



## A Study on Role of Hemolysis as a Prognostic Indicator in Patients Admitted with Poisonous Viper Bites

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### Abstract

*Bites due to poisonous snakes especially vipers, are one of the challenging public health problems in India. Envenomation in such cases often leads to massive intravascular hemolysis. Hence this prospective observational study was done to find out the relation between hemolysis and prognosis in patients with viper bites. 107 patients admitted with confirmed or suspected viper bites in a tertiary care centre were included. The sociodemographic details of the patients, time and site of bite, bite to needle time, presence or absence of local reaction, treatment details and relevant laboratory investigation reports were recorded. Lactate dehydrogenase levels, hyperbilirubinemia and reticulocytosis were taken as markers of haemolysis. Duration of hospital stay, recovery or in hospital deaths were noted. Data analysis was done using Microsoft excel 2010. It was found that 61.7 % were males. Bites occurred between 4 pm and 8 pm in 45.8%. Many had local reaction, active bleeding, prolonged clotting time and evidence of haemolysis and were brought to the hospital within 6 hours of bite. 20 vials of anti-snake venom were needed in 41.1% patients. Duration of hospital stay was less than 5 days in 55.1% patients. 92.5% patients recovered and 8 patients died in this study. Statistically significant relation was seen between haemolysis and death in these patients. Thus, it can be concluded that haemolysis occurring in poisonous viper bites can be taken as a prognostic indicator in such patients.*

**Keywords:** Hemolysis, Poisonous snakes, Viper bite, Clotting time, Envenomation.

### Introduction

Out of the 216 species of snakes found in India, 52 species are poisonous.<sup>1</sup> In India, two lakh persons get snake bite every year and about 35,000 to 50,000 die.<sup>2</sup> Cobra, Krait, Saw scaled viper and Russell's viper are the four major poisonous snakes in India.<sup>3</sup> The envenomation due to Russell's viper often leads to massive

intravascular hemolysis.<sup>4</sup> This is thought to be due to the presence of phospholipase A<sub>2</sub> (which can damage the red cell membrane<sup>5</sup>) and lysolecithin in snake venom. The objective of this study was to assess the role of haemolysis as a prognostic indicator in patients admitted with poisonous viper bites.

**Methods**

A prospective observational study was done in 107 patients admitted with viper bites in this tertiary care centre over a period of one year. All patients admitted with confirmed viper bites, willing to give informed consent were included in this study. Those patients with suspected viper bite having local reaction and /or prolonged clotting time were also included. Patients with unknown bites without local reaction or prolonged clotting time, other poisonous snake bites and those with pre existing jaundice or liver disease were excluded from the study. Institutional Human Ethics Committee approval was obtained prior to the study. The sociodemographic details of the patients, time and site of bite, bite to needle time, presence or absence of local reaction, total number of vials of Anti-snake venom (ASV) used for treatment etc were all recorded in a predesigned proforma. Reports of laboratory investigations done like total leucocyte count, peripheral smear, clotting time, prothrombin time (PT)/international normalised ratio (INR), activated partial thromboplastin time (aPTT), renal function tests, serum bilirubin, urine albumin and lactate dehydrogenase (LDH) were collected and recorded. Raised LDH, hyperbilirubinemia and reticulocytosis seen in blood sample collected on the second day of admission was taken as a marker of hemolysis in this study. All patients were followed up until discharge or death. Outcome of treatment was measured by the duration of hospital stay and recovery or in hospital deaths. Data collected was entered in Microsoft excel 2010, analysed by descriptive statistics and results were expressed in proportions. Chi square test was done to compare the role of hemolysis with outcome of treatment.

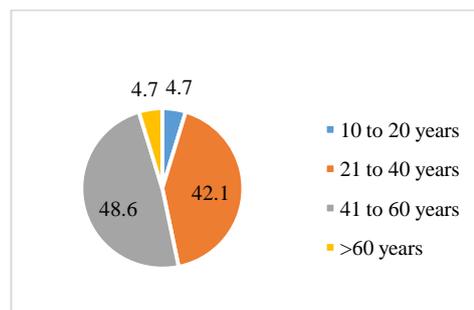
**Results**

Out of the 107 patients enrolled in this study, 61.7 % were males and 38.3% were females. 48.6% were in the age group of 41 to 60 years and 42.1% were between 21 to 40 years of age (Figure 1). In 45.8% patients, the bites occurred between 4 pm

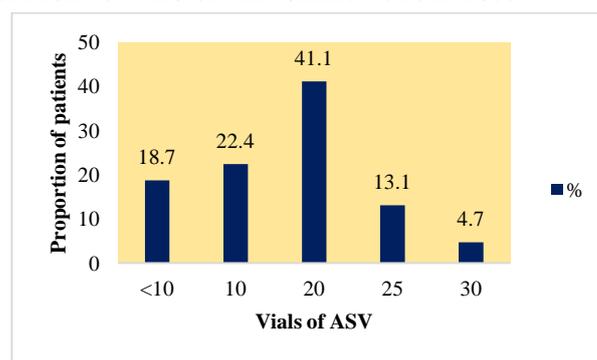
and 8 pm and in 24.3%, it was between 4 am and 10 am. 84.1% patients were bitten in the lower limb. In 15.9% patients, the bite was in the upper limb. 91.6% patients were brought to the hospital within 6 hours of snake bite. Local reaction was present in 94.4% patients. Active bleeding in the form of oozing from bite site, hematuria and hematemesis were seen in 45.8% patients. 41.1% patients were treated with 20 vials of ASV and 22.4% required 10 vials (Figure 2).

Table 1 depicts the proportion of patients showing prolongation in clotting time and time taken for normalisation of clotting time. In 42.1% patients, the clotting time was between 10 minutes to 20 minutes and in 39.3%, it was more than 20 minutes. The clotting time was normalised within 12 hours in 80.4% patients.

**Figure 1:** Percentage distribution of patients based on age



**Figure 2:** Percentage distribution of patients in relation to vials of Antisnake venom used.



**Table 1:** Distribution of study population based on variation in clotting time

Prolongation of clotting time		Normalisation of clotting time	
Time (minutes)	n (%)	Time (hours)	n (%)
<10	20(18.7)	<12	86(80.4)
10 to 20	45(42.1)	12 to 24	16(15)
>20	42(39.3)	>24	5(4.7)

Leucocytosis was seen in 62% of the study population. Urine albumin was positive in 41% and renal function tests were deranged in 24% patients.

Coagulopathy, as suggested by elevated INR and aPTT was seen in 39% patients. Evidence of hemolysis like reticulocytosis and elevated LDH were seen in 30% of the study population. Hyperbilirubinemia, another indicator of hemolysis, was detected as an increase in indirect bilirubin levels in 24% patients.

Outcome of treatment was noted in terms of duration of hospital stay and recovery or deaths. Duration of hospital stay in majority of the patients (55.1%) were less than 5 days. Only 11.2% patients were hospitalised for more than 10 days. In 33.6% patients, it was between 5 to 10 days. 92.5% patients recovered and 8 patients died in this study. Table 2 shows the relation between indicators of hemolysis and duration of hospital stay. There was no statistically significant relation between them. However, hemolysis was seen in all the 8 patients who died. Among them, 7 patients had reticulocytosis, 8 each had hyperbilirubinemia and elevated LDH. This was statistically significant with a p value less than 0.001 (Table 3).

**Table 2:** Relation between indicators of hemolysis and duration of hospital stay

Indicators of hemolysis		Duration of hospital stay ( days)				p value
		<5 days	5-10 days	>10 days		
		n (%)	n (%)	n (%)		
Reticulocytosis	+*	16 (50)	11 (34.4)	5 (15.6)	0.601	
	-*	43 (57.3)	25 (33.3)	7 (9.3)		
Hyperbilirubinemia	+*	15 (57.7)	7 (26.9)	4 (15.4)	0.596	
	-*	44 (54.3)	29 (35.8)	8 (9.9)		
Elevated LDH	+*	16 (50)	11 (34.4)	5 (15.6)	0.601	
	-*	43 (57.3)	25 (33.3)	7 (9.3)		

\* (+) : Present, (-) : Absent

**Table 3:** Relation between indicators of hemolysis and recovery or death.

Indicator of hemolysis		Number of patients		p value
		Recovered	Death	
Reticulocytosis	Present	25	7	<0.001
	Absent	74	1	
Hyperbilirubinemia	Present	18	8	<0.001
	Absent	81	0	
Elevated LDH	Present	24	8	<0.001
	Absent	75	0	

**Discussion**

In this study, a total of 107 patients admitted with viper bites were studied over a period of one year. Maximum number of viper bites were seen in the age group of 21-60 years with a male preponderance as seen in a study by David. This might be because of the fact that males tend to work outdoor more and hence chances of getting bitten are also more. Majority of the bites were in the lowerlimb.<sup>2</sup> This can be explained by bites due to accidental stepping over the snake.

101 out of 107 patients had local reaction in our study. Rodney et al reported local reaction in 73% of his patients.<sup>6</sup> This also correlates well with earlier studies.<sup>7,8</sup> Local reaction occur due to loss of blood and plasma volume into the extravascular space following increase in capillary permeability as a result of ophitoxemia.<sup>9</sup> 45.8% had active bleeding. Majority presented with bleeding from the bite site. In this study, patients also presented with hematuria, hematemesis and echymotic patches and one patient even had intracerebral bleed. This is similar to study done by Rodney et al.<sup>6</sup> In a study conducted in Maharashtra, 15 out of 38 patients had active bleeding.<sup>10</sup> However, a study conducted by Ponlapet et al in Thailand,<sup>11</sup> on pit viper bites, reported systemic bleeding in 17.3% cases only. The toxicity of green pit viper venom is relatively mild as compared to other hemotoxic snake venoms. This might have been the reason for low incidence of bleeding in the Thailand study.

91.6% patients reported to the hospital within 6 hours. This might be due to the greater awareness among people and close proximity to hospitals. A

study done in Northern Kerala reported the average time interval between snake bite and hospitalisation as 2.16 hours. According to Mohd Haneef et al, the average dose of ASV is 160 ml.<sup>12</sup> For correction of abnormal coagulation profile, Lawati et al suggested a mean of 14 ASV vials in patients admitted with snake bite and deranged coagulation profile.<sup>13</sup> In our study, the mean dose of ASV was 200 ml. On an average, Russell's viper injects 63 mg of venom.<sup>14</sup> 1ml of ASV neutralises 0.63 mg of venom. So the total number of ASV required is 100-250 ml. This wide range is because viper venom gets released slowly from the bite site. This recurrent antigenemia can cause delayed systemic envenomation.

Clotting time was between 10 minutes to 20 minutes in 45 patients and more than 20 minutes in 42 patients in this study. It was normalised within 12 hours of ASV therapy. This observation correlates well with studies done by Kularatna et al<sup>8</sup> and Mohd Haneef et al.<sup>12</sup> According to a study conducted in United states, venom induced thrombocytopenia occurs in approximately 30% of envenomations.<sup>14</sup> Hemotoxic venom causes decreased platelet aggregation leading to thrombocytopenia. 30% Patients of our study also had thrombocytopenia. However, all cases reported by Ponlapet et al in his study on pit viper bites had thrombocytopenia.<sup>11</sup> Pit viper bite is a model for combined coagulopathy. The prothrombin time and activated partial thromboplastin time was elevated in 39% of our patients. True vipers such as Russell's viper activate common pathways of coagulation via factor X and V causing prolongation of PT and aPTT. A study done by Joseph et al showed evidence of hemostatic dysfunction in all patients.<sup>15</sup>

62% of our patients had leucocytosis, 24% had deranged renal function and 41% had albuminuria. The indicators of hemolysis observed in this study were reticulocytosis, hyperbilirubinemia and raised LDH levels. Viper venom contains phospholipase A<sub>2</sub> that can destroy the RBC membranes causing hemolysis. This destruction of

RBCs causes rapid cell turn over by the bone marrow resulting in reticulocytosis in peripheral blood. Haemoglobin released is degraded resulting in elevated levels of unconjugated bilirubin. In our study, reticulocytosis and elevated LDH were seen in 30% patients and hyperbilirubinemia in 24% patients. All the three indicators were elevated only in 13 patients. All showed features of renal dysfunction. Intravascular hemolysis was reported by Rodney et al in his study.<sup>6</sup> Two out of five patients studied by Joseph et al showed microangiopathic hemolysis.<sup>15</sup> A study by Dong Zong Hung reported hemolysis as a major symptom in systemic envenomation.<sup>16</sup>

The total duration of hospital stay was less than 5 days in 55.1% patients and this was consistent with studies from North Kerala.<sup>12</sup> No statistically significant relation was seen between duration of hospital stay and hemolysis. However, the p value was significant (< 0.001) when presence of hemolysis and outcome of treatment in terms of recovery or deaths were studied. Death rate in our study was 21-30% and hemolysis was seen in 30% patients. 8 out of 107 patients died in our study and all of them had evidence of hemolysis. 2 had disseminated intravascular coagulation, 1 had intracerebral bleed and the remaining succumbed to renal failure. Viper bites have a mortality ranging from 1-15%.<sup>17</sup> The mortality rate was 2.6% in a study by Kularatne et al.<sup>8</sup> In another study, death occurred in 4.9% in older age group and 11.1% in paediatric age group.<sup>18</sup>

### Conclusion

Envenomation with poisonous viper bites can result in renal damage, spontaneous bleeding and massive intravascular hemolysis. Though not an independent predictor of mortality, hemolysis can play a significant role in prognosis as shown in this study. However, further studies may be taken up to assess the role of hemolysis in the development of renal failure in such patients.

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### Conflict of Interest: Nil

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