiary care teaching hospital and caters to Burdwan, Birbhum, some parts of Bankura districts of West Bengal & parts of adjoining Jharkhand state.

#### Inclusion criteria :

(1) All patients coming to Emergency and Medicine Department with a definite history of Snake bite.

#### Exclusion criteria :

(1) Any patients who showed signs and symptoms of neurotoxic Snake bite like ptosis, Ophthalmoplegia, Dysphagia or present in a comatose condition with developing respiratory paralysis.

(2) Any asymptomatic patient who did not develop any signs and symptoms after 24 hours of observation to exclude nontoxic bites.

(3) History of systemic kidney disease, any Hematological disorders, Gout and any Rheumatological disease.

(4) History of surgery or major trauma in previous month with anticoagulant intake.

It was an institution based observational study and cross-sectional in nature which proceeded after IEC approval vide Memo no.BMC/PG/459. 127 patients were included in the study based on inclusion and exclusion criteria. The confidentiality of the patients was well maintained abiding by the ethical guidelines. 35 patients were grouped under patients with complications out of which 8 succumbed during treatment.

#### The structured case record form had three parts:

The first part included the basic epidemiological parameters of Age, Sex, Education, Place of Bite, Time of Bite, Season of Bite, delay in presentation to hospital and any prereferral treatment received.

The second part included the clinical parameters presence of Local swelling, Bleeding, Pain at bite site, oozing of tissue fluid, any other bleeding site, presence of gangrene, Blood pressure, treatment given, total dosage of Anti-snake venom during treatment and outcome.

The swelling at the site of bite was graded as mild when confined to bite site, moderate when it involved less than half of involved limb and severe when it involved more than half of involved limb or presence of

cellulitis, tissue necrosis and gangrene. The development of gangrene, compartment syndrome, acute kidney injury and severe hypotension due to internal hemorrhage were included under complications. The patients who died during the course of treatment or suffered from complications were compared with those not having any.

The third part consists of laboratory parameters of individual patients collated after detailed study of the case sheets and included whole blood clotting time in 20 min, complete hemogram and renal function test parameters viz serum urea, serum creatinine, serum uric acid and other laboratory parameters of LDH, CPK, CRP, serum sodium and potassium which was taken at the time of admission.

All data were tabulated in Microsoft excel sheet and analyzed with the descriptive statistics, Freusing statistical software SPSS version 23. P value was calculated by chi-square test and p value less than 0.05 was considered statistically significant.

### RESULTS

Our study found 6.76 total Snake bites per 1000 admission /ER visits during the study period and excluding the nontoxic bites it was 4.94 poisonous Snake bites per 1000 admission/ER visits. Out of overall 261 patients who had presented with Snake bite, 127 patients (48.65%) presented with predominantly Vasculotoxic variety which formed our study sample. Bites due to non-poisonous snakes was seen in 85 (32.65%) patients and neurotoxic bites in 49(18.77%) of cases. No cases of myotoxic snake bites found (Table 1).

Our study revealed that over sixty percent of population belong to age group of 20-40 years with a male female ratio of 1.56:1. Snake bites cases was maximum in age group of 31-40 years (43;33.85%) followed by 21-30 years (34;26.77%)(Fig 1).

In our study, majority of the patients with vasculotoxic Snake bites presented with fang marks which presented as two distinct hemorrhagic puncture wounds (111; 87.4%) which often was accompanied by local swelling (72;56.69%) mostly in the lower limbs. Bleeding of bite site was observed where blood oozed out continuously even after wiping was observed in 38.58% cases (Table 2).

Table 1 — Total no of snake bite cases and Sex distribution

Study population	Total patients attending ER/OPD	Total Snake bite cases	Percentage
Male	22673	156	59.77
Female	15916	105	40.23
Total	38589	261	100

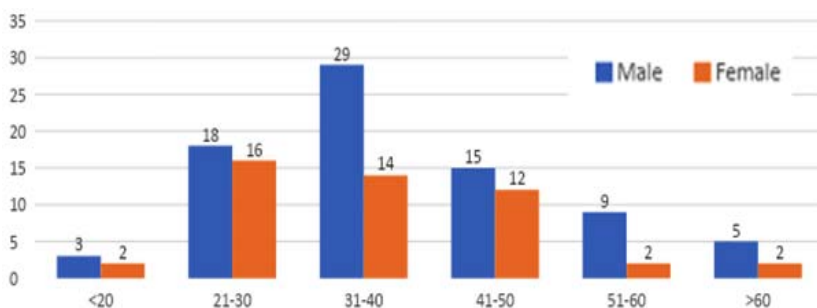


Fig 1 — Age and sex preponderance in predominantly vasculotoxic snake bites

Presenting features	No of patients
Distinct Fang Marks	111
Local swelling	64
Bleeding from bite site	49
Pain at Bite site	37
Bleeding from other sites	11
Blistering	08

A total of 35 patients presented with complications with few patients developed multiple complications. Systemic hypotension was seen in 21 cases. A total of 64 patients presented with swelling with severe swelling was seen in 17 patients with 14 patients (82.35%) developed complications. Moderate swelling was seen in 26 patients with 19 patients (73.07%) developed complications. Only two patients developed complications from 21 patients who had mild swelling at bite site. Compartment syndrome and gangrene developed in two of the patients each who had presented late and received traditional treatments before coming to hospital. 54.28% of patients developed acute kidney injury as a complication. In 8 patients succumbed during the course of treatment (Table 3).

In our study the most convenient bed side test done was 20-minute whole blood clotting test which came positive in 94 patients (74.01%) and complications was observed in 33 patients (35.10%) which was statistically significant.

Majority of the patients (49.60%) arrived late with a delay of 2 to 6 hours followed by 32 patients (25.19%) who arrived the hospital within 2 hours. 4 patients who arrived after 12 hours succumbed during treatment showed a 2/3rd mortality.

Out of the total 127 patients, patients (90; 70.86%) had used pressure bandage on the affected limb before coming to hospital while 19 (14.96%) used traditional patch by indigenous healers. 17 patients directly availed the health facility without any pre-treatment (Table 4).

Time taken to reach hospital after Snake bite	No of cases (n=127)	Pressure bandage Immobilization	Tight tourniquet	Traditional herbal patch	No pre-referral treatment	Mortality
< 2 hours	32	27	0	2	3	0
2-6 hours	63	49	0	5	11	2
>6-12 hours	26	12	2	9	3	2
>12 hours	6	2	1	3	0	4
Total	127	90	3	19	17	8

Majority of the patients in our study (53;41.73%) required 5 to 10 vials of reconstituted lyophilized polyvalent anti-snake venom serum while 39 (30.70%) of patients required 11 to 20 vials. Only 6 patients required more than thirty vials.

There was no significant difference between mean Hemoglobin value between patients with complications and patients without complications. The mean total leucocyte count and ESR was 10992.86 and 58.22 in patients with complications respectively and the result was statistically significant compared to uncomplicated cases.

The mean serum urea and creatinine were significantly raised in patients with complications but the change in serum uric acid level was not significant. The mean serum lactate dehydrogenase and serum creatinine phosphokinase showed higher levels. The mean serum potassium was 5.36±0.56 mEq/L in patients with complications.

The mean duration of hospital stay in patients who developed complications was 8.18 days with standard deviation of 2.78 days. Only 2 patients who developed extensive necrosis with gangrene and 2 patients who had to undergo fasciotomy due to compartment syndrome had a longer hospital stay of 15 days and 18 days respectively. Eight patients succumbed to Acute Kidney Injury and Disseminated Intravascular coagulation (Table 5).

**DISCUSSION**

In our study the hospital admission due to Snake bite was lower than study done at Maharashtra where it remained between 8.45 and 13.31 per 1000 admissions<sup>5</sup>.

Complications	Number of patients affected
Gangrene with extensive necrosis	02
Acute Kidney Injury	19
Systemic Hypotension	21
Disseminated intravascular coagulation	04
Compartment syndrome	02

Table 5 — Hematological, Biochemical parameters and hospital stay

Parameters	Mean Value $\pm$ SD		P value
	Patients without complication	Patients with complication	
Hemoglobin (g/dl)	11.59 $\pm$ 1.46	11.63 $\pm$ 1.56	0.892
Total Leucocyte Count	8327.78 $\pm$ 1445.27	10992.86 $\pm$ 3497.93	<0.0001
Platelet count (lac/mm <sup>3</sup> )	2.87 $\pm$ 0.52	2.52 $\pm$ 0.49	0.0008
Erythrocyte sedimentation rate	23.62 $\pm$ 9.89	58.22 $\pm$ 17.91	<0.0001
Packed Cell Volume	42.74 $\pm$ 4.90	52.39 $\pm$ 7.83	<0.0001
Serum Urea (mg/dl)	29.19 $\pm$ 5.78	64.67 $\pm$ 8.94	<0.0001
Serum Creatinine (mg/dl)	0.92 $\pm$ 0.18	1.86 $\pm$ 0.25	<0.0001
Serum Lactate Dehydrogenase (IU/L)	207.15 $\pm$ 62.48	565.68 $\pm$ 174.81	<0.0001
Serum C-Reactive Protein (mg/dl)	2.56 $\pm$ 0.87	5.63 $\pm$ 3.46	<0.0001
Serum Creatinine Phosphokinase (IU/L)	62.94 $\pm$ 38.23	265.39 $\pm$ 112.91	<0.0001
Serum Uric Acid (mg/dl)	5.14 $\pm$ 1.18	5.55 $\pm$ 1.18	0.0826
Serum Sodium (mEq/L)	134.25 $\pm$ 2.43	135.35 $\pm$ 1.31	0.0124
Serum Potassium (mEq/L)	4.26 $\pm$ 0.54	5.36 $\pm$ 0.56	<0.0001
Hospital stay (days)	3.15 $\pm$ 1.50	8.18 $\pm$ 2.78	<0.0001

In an earlier epidemiological survey done in the same district two decades earlier, reflected about deaths due to poisonous snake bites ranged between 5.28 to 31.75 per 1 lakh population<sup>6</sup>.

Since we had taken into account only vasculotoxic bites, the mortality was mostly due to late arrival of patients due to decision delay and preventable complications could have been managed by timely administration of Anti-snake venom serum<sup>7</sup>.

Although in our study the vasculotoxic variety was predominant but it was quite lower than the study done in Paschim Midnapore district where it constituted 80% of Snake envenomation<sup>4</sup>.

We observed the non-toxic Snake bite cases who come with a definite history of Snake bites and species identification is doubtful often present with anxiety and increased heart rate and without any other symptoms. They get relieved when kept under observation in Casualty.

In our study a higher male preponderance was observed which slightly differed from an earlier study done in Paschim Midnapur district where female to male ratio was 1.07:1 but was quite similar to study done at Burdwan<sup>4,6</sup>.

The age group 31-40 years were mostly affected in our study differed from previous study at Burdwan where 21-30 years was the predominant age group<sup>6</sup>. This could be attributed to the fact that the young age group were now less prone to exposure to snakes due to non-involvement in cultivation and growing employment in other sectors.

The patients who arrived late invariably developed the complications and size of swelling was directly proportional to time delay. Since the fangs of vipers are solid and cylindrical it could penetrate the dress

material easily, fang marks was a prominent feature in our study.

The presenting signs on arrival in our present study were comparable to an earlier study done at Odisha where the commonest symptom was local pain (41.6%) followed by oozing from bite site in 19.1% of vasculotoxic bites<sup>8</sup>. Researchers in India had suggested that 42-55% of patients who presented after 6 hours developed complications<sup>9,10</sup>.

Our study pointed out a marked increase in patient confidence on

modern medical treatment than traditional healers as compared with an earlier study done in the same district two decades back where 65.47% went for traditional healers and only 22.14% received hospital treatment<sup>6</sup>. This could be attributable to social awareness campaign by Government and other allied sectors. Pressure bandage by a saree/dupatta/dhoti were commonly observed in patients who presented at casualty.

Patients who required more than thirty vials had a longer stay and increased mortality. Early initiation of Anti-snake venom serum was more important than cumulative doses a patient received.

Our findings were comparable to studies in India where Total Leucocyte Count, C-reactive protein, creatinine phosphokinase levels and lactate dehydrogenase levels were always elevated in vasculotoxic Snake bite<sup>11,12</sup>. Platelet count, serum creatinine phosphokinase and lactate dehydrogenase levels had been advocated in standard treatment guidelines which helped to monitor the patients with vasculotoxicity<sup>3</sup>.

Serum creatinine and urea levels which represent compromised renal function were quite evident and early indicator of patients developing Acute Kidney Injury. Earlier researchers have proved 61.5% of patients with primary fibrinogenolysis and 38.5% with DIC developed renal failure and coagulation abnormality were commonly noted in vasculotoxic Snake bites<sup>13</sup>. The earlier study done to demonstrate effects of Viperidae venoms on renal structure and function had clearly showed increase in creatinine levels in sublethal doses in animal experiments. The authors had stated that severe hypotension, hemolysis, DIC and direct cytotoxic effect play a significant role in pathogenesis of Acute Renal Failure<sup>14</sup>.

### CONCLUSION

Vasculotoxic Snake bite requires serial monitoring of all crucial parameters with an aim to prevent the progression to Acute Kidney Disease. Early reporting and preventing decision delay is absolutely critical and require a multi-sectorial approach. Awareness campaigns must be strengthened in susceptible areas.

The major limitation of the study was its cross-sectional nature and more prospective studies could substantiate the management protocol.

**Ethical clearance** : Obtained prior to study

**Conflict of interest** : None

**Funding** : Self-funded

**Acknowledgement** : The authors are indebted to Burdwan Medical College and Hospital, West Bengal

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