



Demographic and Laboratory characteristics variations among snake envenomation patients- An Institutional study

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Abstract

Introduction: The actual true worldwide burden of snake bite is not well known and documented because of high level of under reporting and serious misreporting. Snakes have always evoked a feeling of awe and curiosity, Knowledge regarding snakes and the effects of envenomation dates back to centuries.

Aim: The primary aim of the study was to understand the demographic characteristics, details of clinical and laboratory risk factors predicting high disease severity in patients with snake envenomation to a tertiary care center, Christian Medical College and Hospital, Vellore.

Materials and Methods: Prospective observational Cohort study with nested case control design. Every patient was subjected to a 20 min whole blood clotting time (20min WBCT) test at admission. Additional two citrated samples of 3 ml whole blood were taken at admission and 6 hours later from the patient along with the routine blood samples.

Results: Analysis of Demographic, Clinical and Laboratory characteristics was done in the present study, demographic a detail of 72 patient's shows information about Gender distribution of the patients showed males number was higher compared to females. The mean age of the study population was 40.78 years. The incidence of co morbidities as expected was less as the predominant population was between and 21-60 years. The predominant occupation among the study population comprised of farm labourers (34%) and farmers (29%). Among the identified species the most common species was Russell's viper (31%, N=22) followed by krait (5%). Various baseline Clinical Parameters were also assessed among those the most clinical feature was pain at the bite site which was present in 90.28% of the patients followed by local swelling which was seen in 87.5% of the population.

Conclusion: Socio-demographic variables, clinical findings, treatment variables, ASV related data and mortality in our study was found to be consistent with the studies done earlier.

Keywords: Anti Snake Venom; snake bite; clotting time; clinical parameters

Introduction

Snake envenomation is a common medical emergency and estimates that 81,000–138,000 people die each year from snakebites worldwide, and about three times that number survive and but are left with amputations and permanent disabilities (World Health Organization (WHO)- 2019) ^[1]. India not only has the highest number of envenoming's annually but also has the highest mortality rate annually with an estimated 11,000 deaths occurring every year according to current estimates ^[2]. Snake envenomation often leads to significant mortality and morbidity if adequate supportive and treatment measures are not initiated early. Hence snake envenomation's and the resultant deaths are a major and important public health problem in the rural tropics ^[3]. A large body of literature demonstrates a strong association between low socioeconomic status or poverty and a high burden of snakebite envenoming and death. This is particularly due the fact that health services in these areas are not only poorly accessible but are often suboptimal, and in some instances, have a scarcity of antivenom, which is the only specific treatment ^[4]. Traditionally snake envenoming is still managed using routine

tests like 20 min whole blood clotting time (WBCT) and prothrombin time, which form the basis for administration of Anti Snake Venom (ASV) to the patients ^[5]. Therefore it is important to accurately know the coagulation status of the patients at admission for effective administration of ASV. Thromboelastography (TEG) is a relatively new technique that assesses the dynamic coagulation status of the blood ^[6]. Management algorithms based on Thromboelastography for conditions like liver transplantation, massive trauma and cardiac surgery have been shown to decrease both transfusion requirements and intraoperative blood loss. The purpose of the study is to describe the clinico-epidemiological profile of patients with snake bite and to assess the clinical severity in patients with snake envenoming. Hence it can be assessed in future for better management of patients with snake envenomation. Vellore district and its nearby areas are heavily infested with venomous snakes, and the victims are mostly healthy young individuals mostly belonging to the lower socio-economic strata, most of them bread winners of the family. This is a prospective

observational cohort study done on patients presenting with newly diagnosed snake envenomation to Christian Medical College and Hospital (CMCH), Vellore. All patients fulfilling the inclusion criteria were assessed by a clinical research form at admission to casualty in CMCH. Routine blood investigations were done as per protocol and blood samples for Thromboelastography were collected along with the routine investigations. The patients were followed up till discharge or death to assess the final outcome. The primary aim of the study was to understand the demographic characteristics, details of clinical and laboratory risk factors predicting high disease severity in patients with snake envenomation to a tertiary care center, Christian Medical College and Hospital, Vellore.

Materials and Methods

Study type: Analytical study

Study design: Prospective observational Cohort study with nested case control design. The study was conducted among the patients presenting to the Emergency department and Department of General Medicine of Christian Medical College Vellore Hospital for a period of 18 months from January 2013 to June 2014. Around 80 – 100 snake envenomation's are seen every year in the Emergency Department of the hospital. Institutional review board approval was obtained prior to the commencement of the study. Sequentially encountered patients with snake envenomation were recruited after taking written informed consent and were followed up till discharge with a clinical research form.

Type of comparison group

Internal comparison

Duration of the study

The study was conducted between November 2012 and August 2014 on a prospective basis. The recruitment phase spanned over an 18 month period.

Study population

All patients admitted to Christian Medical College Hospital Vellore during the study period, with history of snake bite having noticed the offending snake and patient with doubtful history of snake bite but with definite acute onset of symptoms and signs of local systematic envenomation without any other causes for the same. We included those who consented to participate after careful exclusion criteria.

Patients were recruited principally under 2 clinical categories:

1. Patients with mild/moderate severity of snake envenomation
2. Patients with high severity of snake envenomation.

Sources of information

1. Study participants interview
2. Hospital records examination
3. Laboratory testing results.

Inclusion criteria

- Age more than 15 years
- Newly presenting to the emergency department with alleged history of snake bite with features of snake envenomation like local bite site reaction, hemotoxicity or neurotoxicity.

Exclusion criteria

- Age less than or equal to 15 years.
- Pregnant women
- Patients with known haematological disorders or malignancies that may affect the coagulation pathway.
- Patients on known anticoagulant or antiplatelet medications.
- Patients with known history of chronic liver disease.
- Patient refusing to give consent to be part of the study.

Statistical Analysis

The data collected was statistically analyzed by using *STATA (DATA analysis and statistical software)* version 13.00 for Windows 97 and above. The chi – square test was used for comparison of categorical variables. 'P' value less than 0.05 was considered statistically significant.

Results

A total of 124 patients with newly diagnosed case of snake envenomation, above the age of 15 presented to the emergency department. 22 patients missed invitation to participate at admission and 9 patients refused consent to take part in the study. Hence the remaining 93 patients were assessed for eligibility. 21 patients were further excluded due to various reasons after assessing for eligibility (14 patients had dry bites, 3 were on antiplatelet medication, 1 patients was on anticoagulation, 2 patients were pregnant, 1 patient had history of chronic liver disease). Of the remaining 72 patients, all of the patients data was included in the descriptive analysis while only those for whom the complete data for coagulation testing was available (i.e. 47 patients) were included in the final statistical analysis.

Analysis of Demographic characteristics

There were totally 53 males (74 %) and 19 females (26 %). The male to female ratio was 2.78. The gender distribution is shown below Figure 1.

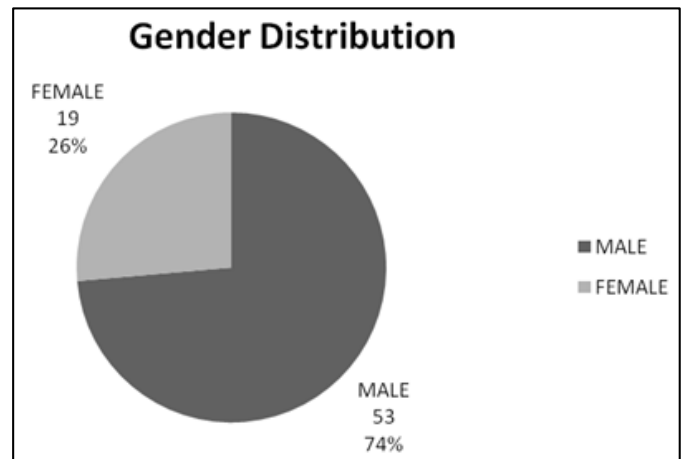


Fig 1: Pie chart showing distribution of patients with snake envenomation based on gender.

Age distribution

Figure 2 shows that the mean age of the study population was 40.78 years with a standard deviation of +/- 13.5 years. The oldest patient was 81 years old while the youngest was 16 years old.

Males: Snake bites were more common among males and a similar trend was present in all the age groups of <20, 21 – 40, 41 – 60, >60 years of age. While 73.6% of all the patients were males, the maximum number of males with snake envenomation belonged to the age group of 41 – 60(23) closely followed by age group of 21 – 40(22).

Females: Equal numbers of females with snake envenomation were present in the age groups of 21 – 40 and 41 – 60 years which also had the highest number of bites. There was only one case below the age of 20 and no patients in this category above the age of 60 years.

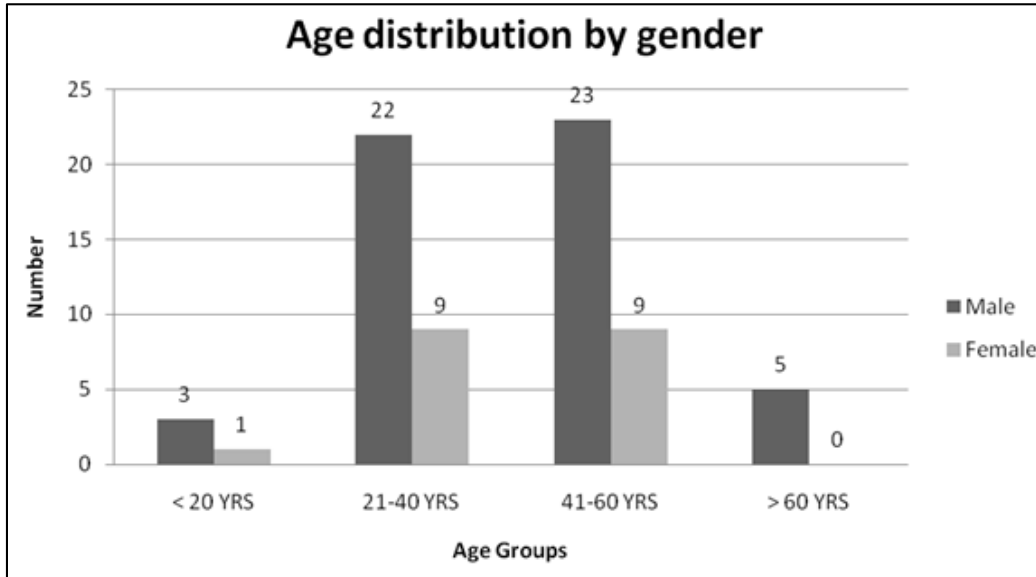


Fig 2: Bar graph showing distribution of patients by age and gender

Baseline characteristics

Table 1: Baseline demographic characteristics of patients at admission.

Characteristic of Patients (N=72)	Frequency N (%)
Mean Age	40.78±13.53 years
Male gender	53 (74)
Co- Morbidities	
Diabetes Mellitus	5 (6.9)
Hypertension	4 (5.5)
Smoking	8 (11.1)
Alcohol	4 (5.5)
Coronary Artery Disease	1 (1.3)
First medical contact in hours (Bite to needle time)	2.61 ± 2.01 hours
Duration of Hospital Stay	6.53 ± 4.65 days

The incidence of co morbidities as expected was less as the predominant population was between and 21-60 years old and were among the strong workforce group. The mean bite to needle time for first medical contact was 2.6 hours with a standard deviation of +/- 2 hours. The minimum time was 0.25 hours (15 min) by a patient who sustained a bite nearby a hospital. The maximum time for first medical contact was 9 hours by a patient who resided in a tribal area over the hills with no primary hospital nearby. The mean duration of hospital stay was 6.5 day with standard deviation of 4.6 days. The maximum duration of stay was 24 days and minimum duration was 2 days (Table 1).

Occupation and Region of residence

The distribution of various occupations among the patients was shown in Figure 3.

The predominant occupation among the study population comprised of farm labourers (34%) and farmers (29%) who together made up more than 60 % of the population. Most of the females with snake envenomation were housewives (84%, 16/19) who also helped in the farm during the harvest periods. Overall 71% [N =51] of study patients were residents of Tamil Nadu. The remaining 29% were from Chittoor district in neighbouring state of Andhra Pradesh (Figure 4).

Time of bite

The maximum number of snake bites occurred in the early morning hours (23 bites) or in the evening hours (22 bites) (Figure 3).

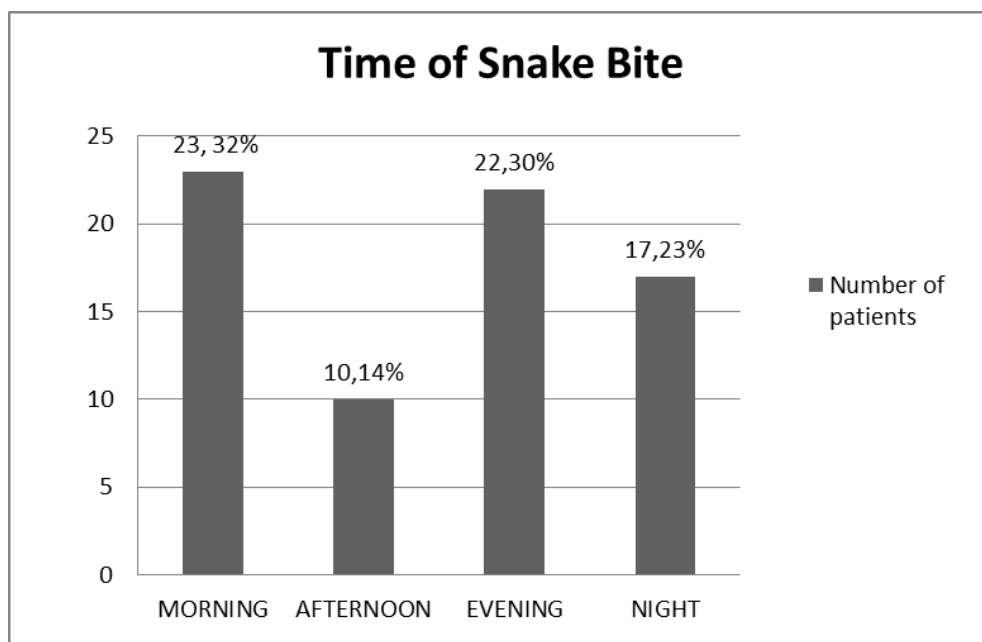


Fig 3: Bar diagram showing the distribution of patients with respect timing of the day during which they sustained the snake bite.

Time elapsed since presentation to the hospital

Figure 4 shows, 57% (N=41) of the patients presented within 6 hours of sustaining the snake bite to the hospital, 10 patients

presented between 6 to 12 hours after the bite, 14 patients presented within 12 – 24 hours after the bite. 7 patients had presented after 24 hours of the snake bite.

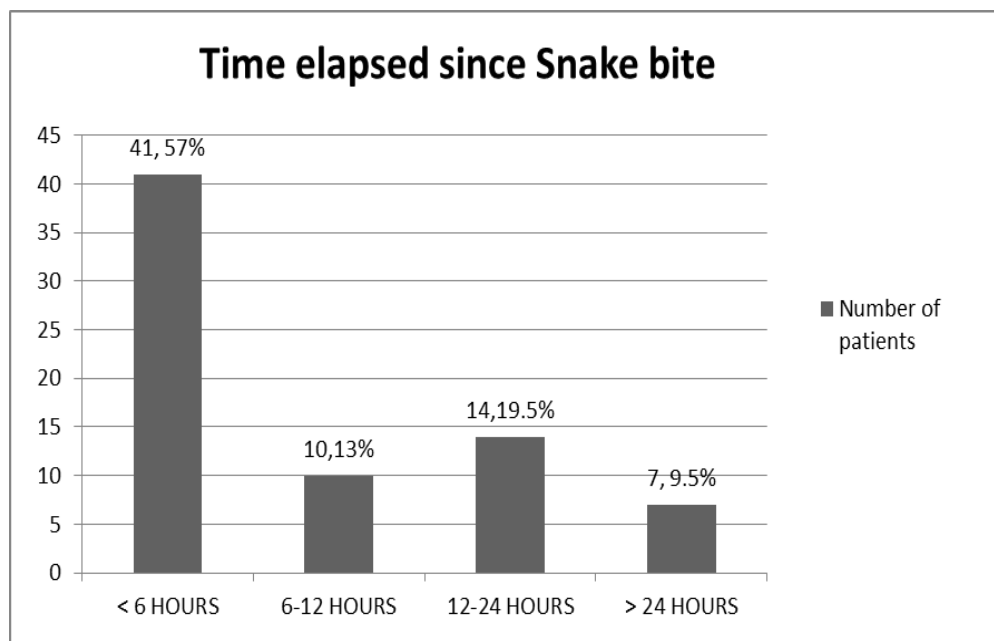


Fig 4: Bar diagram showing the distribution of patients with respect to time elapsed since the bite to presentation to the hospital

Snake brought with the patient and Snake Identification

The present study, show that snake was killed and brought along with the patient in 15% of the patient population (11 patients). The type of snake species was identified in about 42% (N=30) of the patient population. The remaining 58% (N=42) were not able to identify the snake bite. As stated earlier only 11 patients had killed and brought the snake along with them which we were able to identify. 19 more patients could identify the snake or provide the description of the size, shape, colour, pattern of head and

scales based on which assumed the species of snake.

Type of snake species

Majority of the patients (58%, N=42) could not identify the snake species that had bitten them. Among the identified species the most common species was Russell's viper (31%, N=22) followed by krait (5%). There were 2 cases each of documented Saw scaled viper and Indian cobra (**Figure 5**).

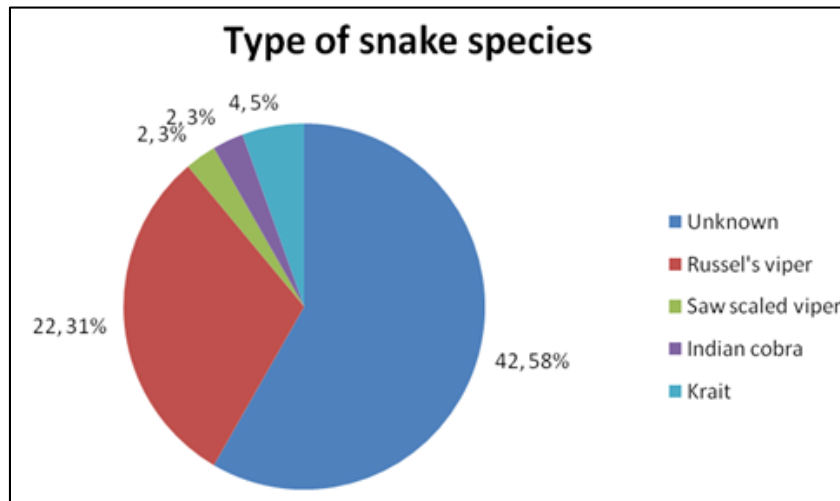


Fig 5: Distribution of patients according to the species of snake that they had been bitten with.

Laboratory Parameters

Baseline laboratory parameters of the patients with snake bite are discussed in table 2

Table 2: Details of laboratory parameters at admission

Variable	n	Mean	S.D.	Median	IQR
Hemoglobin	72	12.75	2.64	13.15	11.3-14.5
Total Count	71	18050	9791	17500	10120-22000
Platelets	71	169459	106492	175000	74000-253000
Total Bilirubin	45	2.83	3.44	1.6	0.7 - 3.5
Albumin	45	3.64	0.66	3.6	3.1 - 4.2
AST	46	130.37	216.39	56.5	29 - 134
ALT	46	30.41	31.62	19.5	12 - 36
RBS	67	169.57	87.93	146	120 - 190
CPK	57	3236.6	5984.68	913	275 - 3427
LDH	28	1825	1330	1459	759 - 2546
Creatinine	72	27.69	18.32	25.5	11 - 43.5
Urea	67	61.63	55.34	36	26 - 88
Sodium	70	137.74	4.99	139	134 - 141
Potassium	70	12.47	5.98	12	8 - 17
Fibrinogen	17	299	190	320	127 - 446.7
Prothrombin time	72	22.65	20.94	14.75	11.95 - 23.5
INR	72	2.01	1.71	1.40	1.10 - 2.15
APTT	72	40.43	36.06	28.25	25 - 35.3

RBS: Random Blood Sugar, **AST:** aspartate aminotransferase, **ALT:** Alanine aminotransferase, **CPK:** creatinine phosphokinase, **LDH:** Lactate dehydrogenase, **INR:** International Normalized Ratio, **APTT:** Actiated Partial Thromboplastin Time

Clinical Parameters

Baseline Clinical Parameters of the patients with snake bite are discussed in table 3

Table 3: Details of clinical parameters (categorical variables) at admission

Clinical features	Percent	Number of patients (n =72)
Pain at the bite site	90.28%	65
Local swelling	87.50%	63
Fang mark	78%	56
Cellulitis	73.6%	53
Tachypnoea (RR>20/min)	69.44%	50
Neurotoxicity	66.67%	48
Local bleeding	63.89%	46
Ptosis/Ophthalmoplegia	54.16%	39
Renal failure	51.39%	37
Vomiting	48.61%	35
Tachycardia(HR>100/min)	36.11%	26
Systemic bleed	34.72%	25
Paradoxical respiration	18.05%	13
Necrotising fasciitis	13.89%	10
Compartment syndrome	8.33%	6

The most clinical feature was pain at the bite sit which was present in 90.28% of the patients followed by local swelling which was seen in 87.5% of the population. Predominant neurotoxic features comprised of ophthalmic manifestation which comprised of almost 84% (ptosis was seen in 47% and diplopia in 37%) (Table 3).

Table 4: Details of clinical parameters (continuous variables) at admission

Variable	n	Mean	S.D.	Median	IQR
ASV vials received outside	72	6.39	6.25	6	1.5-8
ASV vials received in the hospital	72	11.25	5.98	10	7.5-14
Total ASV vials received	72	17.61	7.71	16	14-20
Heart rate	72	99.57	24.43	97	82-112
Systolic blood pressure	72	115.64	23.34	110	100-125
Diastolic blood pressure	72	73.22	14.04	70	60-80
Saturation (Spo2) at admission	72	94.06	8.45	96	93-98

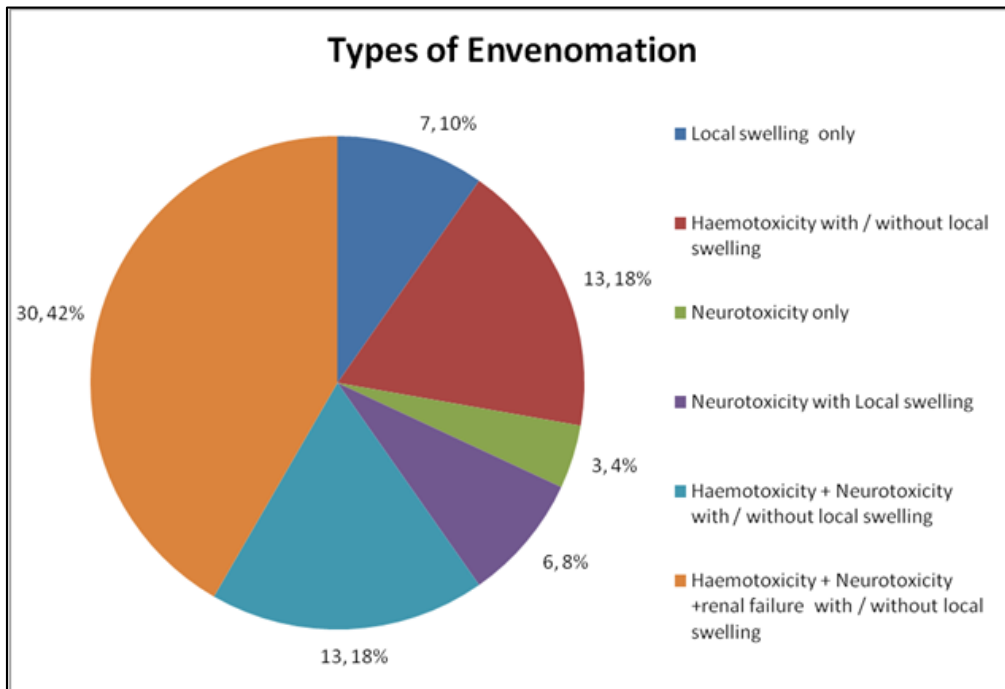


Fig 6: Distribution of patients according to the different clinical syndromes of snake envenomation

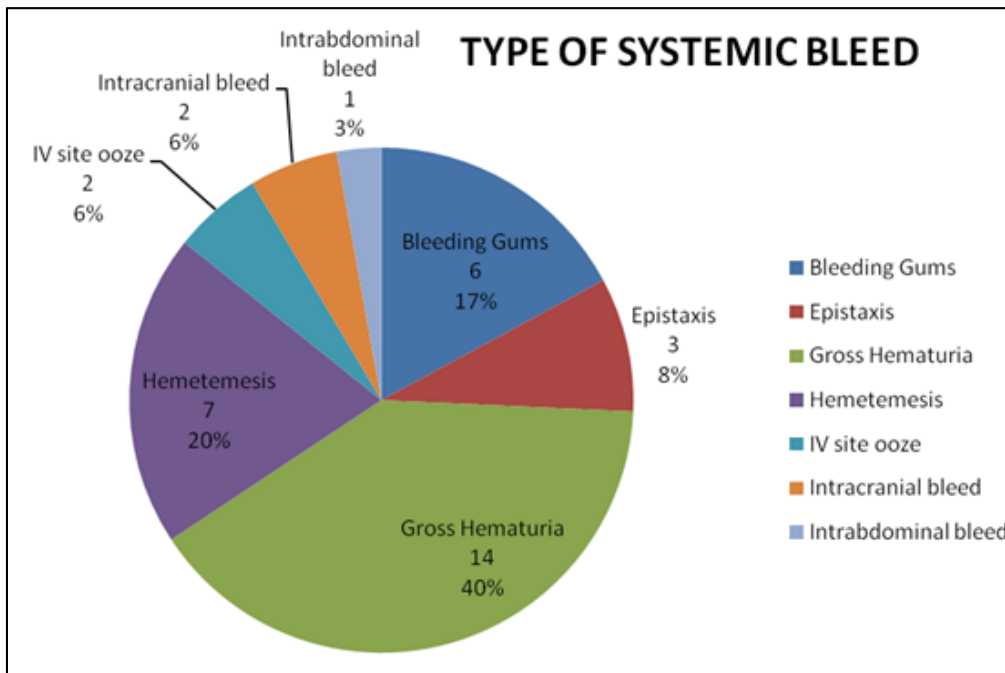


Fig 7: Distribution of various types of systemic bleeding among the patients with systemic bleeding in patient with snake bite

Discussion

Snake bite is an important neglected tropical health disease which has a high socio-economic impact on the community especially in the rural areas. According to recent studies, in India the data regarding incidence and mortality are fragmentary because less than 40% of snake bite patients attend hospitals for medical care rather first consults traditional practitioners or quacks and only subsequently resort to modern medicine [7]. Most of the data regarding the epidemiology of snake bite are very unreliable due to the poor condition of the reporting systems in place in

developing countries. Moreover, the mortality and morbidity secondary to snake bite are a gross underestimation as most of the bites (approximately 80% of all documented cases) occur among non-urban/rural population [8]. The present study was to evaluate the demographic characteristics, details of clinical and laboratory parameters among adult patients admitted with snake envenomation to a tertiary care center, Christian Medical College and Hospital, Vellore.

The present study shows, the mean age of the study population was 40.78 years with a standard deviation of ± 13.5 years. A

significant proportion of the study population was common among males and a similar trend was present in all the age groups of <20 to >60 years of age. The present study results are in accordance with earlier studies conducted by Kulkarni *et al.*^[9] Brunda and Sasidhar^[10] in Andhra Pradesh. The predominant age group being affected between 20-40 years was consistent with all the earlier studies conducted in India, however two studies by Hansdak *et al.*^[11] in Nepal and Rahman *et al.*^[12] in Bangladesh (46%) which could be due to problem of child labour or children being taken to the field.

In the present study majority of the patients were daily wage labourers working in the fields (34%), followed by farmers (29%). This was consistent with the rural predominance and field related occupations like farmers and daily wage labourers being the most common group affected in various studies conducted^[10, 11]

In our study we found that most of the snake bites 32% occurred during the morning period (6am to 12 am) and 30% occurred during the evening period (6pm to 12 pm). This was different to the findings in other studies conducted in Maharashtra by Bawaskar *et al.*^[13]. In our study fang mark was identified in 78% of the patients. Both the lower combined constituted about 80% of the bite sites with rest occurring over the upper limb. We had one patient with a bite over the anterior abdominal wall leading to extensive necrosis and death later. Our lower limb predominance is consistent with studies conducted by Kulkarni *et al.*^[9] in Karnataka and Bawaskar *et al.* in rural Maharashtra^[13] Our study showed that 68% of the patients received some form of first aid prior to presentation to the hospital. Almost all of them received more than one form of first aid. Around 81% of the patients were administered this first aid by untrained personnel (either patient himself or the bystander). The predominant mode of first aid that was used was application of pressure tourniquet which was used by 71% of the patients that received first aid. 19% of the population had received a local anaesthetic injection at the bite site by the local practitioner to relieve the pain. Around 10% of the patients had treatment with native medicine in the form of local application of crushed herbs or special powder. Our study showed that around 42% of the patients were able to identify the snake and Russell's viper was the most common cause in them which was similar to studies conducted by Kulkarni *et al.*^[9] and Kalantri *et al.*^[14] However studies done by Bawaskar *et al.*^[13] in Maharashtra and showed krait being the most common, Sharma *et al.*^[15] showed cobra being the most common suggestive of the regional difference in the distribution of snakes in India.

Of the 72 patients that were studied, fang marks were present in 56 patients. Local swelling was present in 87.50% of the patients. Features of cellulitis (such as local warmth with along with redness, swelling and tenderness) were present in 73.6% of the population. 64% of the patients had some amount of local bleed/ooze at the bite site. 14% went on develop necrotising fasciitis and 8.3% of the patients had compartment syndrome which required fasciotomy. The findings in our study were consistent with studies done by in Maharashtra by Bawaskar *et al.*^[13]

The various syndromes of snake envenomation seen in our study includes Local Swelling, Hemotoxicity with/without Local swelling, Neurotoxicity only, Neurotoxicity with local swelling,

Hemotoxicity + Neurotoxicity + Local swelling, Hemotoxicity + Neurotoxicity + Renal failure + Local swelling. This was consistent with the studies conducted earlier by Kulkarni *et al.*^[9] Bawaskar *et al.*^[13]. The syndrome of combined hemotoxicity, neurotoxicity, renal failure with local envenomation was highest which was in correlation with the high incidence of viper bite that were observed in the study sample. The risk factors for the prediction of severe envenomation were divided into demographic, clinical and laboratory groups.

The demographic risk factor associated with development of severe envenomation was that if the patient was a resident from Tamil Nadu. The possible explanation for this could be that as this was a referral centre more sick patients had come from the home state of Tamil nadu and only few people would have been referred from the neighbouring state. Most of the sick patients from Andhra Pradesh would have been referred to a higher centre in that state itself. However this factor was not found to have independent significance on multivariate analysis. On analysis of various clinical characteristics associated with patients presenting with snake bite, the clinical predictors of severe envenomation were presence of cellulitis at admission of local bleeding of systemic bleeding, features of neurotoxicity at admission, requirement of ventilation during the ward stay presence of renal failure, requirement of blood or blood product transfusion during the course of the hospital stay. Again on unadjusted multivariate analysis none of these factors were found have independent statistical significance.

Clinical features associated with higher risk but not statistically significant were administration of ASV at a local centre, local swelling, local pain, necrotising fasciitis. Though local and systemic bleeding were significant predictors, factors such as specific type of bleed like epistaxis, gum bleed were not statistically significant. Similarly specific manifestations of neurotoxicity like ptosis and paradoxical respiration were not statistically significant in spite of having higher odds ratio on analysis. On analysis of various laboratory characteristics associated with patients presenting with snake bite, the factors associated with statistical significance on univariate analysis were presence of anemia, thrombocytopenia, jaundice, hepatitis, haematuria on urinalysis, prolonged Thromboelastography

Conclusion

Present study found multiple risk factors were significant to predict a severe clinical course in envenomation. Socio-demographic variables, clinical findings, treatment variables, ASV related data and mortality in our study was found to be consistent with the studies done earlier

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