

# Predictors of Mortality in Vasculotoxic and Neurotoxic Snakebite Patients in a Tertiary Care Institute in Jharkhand, India

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## ABSTRACT

**Introduction:** The paper presents a study carried out in vasculotoxic and neurotoxic snakebite cases to find out the predictors of mortality in the state of Jharkhand.

**Materials and methods:** An estimated 58 snakebite patients who fulfilled the inclusion criteria were enrolled into the study. The clinical parameters and epidemiological data were noted during admission. Patients were followed up during their stay in the hospital for the progress of the symptoms and the treatment effects. Data obtained were analyzed using SPSS and Microsoft Excel.

**Results:** There was a significant positive association between the occurrence of GI bleed/epistaxis, DIC, or shock with an increased mortality in vasculotoxic snakebite cases. In the cases of neurotoxic snakebite, the occurrence of cardiac arrhythmias or respiratory failure was foretellers of an increased chance of mortality. Amongst the patients with vasculotoxic snakebite, local bleeding was present in all the patients and the infection was found in 94% of them. The complications included DIC in 36% of patients, GI bleed in 9%, epistaxis or gum bleed in 9%, shock in 21%, acute renal failure in 50%, and neurotoxic signs in 6% of the patients. In the neurotoxic subset, the most frequent symptoms were ptosis and blurring of vision, both in 100% of the cases, generalized paralysis in 79%, and local pain with swelling in 67%. Respiratory failure was seen in 50%, infection in 45%, cardiac arrhythmias in 33%, shock in 12%, and hepatotoxic features in 20%. Most of the patients required 30 vials or less of anti-snake venom serum (ASVS).

**Conclusion:** GI bleed/epistaxis, DIC, or shock are positive predictors of mortality in vasculotoxic snakebite cases, while the occurrence of cardiac arrhythmias or respiratory failure are markers of a poor prognosis in neurotoxic snakebite cases.

**Keywords:** Emergency medicine, Snakebite, Venom.

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## INTRODUCTION

Snakebite is a common occurrence in a country such as India<sup>1</sup> and more so in a tribal state such as Jharkhand, where the majority of the population lives in either villages or hilly areas.

Fatalities due to snakebite is due to wide snake species, poverty, shortage of anti-snake venom, poor compliance with treatment protocols, and a lack of public awareness along with a general state of ignorance about emergency management of snakebite cases across all regions within India. The overenthusiastic and overzealous reliance on faith healers due to a generally low level of social education is another frontier that needs to be crossed for improving care practices.

This study was done to ascertain the factors related to mortality during the course of the disease and treatment.

## AIMS AND OBJECTIVES

- To study the clinical presentation and complications of snakebite.
- To find out the relationship between clinical features, complications, treatment modalities, and mortality

## MATERIALS AND METHODS

Patients admitted to the department of medicine who fulfilled the inclusion criteria were taken for the study and were evaluated using the proforma. Patients were followed up for their duration of stay in the hospital with a close watch being kept on the development

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of clinical features and complications and the treatment being given. Standard laboratory tests were used in the quantification and diagnosis, as was guided by the proforma of the study.

The data so obtained were represented in the form of a master chart using Microsoft Excel and were classified in groups for an easy statistical classification and analysis. IBM SPSS was used for the statistical evaluation. Pie charts and bar figures were used for representation of frequency and the Chi-square test was used for testing of association between various variables (Figs 1 and 2).

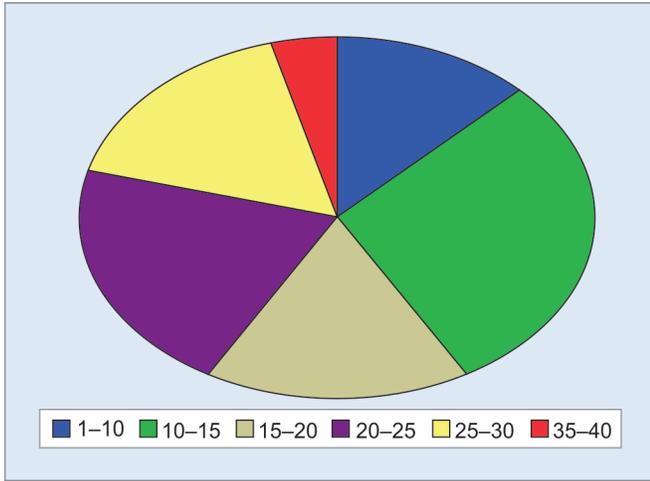


Fig. 1: Use of anti-snake venom serum (ASVS)

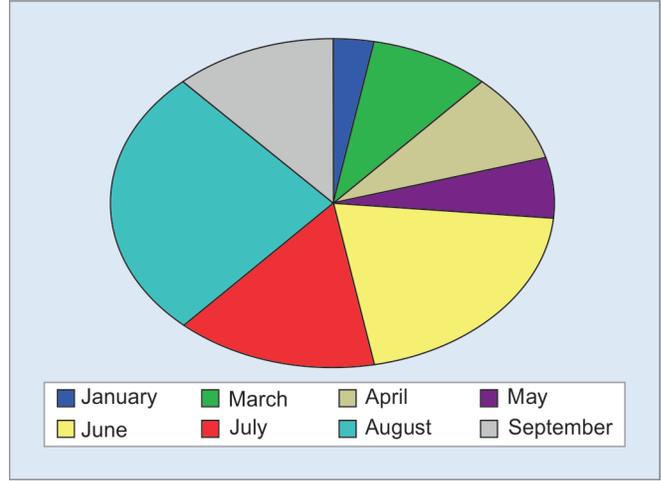


Fig. 2: Months of bite

## RESULTS

Fifty-eight cases were examined, of which 24 (41%) turned out to be neurotoxic and 34 (59%) vasculotoxic snakebite cases. The mean age in both groups was around the 30-year mark, which tells us that the effective management of snakebite cases is all the more important because most of the patients involved are in the peak of their productive life. While most of the neurotoxic bites occurred in the evening and night (84%), the vasculotoxic bites (57%) were reported to occur in the evening and night with the rest of them happening during the daytime. There were no major sex differences in the cases of snakebites amongst both vasculotoxic and neurotoxic groups, with both males and females being affected equally. Maximum cases occurred while the patient was sleeping: neurotoxic (75%) and vasculotoxic (50%). The limbs formed the major site of the bite, with the hands being the most common among the neurotoxic and the legs amongst the vasculotoxic group.

Majority of the cases of neurotoxic bites got to the hospital within the first 4 hours (58%) while it was only 35% in the vasculotoxic group. However, if we take 8 hours as the marker of getting to the hospital quickly for a state such as Jharkhand, where there is a dearth of local transport availability and bad terrain almost 75% of neurotoxic cases and 67% of vasculotoxic cases got to the hospital and had been started on treatment.

Fang marks were identifiable only in 46% of the patients. Most of these and subsequent findings are concurrent with those of other recent papers. In the neurotoxic subset, the most frequent symptoms were ptosis and blurring of vision, both in 100% of the cases, generalized paralysis in 79%, and local pain with blistering in 67%. Respiratory failure was seen in 50%, infection in 45%, cardiac arrhythmias in 33%, shock in 12%, and hematotoxic features in 20%. Ninety-five percent of the patients required less than 30 vials of ASVS with 42% requiring less than 15 vials. Mortality was seen in 4/24 cases (Fig. 3). Looking into the neurotoxic cases, the predictors of outcome and complications were looked into.

There was no significant association with:

- The time of bite
- The part of the body bitten
- The time taken to get to the hospital
- Infection

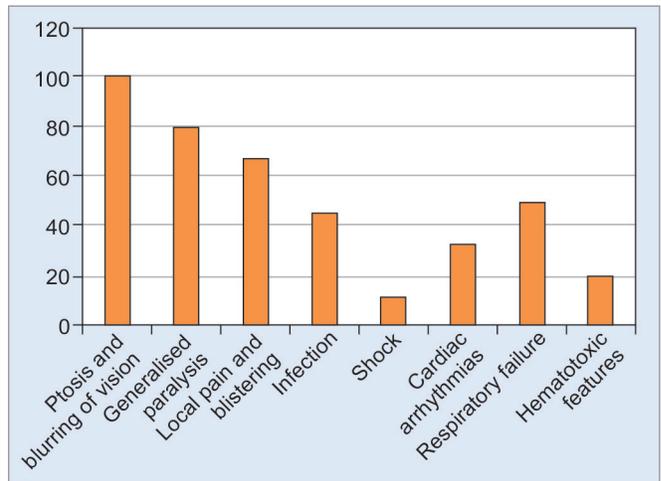


Fig. 3: Symptoms amongst neurotoxic bites

- Blurring of vision
- Ptosis
- Generalized paralysis
- Clotting time, or
- The amount of ASVS used.

However, a positive association was found among cardiac arrhythmias ( $p = 0.01$ ), respiratory paralysis ( $p = 0.02$ ), and mortality.

In the vasculotoxic subset, the whole blood clotting time at admission was deranged in about 80% of patients. Amongst the symptoms and signs of snakebite, local bleeding was present in 100% while the infection was present in 94%. DIC (36%), GI bleed (9%), epistaxis/gum bleed (9%), shock (21%), ARF (50%), and neurotoxic signs in 6% of the cases formed the complications (Fig. 4). Most (97%) of the patients required less than 30 vials of ASVS.

Testing for the parameters that may foretell the prognosis of the case and the likelihood of discharge or complications, there was no significant association with:

- The part of body bitten
- The time taken to get to the hospital
- Local treatment given
- The amount of ASVS used
- Neurotoxic features

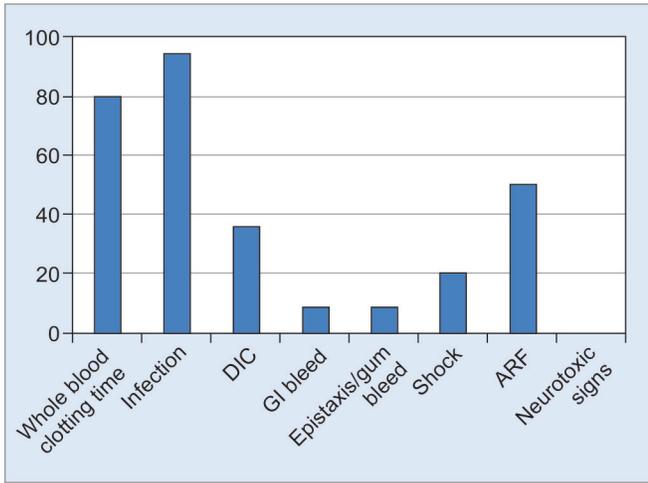


Fig. 4: Symptoms amongst vasculotoxic bites

- ECG changes, or
- Local infection.

Even the presence of acute kidney injury did not have a significant association with mortality. This may be due to the life-saving use of hemodialysis.

However, the development of DIC ( $p = 0.014$ ), shock ( $p = 0.000$ ), and epistaxis/gum bleed ( $p = 0.000$ ) all had a positive association with a bad prognosis.

## DISCUSSION

Snakebite as has already been talked about is a grave danger for a country such as India and more so for a state such as Jharkhand, where the majority of the population lives in villages that are hilly in terrain and often difficult to access and is prone to incidence of snakebite.<sup>1</sup>

Amongst 58 patients evaluated, 24 had neurotoxic snakebite and 34 had vasculotoxic snakebite. The mean age of the patients was 30 years. This group is the most active; hence they have more probability of snakebites.

In the vasculotoxic group, the maximum bite incidence occurred between 6 am and 6 pm (41%) and another 32% incidence is found to occur in the evening. This can easily be explained by the fact that cobra and krait (i.e., the neurotoxic snakes) are active at night, while the vipers are active in the daytime. The neurotoxic snakes may also bite during the day if disturbed while they are looking for food.

In both the groups, we saw that the maximum people were bitten while they were asleep and more so in the neurotoxic group (75%) than in the vasculotoxic group (50%). This has important implications, as it is a modifiable variable where a person may reduce his/her risk of a bite by not sleeping on the floor and trying to build a pucca house, which has fewer avenues for the snakes to come in. In cases of neurotoxic, the incidence of bite occurs on hands (50%), which is higher than in vasculotoxic (35%). Bite on the legs was much more common in vasculotoxic snakebite cases (67%) probably because of the more daytime bites and bites while the patient was either walking or working. In the neurotoxic subset, there were a few (3) cases of bites on the trunk and head neck area, which are considered rare and much more dangerous. Time to get to the hospital varies a lot with the types of bites. In the neurotoxic set, 58% of patients were brought to the hospital within the first four

hours and no patients were brought later than 24 hours after the incident. In the vasculotoxic group, we see that only 35% of patients were brought within the first four hours and some patients (15%) were brought in later than a day.

The symptoms in the cases of neurotoxic snakebites are much more dramatic. Ptosis, respiratory failure, and generalized paralysis along with other symptoms lead the patients and attendants to rush to the hospital as soon as possible, whereas in the vasculotoxic group, the swelling of the part bitten, bleeding from various sites, shock, and acute kidney injury take some time to get established and therefore the patient is brought in a little later.

Pain and blistering is a common sign that occurs very early and was found to be present in 68% of the patients. It is one of the symptoms which are important because it draws the attention of the patient as well as attendants before the patient's condition becomes unsalvageable.

It is very interesting to note that 100% of the patients in the neurotoxic group had blurring of vision; therefore, this could be an important marker for being sure about the neurotoxicity of the case. Ptosis like a blurring of vision was also present in 100% of the patients. Generalized paralysis was present in 80% of the patients involving the limbs, which recovered on ASVS treatment. Respiratory failure (one of the most dangerous complications) occurred in exactly half of the patients studied. These patients needed mechanical ventilation for a duration of 1–7 days using GE Engstrom Carestation machine and made a good recovery.

Cardiac arrhythmias (67%) range from ST changes to arrhythmias, and in one case, frank ST-elevation myocardial infarction was seen. It may be due to cardiotoxins present in the snake venom. The hemodynamic shock was present in a few patients (3/24).

Visible fang marks were present in only 46% of the patients, and 54% of the patients had no fang marks. Therefore, fang marks can be considered as a reliable sign of envenomation.

Thirteen percent of patients got relief with a mere 10 vials of ASVS, which is only the first dose. An estimated 43% patients were treated in 15 vials and almost 60% in 20 vials. Totally, 80% of the patients needed less than 25 vials and only 5% needed more than 30 vials. In neurotoxic snakebite, the toxin is injected all at once and therefore a lesser number of ASVS is required for the treatment.

Clotting time was deranged in 71% of patients with vasculotoxic snakebite compared to 42% in a neurotoxic bite.

Like blurring of vision and ptosis were present in 100% of the patients of neurotoxic snake bite, local bleeding from the site of bleed was present in 100% of the vasculotoxic cases. Infection was present in 94% of the patients. Infection is very common in vasculotoxic cases because while the snake releases the toxins there is a greater chance of infection from the flora of the snake's teeth. The incidence of infection is much more in vasculotoxic than in neurotoxic cases (46%) as the toxin is present in the local tissue for a long time and leads to severe necrosis of the local tissue with subsequent gangrene and more avenues for infection. Higher and more prompt institution of antibiotics is important in the cases of vasculotoxic cases as otherwise there are other complications owing to sepsis. Disseminated intravascular coagulation (DIC) is a frequent manifestation of vasculotoxic snake bite owing to consumptive coagulopathy caused by the toxin especially in cases of vasculotoxic snakebite cases. It leads to severe bleeding from both external sites and tissue, including visceral bleed, retroperitoneal hemorrhage, cerebrovascular accident (commonly hemorrhage but in a rare

case a patient had parietal infarct) and system damage owing to hypoperfusion. DIC is also precipitated by the increased incidence of septicemia that is a frequent accompaniment in cases of vasculotoxic snakebite cases. It rapidly changes the treatment paradigm because now the coagulopathy is not only due to the direct effect of the toxin but as a result of the cascade of consumptive coagulopathy that is set into motion. Prompt ASVS therapy with well-targeted antibiotics and blood products such as fresh frozen plasma, cryoprecipitate are the mainstay of the treatment. Along with it the patient is treated for any system failure that might ensue most commonly the renal system. The incidence of GI bleed and epistaxis was very less, which about 9% each in the patients surveyed. The shock was found in about 21% of the patients and is more common in vasculotoxic cases compared to 13% in neurotoxic. The mechanism is a little different. While in neurotoxic the shock is caused by a direct cardio depressant effect and autonomic disturbances, the shock in vasculotoxic cases is caused by increased vascular permeability, leading to leakage of fluid into extravascular spaces and increased exudation. There is vasodilation and resultant hypotension, often leading to tissue hypoperfusion and failure of various systems. ARF or acute renal failure is another common complication in case of vasculotoxic snakebite cases. The incidence was 50% of the total patients.

Neurotoxic features that is ptosis, blurring of vision, and difficulty in breathing are generally signs of neurotoxic snake bite cases, but in a few cases (2/34), these features were also found in the vasculotoxic subgroup. The effects are well documented in some cases of bites by *Dabiola russeli*, which is the most common vasculotoxic snake found in our part of the world.

The mortality rate in cases of vasculotoxic cases were about 9%, which was mostly due to shock and acute kidney failure that did not even respond as a result of vigorous renal replacement therapy.

Testing for association between two-factor Chi-square and Fischer exact test were applied and the cross-tabulation was done.

### Vasculotoxic Snakebites

There was a positive association between the part of the body bitten and the whole blood clotting time amongst vasculotoxic cases ( $p = 0.04$ ) with more cases with deranged clotting time were bitten on the hands. Testing for the parameters that may foretell the prognosis, there was no significant association with

- The part of the body bitten
- The time taken to get to the hospital
- Local treatment given
- The amount of ASVS used
- Neurotoxic features
- ECG changes or
- Local infection.

Even the presence of acute kidney injury did not have a significant association ( $p = 0.07$ ), which is most probably due to the widespread use of hemodialysis. However, the development of DIC ( $p = 0.014$ ), shock ( $p = 0.000$ ), and epistaxis/gum bleed ( $p = 0.000$ ) all had a positive association with a bad prognosis. Amongst the other factors (the amount of ASVS required, the time taken to get to the hospital, the part of the body bitten, the time of the bite or whether the person was sleeping or awake), no strong association was found.

### Neurotoxic Cases

Looking into the neurotoxic cases, the predictors of outcome and complications were looked into. There was no significant association with:

- The time of bite
- The part of the body bitten
- The time taken to get to the hospital
- Infection
- Blurring of vision
- Ptosis
- Generalized paralysis
- Clotting time or
- Amount of ASVS used.

However there were following strong associations:

The occurrence of respiratory paralysis ( $p = 0.02$ ) and cardiac arrhythmias ( $p = 0.01$ ) have a significant positive association with a worse outcome.

Sharma et al.<sup>2</sup> presented a study of 142 snakebite cases. Neuroparalytic cases were predominant, with their number being 86; there were 52 vasculotoxic cases. Average time to arrival at their hospital after the bite was 9 hours and the mean duration of hospital stay was 8 days. Twenty-seven cases had acute renal failure and 75% of all neurotoxic bites required assisted ventilation. The average dose of antivenom was 51.2 vials for neurotoxic bites and 31 vials for haemotoxic bites.

Bawaskar et al.<sup>3</sup> in their 91 snakebite cases at Mahad of Mumbai in western Maharashtra found that Forty-five (49.5%) patients had snakebite without envenoming. Twenty-six (28.6%) patients were paralyzed and ten (11.0%) patients died.

In the study of Suchithra et al.,<sup>4</sup> 200 (34%) of 586 cases with snakebites had envenoming. Snake species could be identified in 34.5% of the venomous bites. 93.5% had signs of local envenoming. Failure of coagulation, respiratory failure, and intracerebral bleed were the determinants of mortality.

Bawaskar et al.<sup>5</sup> did a study on 182 snakebite cases. Totally, 55 (30.2%), 38 (20.8%), 48 (26.3%), 41 (22.5%) cases were bitten by *Echis carinatus* (Eh), Russell's viper (Rv), krait (Kr), and cobra (Cr), respectively.

In Hayat et al.<sup>6</sup> study, one hundred (100) cases from both genders, from 8 years to 55 years age were reviewed. There were 57 (95%) hemotoxic having hemostatic abnormalities and 3 (5%) neurotoxic bites presented with neuromuscular symptoms. The average dose of anti-venom was 60 vials for viper bites and 10 vials for elapid bites. The overall mortality rate was 4%. An estimated 13 (86.66%) patients had respiratory paralysis requiring ventilatory assistance. Totally, 17 (19.31%) patients had clinical and laboratory parameters favoring DIC. A total of 12 (13.62%) patients had ARF in the study, and 2 (2.27%) patients succumbed amongst vasculotoxic snakebite cases.

Bawaskar et al.<sup>7</sup> studied 30 subjects of presumed snake envenoming (krait = 23 cases, cobra = 7 cases). Of the 23 subjects (11 male, 12 female) bitten by kraits, 2 were deceased upon arrival, 7 died in the hospital, and 14 recovered. Of the 14 survivors, 4 required artificial respirations. Of the 7 subjects (5 male; 2 female) who encountered cobras, 2 were deceased upon arriving at the hospital, and 1 died suddenly of an apparent cardiac arrest. Four subjects recovered with ASV, anticholinesterase drugs, and/or artificial respiration.

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