

## Original Research Article

# Assessment of clinical parameters among patients with snake poison induced coagulopathy

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### ABSTRACT

**Background:** Snakes are poikilothermic carnivorous reptiles that have evolved the venomous apparatus for the purpose of procurement of food. Snake bite can result in local and systemic complications. Major systemic complications include acute renal failure, neurologic abnormalities requiring ventilator support and disseminated intravascular coagulation. Disseminated intravascular coagulation can result in serious life-threatening systemic complications like haemorrhage, infarction and even death if the treatment is delayed. The present study was undertaken to study the clinical profile of the snake bite patients who develop coagulopathy and to study the role of coagulation markers to evaluate the morbidity and mortality of snake bite victims.

**Methods:** Hundred patients consecutively admitted with history of snakebite were studied. Patients who have developed local signs of envenomation due to snake bite were included in the study group. The coagulation profile was assessed by doing blood investigations.

**Results:** In this study, patients who developed coagulopathy had prolonged hospital stay and requirement of more blood products transfusion causing increased morbidity. 43 patients (35.8%) had platelets less than 1 lakh and approximately hospitalized for 26 days and INR was more than 1.5 in 112 patients (93.3%) and hospitalized for 22 days and they received fresh frozen plasma. The survival rate in this study was 86% followed by 13.3% deaths.

**Conclusions:** Use of clinical and laboratory parameter evaluation needed to identify the coagulopathy very early to reduce the hospital stay and mortality.

**Keywords:** Coagulopathy, INR, PT, Snake bite, WBCT

### INTRODUCTION

According to the World Health Organization (WHO), around five million snake bites occur each year, although venom is only injected in just over half of cases. From blindness to amputations, hundreds of thousands of people are left with permanent disability after being attacked by snakes. The WHO describes such cases as among the most neglected tropical diseases. The majority of snake bites take place in densely populated areas of sub-Saharan Africa, South Asia and South-East Asia. Poor, rural populations are at particular risk from snake bites, as they often lack access to antidotes or may turn to

traditional treatments. Annual mortality from snakebites continues to be as high as 30 to 40 thousand in the world. Snake bite is almost always an accident. Snakes are legless cold-blooded reptiles. Of the 2500 - 3000 species, about 500 belong to the four families of venomous snakes and only about 200 species are poisonous. Nearly 3500 species of snakes exist in the world. India has about 216 varieties of snakes of which about 52 are venomous and of these only 4 varieties of snakes are commonly encountered as the cause of snakebite poisoning. These are Russell's viper, *Echis Carinatus* (Viperidae), Cobras (Elapidae) and pit viper (Crotalidae).<sup>1,2</sup>

Bites usually result from an unfortunate accidental interaction between a snake and a human victim. It occurs mostly when the people are at work like cultivation, gardening, plantation, wood collection, watching the crops even during walking. However, bites are fairly common when victims are at sleep. During the bite it is unlikely that people can identify the offending snake. Venomous snake bites can be presented with local or systemic features of envenoming-neurological, haematotoxicities, myotoxicities, organ failure and some nonspecific features. One expects complete neutralization of effects of venom with zero morbidity and mortality, but this is not the fact. Snakebite envenomation can present mainly as haemotoxicity or neurotoxicity. Haemotoxicity (prolonged whole blood clotting time/PT/APTT) can present as bleeding manifestations, capillary leak syndrome or disseminated intravascular coagulation (DIC) and acute renal failure.<sup>3,4</sup>

Snake venoms are extremely complex substances. It contains proteic and non-proteic fractions which may produce local changes, like acute inflammatory activity, edema, ecchymosis, blisters and necrosis. Various systemic changes, such as hemorrhage, blood pressure alteration, neurotoxicity, hemolysis, rhabdomyolysis and acute kidney injury are also observed.<sup>5</sup>

Due to snake bite, haematological complications are more often seen than any other complications. A simple 20 Minute Whole Blood Clotting Test (20WBCT) considered the most reliable test of coagulation and can be carried out at the bedside without special training to diagnose and treat early haematological complications of snake bite. Snakebite is a common acute medical emergency faced by rural populations in tropical and subtropical countries. In India more than 20, 00,000 snake bites are reported annually, of which 35,000 to 50,000 people die.<sup>6</sup>

Snake bites are a neglected public health problem in all the tropical countries. It is the common reason for morbidity and mortality. In India, approximately 216 species of snakes, out of which only four are venomous snakes (cobra, krait, Russell's viper and saw scaled viper). These are rich in protein and peptide toxins that have specificity for a wide range of tissue receptors, making them clinically challenging and scientifically interesting, especially for drug design. Although the full burden of human suffering attributable to snake bite remains uncertain, hundreds of thousands of people are known to be envenomed and tens of thousands are killed by snakes every year.<sup>7,8</sup>

Hematologic abnormalities are the most common effects of snake envenoming globally. Venom-induced consumption coagulopathy (VICC) is the commonest and most important. Other hematologic abnormalities are an anticoagulant coagulopathy and thrombotic microangiopathy. Venom-induced consumption coagulopathy is a venom-induced activation of the

clotting pathway by procoagulant toxins, resulting in clotting factor consumption and coagulopathy. The type of procoagulant toxin differs between snakes and can activate prothrombin, factor X, and factor V or consume fibrinogen. The most useful investigation in venom induced consumption coagulopathy is a prothrombin time/international normalized ratio.<sup>9</sup>

Poorly informed population often apply inappropriate first-aid measures and major time is lost before the victim is transported to a treatment centre, where cost of treatment can constitute an additional hurdle. The deficiency of snake bite management in such areas is multi-causal and requires joint collaborative efforts from researchers, anti-venom manufacturers, policy makers, public health authorities and international funders.<sup>10</sup> The main objective of the present study was to describe the clinical profile of the snake bite patients who develop coagulopathy and also to evaluate the mortality and morbidity of snake bite victims.

## METHODS

This was an observational study and the records of the snakebite victims who attended the RIMS hospital were obtained from the medical records department. Clinical data including age, sex and occupation of the victims, the site of bite, time of bite, time between bite and presentation, clinical manifestations, complications and outcome were obtained from the case records. 120 patients consecutively admitted with history of snakebite were included in the study after obtaining ethical committee clearance as well as informed consent from all patients. All patients were evaluated with a detailed history and clinical examination. Patients with risk factors like diabetes, hypertension, connective tissue diseases, and chronic infection. Those with pre-existing coagulopathy, receiving anti-coagulants or anti-platelets drugs and with history of renal diseases were excluded from the study.

Detailed history with clinical examination and appropriate investigations were recorded with the help of a proforma. Following history and clinical features were assessed:

- Investigations include Haemoglobin (Hb), Total count, Platelet count, Bleeding time, Clotting time, Whole blood clotting test (WBCT), Prothrombin time (PT), Activated partial thromboplastin time (APTT), International normalized ratio (INR).
- Snake bite site and snake bite time.
- Lapse of time (in hours) after snake bite.
- Weather tourniquet applied or not.
- Identification of snake and fang marks.
- Local swelling at the site of bite and increasing the swelling with time.
- Bleeding from the bite sites and bleeding from gums.
- History of passing black or brown urine to rule out intravascular haemolysis.

- Symptoms like nausea, vomiting, fever, breathlessness and decreased urine output.
- Number of anti-snake venom serum (AVS) given.

## RESULTS

In the present study, majority of the patients (33%) were found to be in the age group between 41-50 years followed by 28.3% in 51-60 years and (26.6%) in 21-30 years. Only 10 patients (8.3%) were found to be in the age group 31-40 years. Very few patients (3.3%) were observed in the age group of more than 60 years. Out of 120 patients, 90 patients (75%) were males and 30 patients (25%) were females. Age group 41-60 years had higher number of systemic envenomation following snakebite (Table 1).

**Table 1: Age distribution of patients.**

Age in years	No. of patients	Percentage (%)
21-30	32	26.6%
31-40	10	8.3%
41-50	40	33.3%
51-60	34	28.3%
>60	4	3.3%
Total	120	100.0

In the current study, the haemoglobin concentration of 60% of patients was found to be <10% and only 40% patients were having more than >10% concentration.

**Table 2: haematological profile of patients suffering from snake bite.**

Haematological parameters	No. of patients	Percentage (%)
<b>Hb in gms</b>		
<10%	72	60%
>10%	48	40%
<b>TLC</b>		
<4,000/cubic mm	12	10%
4,000-11,000/cubic mm	88	73.3%
>11,000/cubic mm	20	16.6%
<b>Platelet count</b>		
<1.5 Lakh	43	35.8%
>1.5 Lakh	77	64.1%
<b>WBCT</b>		
<20 minutes	25	20.8%
>20 minutes	95	79.1%
<b>Prothrombin time (INR)</b>		
0.8-1.2 seconds	18	15%
>1.2 seconds	102	85%
<b>APTT</b>		
<28.0 seconds	8	6.6%
>28.0 seconds	112	93.3%

Total Leucocyte count (TLC) was in the range of 4,000-11,000 among 73.3%. It was found that only 16.6% of the patients were having >11,000 TLC count and 10%

patients were having less than 4,000 TLC count. The platelet count (PC) was found to be more than 1.5 lakhs among 64.1% patients.

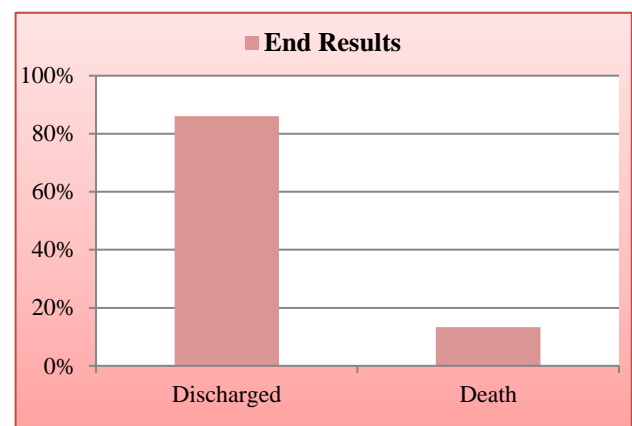
Only 35.8% patients were having less than 1.5 lakhs platelet count. It was seen that the whole blood clotting time (WBCT) of more than 20 minutes was found to be maximum among 79.1% patients and less than 20 minutes among 20.8% patients.

Prothrombin Time (INR) international normalized ratio was found to be more than 1.2 seconds among 85% of the patients and between 0.8-1.2 seconds was seen among 15% of the patients. It was observed that APTT (activated partial thromboplastin time) was found to be more than 28 seconds among 93.3% of the patients and very few (6.6%) patients were found to be having less than 28 seconds (Table 2).

**Table 3: International normalized ratio (INR) and duration of stay in hospital among snake bite patients.**

INR	No. of patients	Mean±SD	Duration in hospital in days	p value
0.8-1.2	86	21.42±4.21	22	0.02
>1.2	34	12.24±3.16	28	0.05

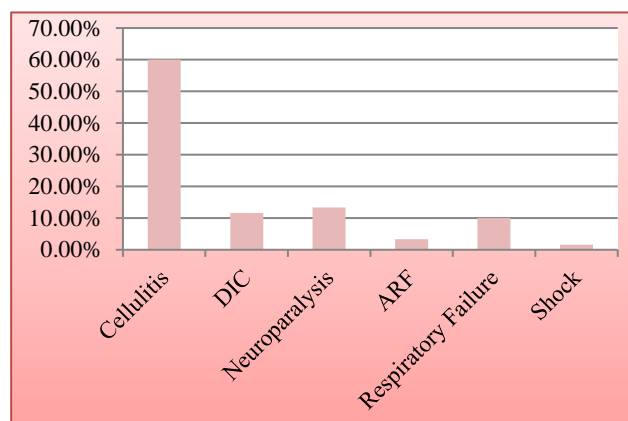
In this study, it was seen that the international normalized ratio was found to be between 0.8-1.2 among 86 patients with duration of 22 days in a hospital followed by 34 patients having more than 1.2 seconds of INR with a stay of 28 days in a hospital which was found to be statistically significant (Table 3).



**Figure 1: Survival and mortality rate of snake bite patients.**

In the present study, Figure 1 shows that the survival rate of the patients which was found to be 86% and the mortality rate was found to be 13.3%. Figure 2 shows complications in snake bite patients. The most common complication was cellulitis (60%) followed by neuroparalysis (13.3%) and DIC (disseminated

intravascular coagulation) 11.6%. Very few were seen affected with respiratory failure (10%) and shock (1.6%).



**Figure 2: Complications in snake bite patients.**

## DISCUSSION

Snake bite is a leading public health occupational hazard in developing countries where farmers, plantation workers, outdoor workers and rural dwellers working bare-foot in fields or sleeping outdoors predisposed to frequent contact with poisonous snakes. The morbidity and mortality of these patients is found to be high globally because even today most of the victims at initial stage approach traditional healers for treatment and are not even registered in the hospital.<sup>11</sup>

The toxic component of snake venom consists of enzymes, polypeptides and glycoproteins. Phospholipase A2 is the major enzyme which is present in the venom of poisonous snakes. It damages red blood cells, leukocytes, platelets, skeletal muscle and myoneural junction. Hyaluronidase helps in the transmission of venom through tissues and proteolytic enzymes are responsible for the local edema, blistering and necrosis. Proteases are divided into serine proteases and snake venom metalloproteinases. Proteolytic enzymes are mainly responsible for tissue necrosis, haemorrhage and bleeding disorders.<sup>12</sup>

The three major families of venomous snakes are the Elapidae, the Viperidae and the Hydrophidae. In present study pit vipers constituted for 70% of the total snakebites. They have a special sense organ, the pit organ, to detect their warm-blooded prey. Among viper bite causes rapid progression of swelling at the bite site and systemically causes coagulopathy.<sup>13</sup>

In this study, out of 120 patients, it was found that there were 72 male and 48 female patients. Most of the patients had venomous bite with species Krait and Russell's pit viper and very few were observed to be bitten with saw-scaled viper bite.

Venomous bites were defined by the presence of signs and symptoms of local and/or systemic toxicity. 68.3% of the patients were bitten by the venomous snakes and 31.6% were bitten by the nonvenomous snake species.

In this study, maximum number of bites 76% were observed in the lower third of leg and feet and 14% of patients were bitten on thighs and buttock because of defecating in open fields and 10% of patients while cutting grass were bitten on fingers. In India, approximate of 200,000 person/year fall prey to snake bite. The incidence of envenomation is higher in tropical countries where snakes are abundant and where human activities like field work increases the risk of man-snake encounters.<sup>14</sup>

A study conducted by Shiao et al, indicated that poor toileting facilities (trench toilets) increased the incidence of biting. They suggested that this risk might be associated with the temporary types of field sanitation infrastructure being exposed to arthropods and snakes. Low cost made toilets build snake pits around designated sanitation area and increases the chances for snake bites. Cleaning of toilets help minimize the incidence of snake bite in such areas. Use of herbal medicines was observed in our study and tight tourniquets were also applied in two-third of the cases.<sup>15</sup>

In this study patients who developed coagulopathy had longer duration in hospital and requirement of more blood products and transfusion causing increased morbidity. 72 patients (60%) had haemoglobin less than 10gms/dl and approximately hospitalized for 22 days and they received packed red cells. 43 patients (35.8%) had platelets less than 1 lakh and approximately hospitalized for 28 days and they received platelet units. INR was more than 1.5 in 112 patients and hospitalized for 28 days and they received fresh frozen plasma. Whole blood clotting time was prolonged more than 20 minutes in 95 patients and approximately hospitalized for 24 days and they received ASV vials. This finding was similar to the studies done by Harshvardhan et al.<sup>16</sup>

The variation in the snake bite may be due to geographical distribution in various parts of world. The most common complication was cellulitis followed by neuroparalysis and DIC. Many other studies have similar findings due to vasculotoxic or neuroparalytic cases. In present study, about 104 patients were discharged from the hospital and 16 patients died of respiratory failure. In the present study, higher incidence was found in summer (March to May), 69 (56.09%) were total snake bites in summer, among them 39 were poisonous bites and 30 were non-poisonous bites. Neuroparalytic snake bites were more at the end of summer and beginning of monsoon. These findings were similar to the studies done by Lingayat AM et al.<sup>17</sup>



Incidence of VT bites was comparatively more in winter. Study conducted by Banerjee et al, noted that incidence of 70-80% during May to October. Most human snakebites occur during the monsoon season because of flooding of the habitat of snakes and their prey. It is the life cycle of the natural prey of these reptiles that govern contact with humans. The breeding habits of frogs closely follow the monsoons and rats and mice are always in close proximity to human dwellings.<sup>18</sup>

Whole blood clotting test which is done for twenty minutes is considered to be the most reliable test for coagulation and can be carried out at the bedside without specialist training. The test should be carried out every 30 minutes from admission for three hours and then hourly after that. If uncoagulated blood is discovered, the 6 hourly cycles will then be adopted to test for the requirement for repeat doses of ASV.<sup>19</sup>

In present study, low platelet count was observed (35.8%) which is in concordance with the study done by Ishfaq et al. Prolonged in present study (79.1%) was comparable with the study of Dasgupta PJ et al (74%). Snake bite is a common life-threatening emergency in the study area. Spreading cellulitis, DIC and AKI were the common complication with vasculotoxic snakebite. Unusual complications like pulmonary edema, intracerebral hemorrhage, disseminated intravascular coagulation (DIC), intracerebral hemorrhage with infarcts were observed in present study. Delay in hospitalization is associated with poor prognosis and increased mortality rate due to consumptive coagulopathy, acute kidney injury, and respiratory failure.<sup>20,21</sup>

Ready availability and appropriate use of anti-venom, ventilatory support, hemodialysis, and treatment of DIC and close monitoring of patients in the hospital will help to reduce mortality from snakebites. Early administration of AS prevents respiratory paralysis after neuromuscular snake bite. Patients with evidence of respiratory insufficiency after neurotoxic venom poisoning require timely intubation and artificial ventilation. There is a definite need to educate the public about the hazards of snakebite, early hospital referral and treatment. There is a need to educate the public especially rural regarding warning signs of envenomation and hazards of delayed hospitalization.<sup>22</sup>

## CONCLUSION

Haematological manifestations are very commonly found in snake bite patients. Therefore, the use of clinical and laboratory parameters is useful in identifying the coagulopathy very early to reduce the hospital stay and mortality.

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