

A STUDY ON COAGULATION PROFILE AND ITS PROGNOSTIC SIGNIFICANCE IN PATIENTS WITH SNAKE ENVENOMATIONRamamurthy P¹, Deepak P. Kurahatti², Sunil Kumar N³, Malappa⁴, Vishwanatha Huggi⁵**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: BACKGROUND: Snakebite envenomation is a treatable occupational hazard in India which can present mainly as haemotoxicity or neurotoxicity. Haemotoxicity includes bleeding manifestations, capillary leak syndrome or disseminated intravascular coagulation and acute renal failure. Coagulation abnormalities like prolonged whole blood clotting time/prothrombin (PT)/activated partial thromboplastin (APTT) can determine the prognosis in these patients and is also essential to triage such patients for regular monitoring and follow up. **MATERIALS AND METHODS:** 50 snakebite cases admitted with systemic envenomation in the form of haemotoxicity (prolonged whole blood clotting time/PT/APTT) to VIMS Hospital, Bellary, during the period January 2012 to June 2013 were studied to determine the coagulation profile in relation to prognosis of patients. **RESULTS:** In this study, out of 50 patients, 35 were males and 15 were females. Age group between 20 to 40 years had higher number of systemic envenomation following snakebite. 26 patients had hematocrit >40%, of which 7 had PT/APTT of more than 1 minute. Out of 8 patients with clotting time more than 30 minutes, 7 patients had PT/APTT more than one minute. Out of 40 patients with prolonged PT/ APTT, 8 patients developed capillary leakage syndrome. Also, 6 developed early onset hypotension (<24 hours) and another 6 developed late onset hypotension (>24 hours). Complications included hypotension, acute renal failure, multi organ failure and DIC. Six patients died of complications secondary to snake envenomation of which, three patients died of multi organ failure, one died of sudden onset cardiorespiratory arrest and two patients died of acute renal failure. **CONCLUSION:** We have found a significant correlation of prolonged PT/APTT, clotting time >30 minutes and raised hematocrit with morbidity and mortality in hemotoxic snake bite and treating physicians should monitor such patients meticulously to prevent complications associated with it.

KEYWORDS: Snakebite, haemotoxicity, hematocrit, clotting time, capillary leak syndrome.

INTRODUCTION: Snake bite is a major health problem in India due to prevailing climatic conditions and the fact that major portions of population are rural and agrarian. Envenoming by snakes is an occupational health hazard often faced by farmers and farm laborers of tropical and subtropical countries like India.¹

Nearly 216 species of snakes are identified in India, of which 52 are known to be poisonous. Every year about 40000 to 50000 people die out of snake bites in India.²

The habit of moving about bare footed in these areas contribute to its higher incidence.³ Early administration of appropriate anti-snake venom is the specific treatment in snake envenomation.⁴

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.

ORIGINAL ARTICLE

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.

According to the Indian snake bite treatment protocol, In case of hemotoxic poisoning repeat dose of ASV is usually required. The correction of coagulopathy is the most important criteria to continue the ASV treatment. After the first dose of bolus ASV, it should be repeated after six hours depending on the coagulation profile and may be repeated till the coagulation profile is corrected. The suggestion of total requirement of dosages lies between 10-30 vials of ASV. Coagulation abnormalities like prolonged whole blood clotting time/PT/APTT can determine the prognosis in these patients and is also essential to triage such patients for regular monitoring and follow up.

OBJECTIVES OF THE STUDY: The study has been conducted to assess clinical and coagulation profiles and to analyse the outcome in relation to PT/APTT values of patients admitted with snakebite and systemic envenomation.

MATERIALS AND METHODS: 50 snakebite cases admitted with systemic envenomation in the form of haemotoxicity to VIMS Hospital, Bellary, during the period January 2012 to June 2013 were studied. Patients with prior history of bleeding disorders, associated neurotoxicity due to envenomation were excluded from the study. Data were analyzed in Microsoft excel SPSS and significance was calculated.

RESULTS AND OBSERVATIONS: This study included 50 patients with signs of systemic envenomation following snakebite. Out of 50 patients 35 were males and 15 were females as shown in table no.1. Age group between 20 to 40 years had higher number of systemic envenomation following snakebite. Age distribution of patients in our study is depicted in table no.2.

	NUMBER	PERCENTAGE
Female patients	15	30%
Male patients	35	70%
Total	50	100%

TABLE 1: SHOWING GENDER DISTRIBUTION IN OUR STUDY

AGE IN YEARS	TOTAL NO. OF PATIENTS	MALES	FEMALES
<20	8	6	2
21-30	16	12	4
31-40	16	11	5
41-50	6	4	2
51-60	3	2	1
61-70	1	0	1
TOTAL	50	35	15

TABLE 2: SHOWING AGE DISTRIBUTION IN OUR STUDY

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The months of August, September, October and November saw higher number of snake bite cases with six, four, seven and six respectively. The months of January, March, April, May and June had zero incidence of envenomation following snakebite. In our study, there is no significant correlation between time interval from snake bite to ASV administration with PT/APTT prolongation. Major symptoms at the time of admission and during initial 24 hours were pain at site of bite, local reaction, abdominal pain, bleeding from bite site, greying of vision and dizziness. Other rare symptoms were malena, hematemesis and sub conjunctival hemorrhage. Pain, tenderness and enlargement of local lymph nodes were the other symptoms. Symptoms of compartmental syndrome have been noted in 5 patients.

Out of 50 patients two patients had clotting time (CT) < 20 seconds, 15 patients had CT between 20-25 seconds, 25 patients had CT between 25-30 seconds and 8 patients had CT >30 seconds. This is depicted in table no3.

CLOTTING TIME	PT/APTT>1MINUTE	PT/APTT PROLONGED BUT <1MINUTE	PT/APTT NORMAL
Clotting time <20	0	0	2
Clotting time>20<25mnts	0	9	6
Clotting time>25<30mnts	5	18	2
Clotting time>30mnts	7	1	0
Total columns	12	28	10

TABLE 3: SHOWING CLOTTING TIME IN RELATION WITH PT/APTT

CHI-SQUARE=35.5; P<0.05 (SIGNIFICANT)

In this study, 26 patients had hematocrit >40%, of which 7 had PT/APTT of more than 1 minute. Out of 8 patients with clotting time more than 30 minutes, 7 patients had PT/APTT more than one minute and 1 patient had PT/APTT less than one minute. In our study, out of 40 patients with prolonged PT/ APTT, 8 patients developed capillary leakage syndrome in the form of ascites, pleural effusion, facial edema and conjunctivaedema. Patients with prolonged PT/ APTT had higher incidence of capillary leakage syndrome.

Out of 50 patients, 6 developed early onset hypotension (<24 hours) and another 6 developed late onset hypotension (>24 hours). All patients with late onset hypotension had severe systemic envenomation as evidenced by PT/APTT of more than 1 minute and a clotting time of more than 30 minutes as shown in table no. 4.

HYPOTENSION IN SNAKE ENVENOMATION	PT/APTT> 1MIT	PT/APTT PROLONGED BUT<1MIT	PT/APTT NORMAL	TOTAL ROWS
LATE ONSET HYPOTENSION	4	2	0	6
EARLY ONSET HYPOTENSION	3	2	1	6
NO HYPOTENSION	5	24	9	38
TOTAL COLUMNS	12	28	10	50

TABLE 4: SHOWING HYPOTENSION IN RELATION WITH PT/APTT

CHI-SQUARE=11.04; P=0.026 (SIGNIFICANT)

ORIGINAL ARTICLE

Out of 50 patients, 15 patients went into acute renal failure and 7 underwent dialysis among them. Of this, 12 patients had PT/APTT more than 1 minute among which, 3 had evidence of hypotension and 2 had capillary leak syndrome. The total no. of antsnake venom (ASV) given to patients in relation to PT/APTT is shown in table no. 5. This shows that patients with prolonged PT/APTT required higher doses of ASV, which was statistically significant.

NO. OF ASV GIVEN	PT/APTT >1 MINUTE	PT/APTT PROLONGED, <1 MINUTE	PT/APTT NORMAL
0-10	1	10	5
11-20	6	14	4
21-30	5	4	1
TOTAL	12	28	10

TABLE 5 SHOWING NO.OF ANTI SNAKEVENOM (ASV) GIVEN IN RELATION WITH PT/APTT

CHI-SQUARE=7.174; P=0.127 (SIGNIFICANT)

Complications included hypotension, acute renal failure, multi organ failure and DIC. Six patients died of complications secondary to snake envenomation.as shown in table no. 6. Three patients died of multi organ failure, one died of sudden onset cardiorespiratory arrest and two patients died of acute renal failure. Mortality rate linearly increased with the prolongation of PT/APTT as shown in table no. 6.

Total no. of deaths in PT/APTT prolonged > 1mnt group	4
Total no. of deaths in PT/APTT prolonged but< 1mnt group	2
Total no. of deaths in PT/APTT normal group	0

TABLE 6: SHOWING MORTALITY RATES IN RELATION WITH PT/APTT

DISCUSSION: This study was conducted to determine the correlation of coagulation profile with the severity of hemotoxic snake envenomation and its prognostic significance. In this study males (70% vs. 30% in females) were more commonly affected with snake bite. Similar observations were seen in JIPMER hospital⁵ and JN Medical College, Aligarh Muslim University, Aligarh, UP, India⁶. However the present study shows a higher mortality rate among females (20% vs. 8%).

Regarding age distribution, most of the victims belonged to the age group of 20- 40 years (32 patients) followed by 40- 60 years (10 patients) and 8 patients belonged to the teenage group. A study in Kerala showed that 52% were aged 31-50 years.⁷There was no statistically significant increase in incidence in the severity of envenomation in any age group. However an increased incidence of late onset hypotension was noted in the 30- 35 years age group. The incidence of late onset hypotension is higher among males belonging to this age group.

In the present study, more than 50% of the cases were seen from August to December. Similar observations were seen in JIPMER hospital.⁵ Previous studies has shown a clustering of bites during this period, as it corresponds with the monsoon rainfall in the state, which compels the reptiles to come out of their pits and shelters. Early pain at the bite site is the most common symptom encountered.

ORIGINAL ARTICLE

Local swelling usually appears within a few minutes but is sometimes delayed for 1 hour or more. Systemic symptoms include retching, recurrent vomiting, abdominal colic, greying of vision, dizziness, profuse sweating, shock, facial puffiness, chemosis of conjunctiva, angioedema of the lips, gums and tongue.

Bleeding manifestations include bleeding from bite site or venepuncture sites. Bleeding from bite site (10 patients) is most common form of bleeding tendency seen followed by gingival sulcal bleeding (8patients). Hematemesis (2), malena (2), hemoptysis and hematuria are rather uncommon. Clotting time is a reliable screening test for assessing systemic envenomation especially due to viper bite.

Clotting time more than 20 minutes is a sure sign of systemic envenomation, whereas clotting time more than 30 minutes seems to be a definite sign of severe systemic envenomation. Two patients had normal clotting time at the time of admission. Repeated testing within 2 hours among them showed prolongation of clotting time to more than 20 minutes. This shows that no patient with a history of snake bite should be discharged before 24 hours and the need for close monitoring of clotting time even if it is within normal limits at the time of admission.

A clotting time of more than 30 minutes is usually associated with a PT/APTT value of more than 1 minute, signifying its correlation and usefulness in monitoring. However, it did not show correlation in patients with clotting time less than 20 minutes. Patients with high hematocrit values had late onset hypotension and capillary leak syndrome. Out of 26 patients with raised hematocrit, only 7 had raised PT/APTT, which was statistically insignificant. Higher hematocrit did not show correlation with derangements in PT/APTT or clotting time.

High hematocrit values in these patients are probably due to shift of intra vascular fluid into extra vascular space or in other third spaces. The contributing factors to high hematocrit value include hypovolemia and DIC. In this study 12 patients had hypotension out of which 6 had early onset and the other 6 had late onset hypotension. Previous studies have shown an incidence of hypotension in snake envenomation as 22%. One Study in north India showed 6.7% hadhypotension.⁸

Another study showed 41% were hypotensive.⁹ The present study shows an incidence of 24 %. Anaphylactic reaction to anti-venom is likely to be the most common cause of hypotension, which can be easily corrected. The commonest cause of late onset hypotension is hypovolemia. All patients with late onset hypotension had severe systemic envenomation as evidenced by PT/APTT of more than 1 minute and a clotting time of more than 30 minutes. Capillary leak syndrome was noted among 3patients and 1 of them had moderate to severe renal failure also.

Late onset hypotension is associated with increased incidence of moderate to severe renal failure in snake bite with systemic envenomation. The important causes of late onset hypotension are hypovolemia, DIC and capillary leak syndrome. Renal failure is common in viperidae bites. 15 patients had renal failure in our study. Of this, 12 patients had PT/APTT more than 1 minute among which, 3 had evidence of hypotension and 2 had capillary leak syndrome. Factors which contributed to renal failure in the study are hypovolemia, hemo concentration due to capillary leak syndrome, late onset hypotension and DIC.

Renal failure develops within a day or two after snakebite envenomation. Renal failure is a significant cause of morbidity and mortality after snake bite envenomation. According to a study, snake bite induced ARF has mortality of 15.5%.¹⁰

ORIGINAL ARTICLE

The factors associated with mortality were presence of coagulopathy and uremic encephalopathy. Correction of hypovolemia and shock is very important in the prevention and treatment of renal failure.

A total number of 6 deaths were observed in this study in which 3 were males and 3 were females. According to a survey, snakebite deaths occurred were more common in males (59%) than females (41%), and peaked at ages 15–29 years (25%) and during the monsoon months of June to September.² In our study, it was observed that the PT/APTT values among 4 of the deceased was greater than 1 minute and among the remaining 2 victims the PT/APTT values was less than 1 minute. Multi organ system failure and renal failure were the cause of death in the PT/APTT prolonged for more than 1 minute group.

CONCLUSION: This study was conducted to assess the clinical and coagulation profile of patients with hemotoxic snake bite. Our study has shown statistically significant correlation between clotting of more than 30 minutes, bleeding manifestations and higher hematocrit with capillary leakage syndrome, hypotension and acute renal failure. A hematocrit value of more than 40 is associated with capillary leak syndrome, hypotension and renal failure. Reaction to ASV is the commonest cause of early onset hypotension.

The incidence of late onset hypotension is 12% in the present study and was common in males associated with hypovolemia. Other causes of late onset hypotension are haemo concentration due to capillary leak syndrome. The requirement of ASV is upto 30 vials in 41.6% of patients with PT/APTT prolonged for more than 1 minute group. The role of ASV after 24 hours of the bite is doubtful as it will not neutralize the venom which is already fixed to the target tissues.

Adequate hydration of the patients in the initial stages after the bite with severe systemic envenomation found to be beneficial in the prevention of oliguric renal failure (ATN), though not completely preventing renal failure but rather helps in converting an impending ATN to a non oliguric renal failure. The morbidity and mortality is high if patient has prolonged PT/APTT of more than 1 minute.

The morbidity and mortality is high if severe prolongation of PT/APTT as in our study, 4 patients with PT/APTT of more than 1 minute, 2 patients with PT/APTT prolonged but less than 1 died, whereas no patients with normal PT/APTT had mortality. In conclusion, we have found a significant correlation of prolonged PT/APTT, clotting time >30 minutes and raised hematocrit with morbidity and mortality in hemotoxic snake bite and treating physicians should monitor such patients meticulously to prevent complications associated with it.

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ORIGINAL ARTICLE

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