Original article

To study the utility of serum LDH values as a marker of hemotoxicity in snake bite victims in HSK hospital: An observational study

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Abstract:

Introduction: Snakebite in India is a commonly occurring occupational hazard among the agrarian population living in suburban and rural areas. Snake bites can either be neurotoxic, haemotoxic, myotoxic or a combination of these and are considered a grave medical emergency which requires immediate identification and treatment. Most of snakebite patients in this part of the country present with haemotoxic manifestations. Research work in this area previously has revealed the potential utility of serum LDH activity in the diagnosis and prognosis of haemotoxic snake bite and hence its levels may provide an insight into the severity of envenomation.

Materials and methods: This observational study was conducted over a period of eighteen months at the S. N. M. C Medical College HSK Hospital. The study comprised of 65 patients with snakebite after satisfying the inclusion and exclusion criteria.

Observation and results: Most of our patients were in the younger age group (75%) and presented with features suggestive of hemotoxic envenomation (70.17%). Elevated WBCT was the most commonly occurring haematological abnormality (75.92%) while 34% of our patients required more than 30 vials of polyvalent ASV. A stastically significant correlation was found between SerumLDH(p value 0.00) levels of the no and severe envenomation group at the time of presentation.

Conclusion: Hemotoxic snake bites with features compatible with moderate envenomation were found most commonly in our study population. It is perhaps due to the higher number of viperidae in this geographical area. Serum LDH levels at admission and 24 hours later may help differentiate between patients with severe envenomation and other grades of envenomation

Keywords: Snake Bite, Hemotoxic envenomation, S. CRP, S. LDH.

INTRODUCTION

In rural population of tropical and sub tropical countries like India, morbidity and mortality due to snake bite is high. Therefore snake bite is a significant health concern and needs immediate medical attention. Snake bite is an occupational hazard mainly in labourers, plantation workers and farmers, but remains unreported largely. India is estimated to have the highest snakebite mortality in the world. According to World Health Organization (WHO) estimation, the number of snake bites are 83,000 per annum with 11,000 deaths[1]. Most of the time there is delay in patients reaching the hospital, either due to negligence or due to adoption of trivial care or quackery. Lack of confidence among PHC workers also contribute to morbidity. Early

administration of ASV is required to neutralize the venom and prevent complications due to snake bite. Hematotoxic envenomation exceeds in number in this part of country as compared to neurotoxic envenomation. Detecting the grade of envenomation at presentation is difficult and novel markers serve as a good guide.

Table 1: Grading of severity of envenomation:[2]

The following scale was used to grade the severity of envenomation

No envenomation:	
Local manifestations	Mild pain
Systemic manifestations	None
Laboratory findings	None
Mild envenomation	
Local manifestation	Swelling, eythema or echymosis confined to the site of bite
Systemic manifestations	None
Laboratory findings	None
Moderate envenomation	
Local manifestation	Progression of swelling, eythema or echymosis beyond the site of bite
Systemic manifestations	Non life threatening signs and symptoms.Perioral and peripheral paresthesia, nausea, vomiting, diarrhea, ptosis, diplopia.
Laboratory findings	Mildly abnormal coagulation profile with no features of systemic bleeding. Mildly abnormal other laborotary tests.
Severe envenomation	
Local manifestation	Rapid swelling, eyrthemaechymosis involving the entire part or body
Systemic manifestation	Hypotension, tachycardia,tachypnoea respiratory paralysis, seizures, fasciculation, altered mental status
Laboratory findings	Systemic bleeding or markedly abnormal coagulation profile, unmeasurable INR, APTT and platelet count <20,000

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The phospholipase, an important component of snake venom is thought to produce hemolysis, a common manifestation of snake bite envenomation. Serum LDH level serves as one of the sensitive marker in the diagnosis and prognosis of snake bite cases, although the research for newer and other sensitive markers for systemic envenomation is still going on. In a study done by Kandasamy .S et al[3], there was a statistically significant increase in the S. LDH values in the 30 snake bite patients at the time of admission and 24 hours later as compared to the control group of 30. In a similar study done in Maharashtra S.LDH values showed significant rise in the envenomed group as compared to the control group[4]. Early rise in serum LDH levels within 48 hours of bite correlated with the degree of haemotoxicity of the bite. This was seen in a prospective study from Brazil that included children with moderate to severe snake bite envenomation[5].

AIMS AND OBJECTIVES:

To study the utility of serum LDH as a marker of hemotoxicity in snake bite victims in HSK hospital: An observational study**.**

MATERIALS AND METHODS

Source of data:

The data was collected from patients admitted to S. Nijalingappa Medical College and HSK Hospital with a history of snakebite.

Method of collection of data:

Study Design:

Observational study.

Sample Size:

A Sample size of 65 was selected for the study using purposive sampling technique based on inclusion and exclusion criteria.

On admission vital signs [pulse rate, respiratory rate, blood pressure, saturation of peripheral oxygen (SpO_2)], and site of bite were recorded.

Patients presenting with history suggestive of snakebite, the following lab tests were included. Hemoglobin, TC(total count), DC(differential count), ESR(erythrocyte sedimentation rate), platelet count, PCV(packed cell volume), Peripheral smear, Urine routine and micro analysis, Serum CRP, LDH, Albumin, APTT (activated partial thromboplastin time), PT-INR (prothrombin time with international normalized ratio) all of which were repeated twice, at admission and following 24 hours thereafter.

Bleeding time, clotting time and a 20 minute whole blood clotting test were repeated 6^{th} hourly for the first 24 hours of hospital admission.

Dry bites were defined as patients with a history of snakebite but without symptoms or signs of local or systemic envenomation or lab abnormalities even after 24 hours of observation in the hospital.

Patients were thereafter divided into no, mild, moderate and severe envenomation group based on a predetermined scale.

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The above values were noted and a correlation was drawn with values of serum LDH and grade of envenomation.

Inclusion Criteria:

1.Patients with alleged history of snakebite.

2.Patients with a history of unknown bite but with symptoms and signs compatible with snake bite envenomation.

Exclusion Criteria:

1.Known case of any bite not caused by a snake.

2.Patients with history of bleeding disorder

3.Patients who received ASV before arriving to the hospital.

4.Patient with a history of vasculitis

5.Patient with a history of acute or chronic liver disease

6.Patient with history of malignancy

7.Patient with history of acute myocardial infarction

8. Patient with history of acute pancreatitis

Data Analysis:

Data was tabulated in MS excel 2013 and analysed using SPSS 20.2 trial version. The data was presented in percentages, mean, standard deviation and statistical tests like ANOVA and t test were used wherever necessary. By using above mentioned tests, test of significance was calculated. A 'p' value less than 0.05 is statistically significant

RESULTS

This study was done in patients admitted to S. N. M.C and HSK hospital, Bagalkot. A total of sixty five patients with history of snakebite or evidence of envenomation admitted to our hospital were studied and followed up for the first 24 hours. The data in the form of investigations and profile of the patients is presented below.

1. **Sex distribution**

Table 2: Sex distribution of 65 cases of snakebite

Sex	Frequency	Percent
MALE	33	50.8
FEMALE	32	49.2
Total	65	100.0

Graph 1: Sex distribution of 65 cases of snakebite

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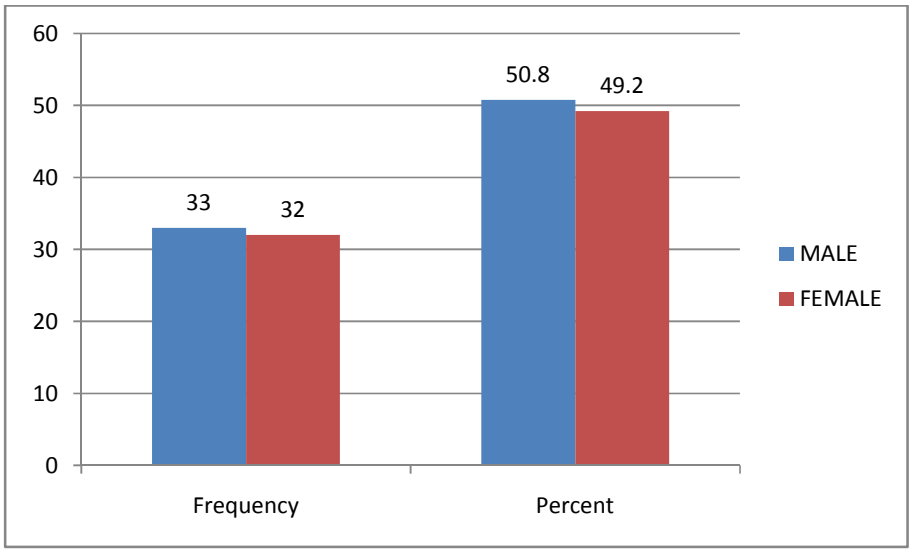


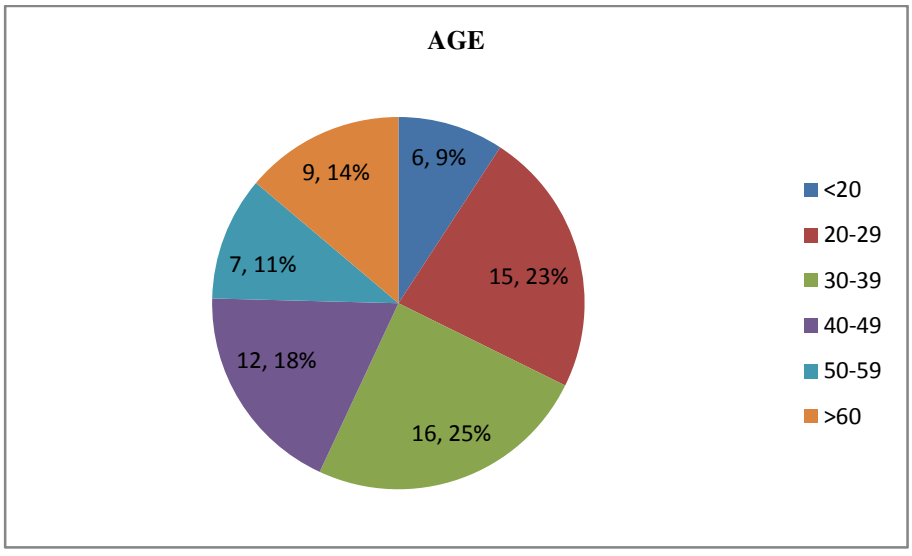
In our study male patients with snake bite were 33(50.8%) and that of female were 32(49.2%).

2.Age distribution

Table 3: Age distribution of 65 cases of snakebite

Age	Frequency	Percent
<20	6	9.2
20-29	15	23.1
30-39	16	24.6
40-49	12	18.5
50-59	7	10.8
>60	9	13.8
Total	65	100.0

Graph 2: Age distribution of 65 cases of snakebite



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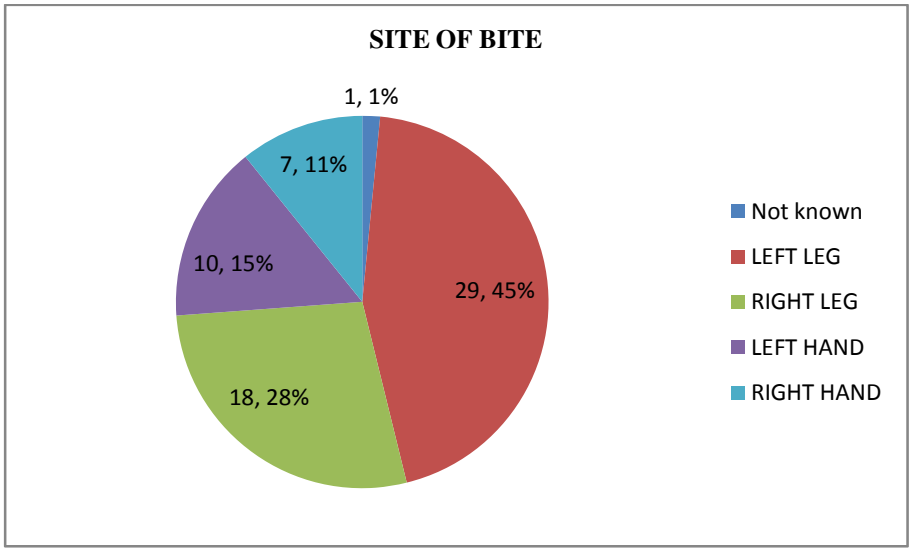
In our study the age distribution was found between 13 and 80 years. Most of our patients were in the age group of less than 49 years (75.4%). The mean age of the patients was 38.11 years.

3. Site of snakebite

Table 4: Site of snakebite

Site of bite	Frequency	Percent
Not known	1	1.5
LEFT LEG	29	44.6
RIGHT LEG	18	27.7
LEFT HAND	10	15.4
RIGHT HAND	7	10.8
Total	65	100.0

Graph 3: Site of snakebite



Lower limbs were the most common site of bite in our study group. Among the 65 patients, 47 (72.31%) and 17 (26.15%) were bitten on their lower and upper limbs respectively. Site of bite in 1(1.54%) of our patient was not known.

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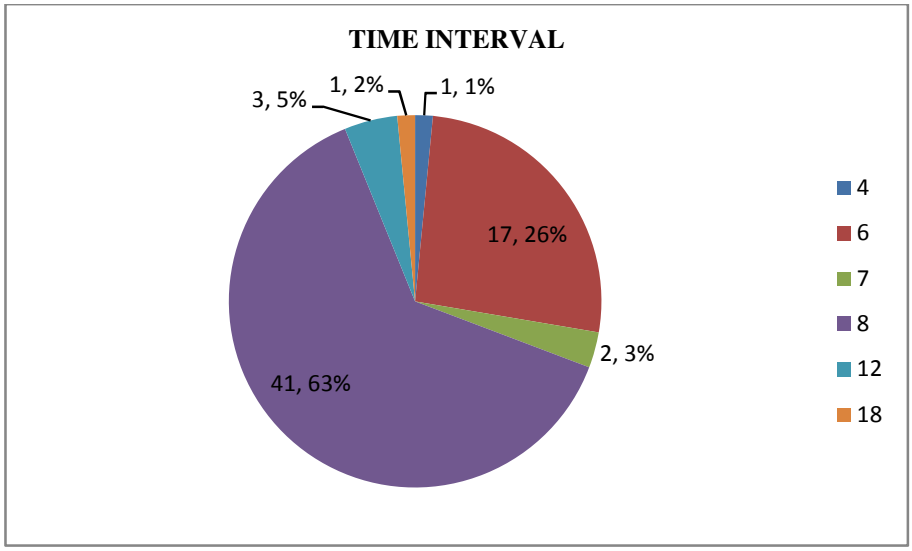
4. Time interval between snakebite and presentation to hospital

Table 5: Time interval between snakebite and presentation to hospital

Time interval	Frequency	Percent
4	1	1.5
6	17	26.2
7	2	3.1
8	41	63.1
12	3	4.6
18	1	1.5
Total	65	100.0

Graph4: Time interval between snakebite and presentation to hospital



In our study 61 patients (93.8%) presented within 8 hours of snakebite while the rest 4(6.15%) within 24 hours of snakebite.

5: Grade of Envenomation

Table 6: Grade of Envenomation

Grade of evenomation	Frequency	Percent
NO	11	16.9
MILD	14	21.5
MODERATE	34	52.3
SEVERE	6	9.2
Total	65	100.0

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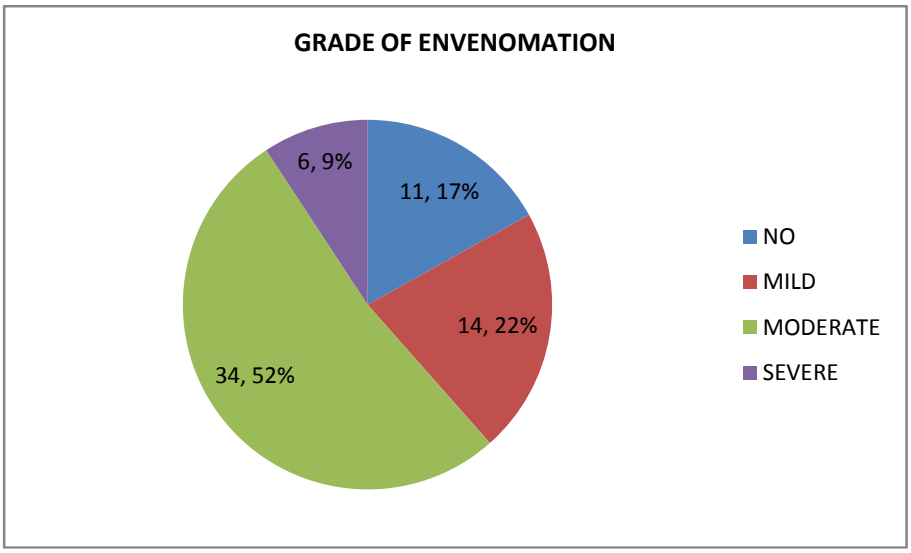
Graph 5: Grade of Envenomation

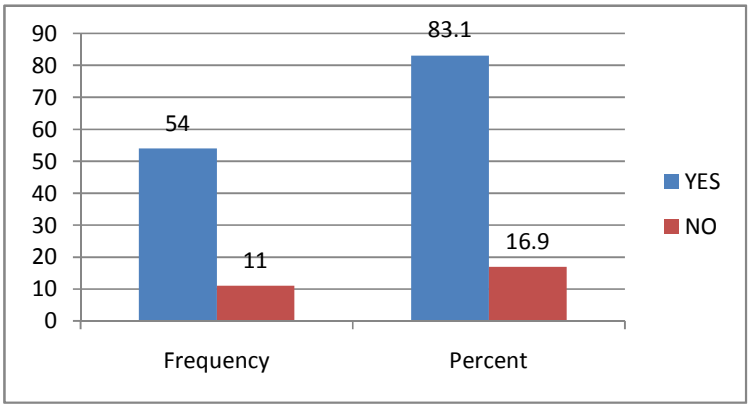


In our study most of our snakebite victims presented with features compatible with moderate envenomation. Of the study group, 34 (52.3%) had evidence of moderate envenomation, while 6(9.23%) had severe, 14(21.54%) had mild and 11(16.92%) had no features suggestive of envenomation.

6.Bleeding manifestations-

Table- 7: Bleeding manifestations in snake bite victims

Bleeding manifestations	Frequency	Percent
YES	54	83.1
NO	11	16.9
Total	65	100.0



Graph 6: Bleeding manifestations in snake bite victims

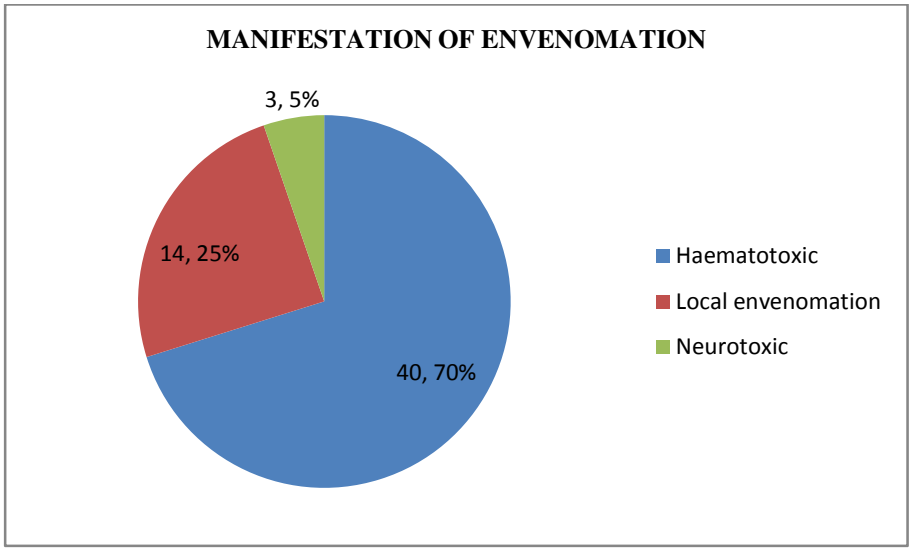
Most of the patients in our study presented with bleeding manifestations. In our study group bleeding manifestations were seen in 54(83.1%) patients and 11(16.9%) with no bleeding manifestations.

7: Manifestation of Envenomation

Table : 8: Manifestation of Envenomation

Manifestation of Envenomation	**No. of patients**	**Percentage**
Haematotoxic	40	70.17%
Local envenomation	14	24.56%
Neurotoxic	3	5.26%
	57	

Graph 7: Manifestation of Envenomation



In our study group 40 patients (70.17%) presented with features compatible with Haematotoxic envenomation.

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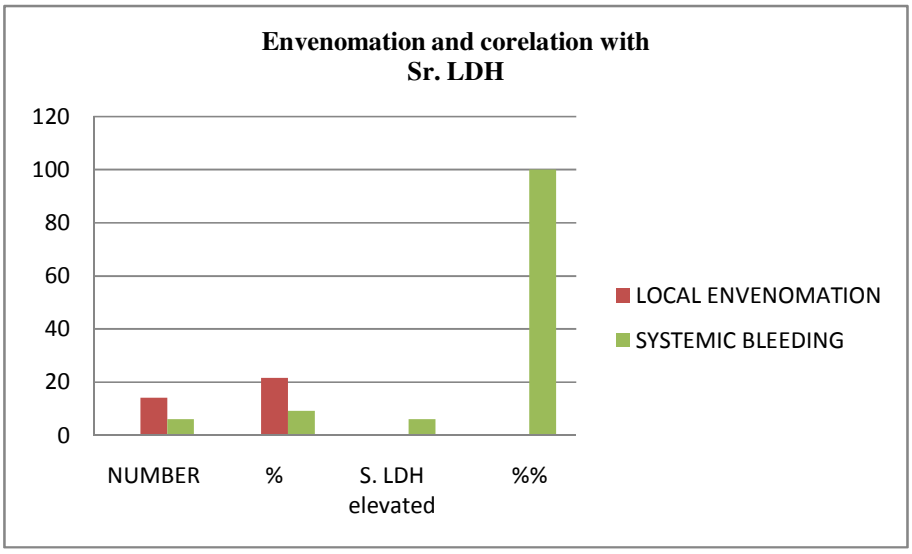
8. Envenomation and Correlation with Sr. LDH

Table:9: Envenomation and Correlation with Sr. LDH

SYMPTOMS	NUMBER	%	Sr.LDH elevated	% %
LOCAL ENVENOMATION	14	21.54	0	0
SYSTEMIC BLEEDING	6	9.23	6	100



Graph 8: Envenomation and Correlation with Sr. LDH

In our study group 14 patients(21.54%) presented with features compatible with local envenomation while 6 patients(9.23%) had systemic bleeding manifestations. Sr. LDH were raised in all the patients with systemic bleeding.

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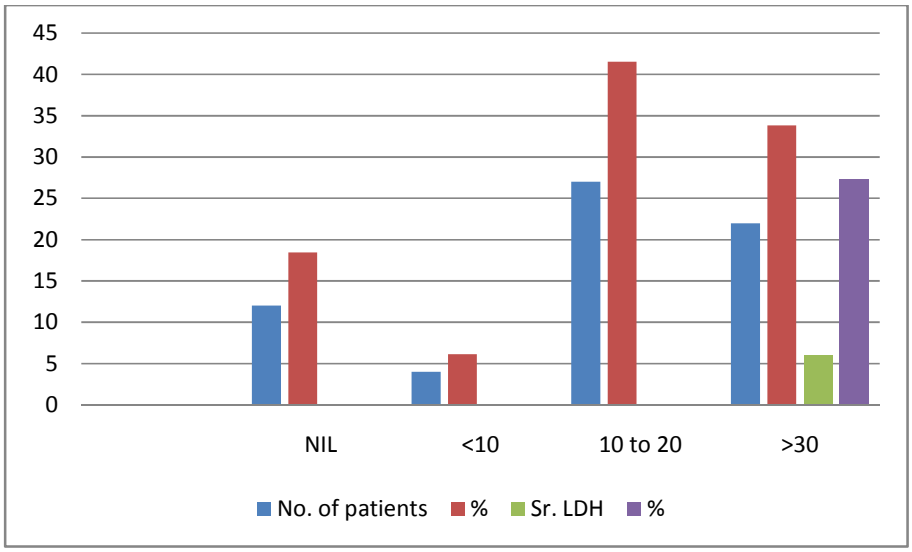
9.Polyvalent ASV used and its comparison with Sr. LDH levels

Table 10: Polyvalent ASV used and its comparison with Sr. LDH levels

Number of vials of ASV	No. of patients	%	Sr. LDH Elevated	%
NIL	12	18.46	0	0
<10	4	6.15	0	0
10 to 20	27	41.53	0	0
>30	22	33.84	6	27.27
	65			

Graph 9: Polyvalent ASV used and its comparison with Sr. LDH levels



In our study 22(33.84%) of the patients received more than 30 vials of polyvalent ASV whereas 27(41.53%) received 10-20 vials and 4(6.15%) received less than 10 vials. Sr LDH was raised in 6 patients who received more that 30 vials of ASV.

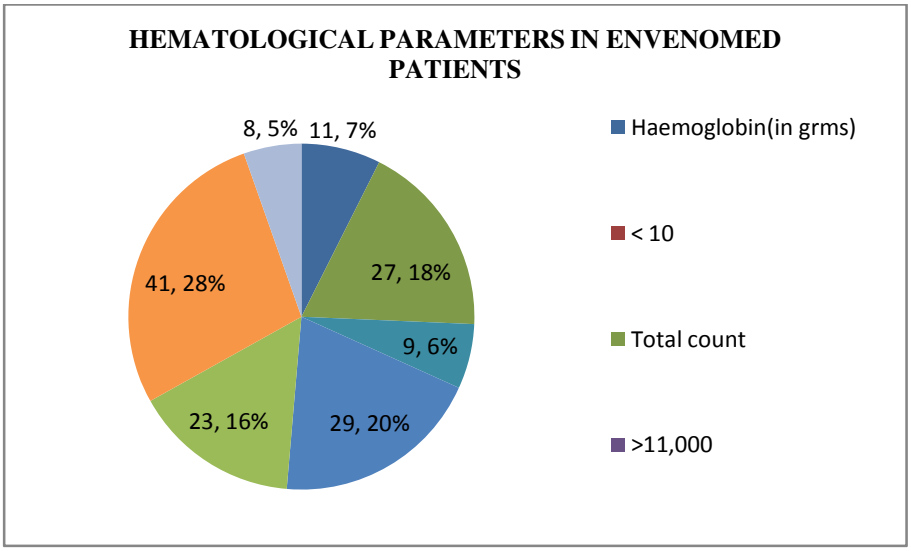
10.Haematological parameters in envenomed patients

Table 11: Haematological parameters in envenomed patients

Haematological parameters	No. of Patients	%
Haemoglobin(in grms) < 10	11	20.37

Total count	27	50
>11,000		
Platelet count	9	16.66
<100,000		
Prothrombin Time (in secs)	29	53.77
>15 sec		
Activated Partial Thromboplastin Time (in secs)	23	42.59
>30 secs		
WBCT		
>20 minutes	41	75.92
INR> 1.5	8	14.81
	54	

Graph 10: Haematological parameters in envenomed patients



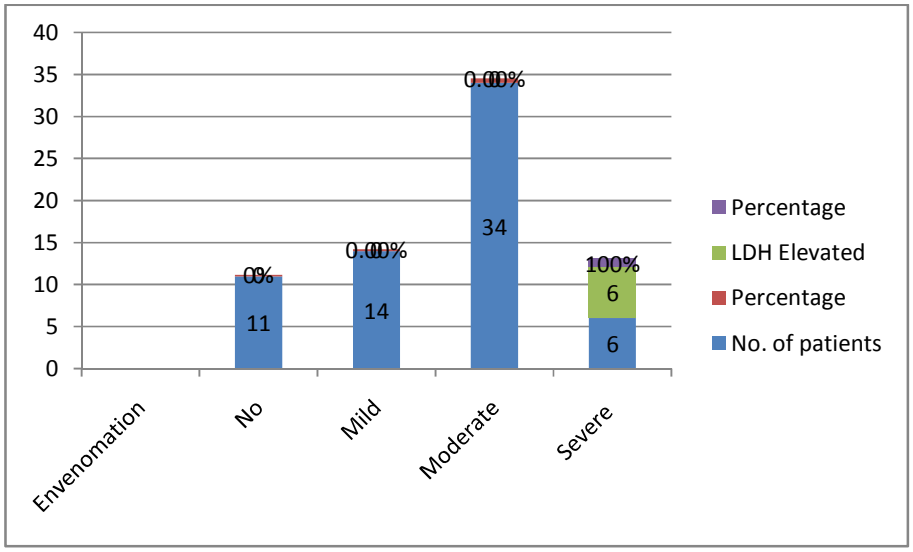
In our study 41(75.92%) patients with features of envenomation had elevated WBCT while only 11(20.37%) patients had haemoglobin level of less than 10. 29(53.77%) patients had raised PT and 8(14.81%) had INR>1.5.

11.Grade of Envenomation and its correlation with Sr. LDH values

Table 12 : Grade of Envenomation and its correlation with Sr. LDH values

Grade of Envenomation	No. of patients	Percentage	LDH Elevated	Percentage
No	11	17%	0	0%
Mild	14	22%	0	0.00%
Moderate	34	52%	0	0.00%
Severe	6	9%	6	100%
Total	**65**			

Graph 11: Grade of Envenomation and its correlation with Sr.LDH values



In our study all 6(100%) patients with severe envenomation showed increased levels of Sr.LDH, whereas in the moderate envenomation 0(0%) showed elevation in its values at presentation.

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12.Serum LDH values in envenomed patients-

Table 13- S. LDH values in envenomed patients at presentation and 24hrs later-

At presentation	237.59± 196.99
24hrs later	277.586±256.49
p-value	<0.05

In our study there was found to be statistically significant difference in S.LDH values at the time of admission and 24 hours later (**p value< 0.05**) in the envenomed group.

13. Grades of envenomation and its comparison with Sr LDH values-

Table 14:Grades of envenomation and its comparison with Sr LDH values at presentation and 24hrs later-

ENVENOMATION	S LDH AT PRESENTATION Mean±SD	S LDH AT 24 HOURS Mean±SD
No	140.28±14.2	159.41+/-32.13
Mild	160.92±63.15	177.5+/-64.22
Moderate	211.23±67.81	240.24±72.55
Severe	744.23±324.87 *	939.33±448.125*
F value	48.527	48.612
P value	.000	.000

Post hoc Dunnets

There is significant difference in LDH at presentation between the groups, determined by ANOVA test with F value of 48.527 and p value of 0.000. Post hoc dunnets showed that there is significant difference between no group and severe group.

There is significant difference in LDH at 24hrs later between the groups, determined by ANOVA test with F value 48.612 and p value of 0.000. Post hoc dunnets showed that there is significant difference between no group and severe group.

In our study it was seen that there was statistical significant difference in Sr LDH values at presentation and 24hrs later in envenomed group. A significant difference was also noted in patients who presented with severe as compared to those with no envenomation. And also it was observed that S. LDH values increased as the grade of envenomation increased.

DISCUSSION

A greater number of snakebite patients in this part of the country present with haemotoxic envenomation and its complications. While a small number of studies have been done demonstrating the role of serum LDH as a marker of haemolysis, there have been no noteworthy studies done showing a correlation between grade of envenomation and serum LDH in snakebite victims. Hence in this study we aimed to analyze the relationship between serum LDH with grade of envenomation and haematological profile, and their values at presentation and 24hrs later and to ascertain their utility as markers of haemotoxicity in snakebite victims.

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The present study involved a total of 65 patients who were admitted to S. Nijalingappa medical college and HSK Hospital with history of snakebite This study showed that the occurrence of snakebite was higher in the working age group. A majority(75%) of patients were below 49 years of age and the mean age was 38.11 years. This correlated with other studies done by Suchithra N, et al.[6], Monteiro FN, et al.[7] and Sharma SK, et al.[8] where the mean age was 40, 40.7 and 32 years respectively. As most patients affected fall in the working age group it places a great economic burden on the family

In the present study the incidence of snakebite was seen to be same in males and females, the ratio being 1.03:1. The might be attributed to higher exposure of both the sexes to outdoor environment and hence the risk of snakebite. But other studies showed male preponderance, like the one by Monteiro FN, et al.[7] where the ratio was 1.38:1 and by Kulkarni ML, et al.[9] where the ratio was 2.17:1

In our study lower limb were the commonest site of snakebite. The ratio of lower limb to upper limb bites was 2.8:1. A study done by Saravu K,et al.[10] showed a ratio of 3.48:1. Another study done by David S, et al.[11] showed that lower limb bites were 3.44 times more common than those of upper limb bites. As most of these bites happen outdoors especially either at night on accidental stepping or while working in the fields, lower limbs tends to have higher incidence of bite site than upper limb.

In the present study haemotoxic envenomation with coagulopathy was higher in occurrence compared to neurotoxic envenomation. A Study done by Kulkarni ML, et al.[9] at Davangere showed a similar result with 58.6%patients developing coagulopathy after snakebite. A study done by Suchithra N, et al. [6] in Kerala showed 71% of patients demonstrating coagulopathy after snakebite. This probably could be attributed to the higher number of viperidae in this part of country compared to elapids.

The present study showed that local envenomation as well as systemic bleeding tendencies were less common in our study group. In a study done in Bangalore by Harshavardhana HS, et al.[12] the incidence of systemic bleeding manifestations was 50% and local envenomation 40%. This might be attributed to later onset of presentation to hospital as well as higher incidence of bites caused by viperidae in their study group. An observation was made in our study that all of 6 patients with systemic bleeding manifestations had elevated levels of Sr.LDH.

In our study group most of the patients received more than 10-20 vials of ASV after admission. In a study done in Maharashtra by Pore SM, et al.[13] 49% of the patients received less than 10 vials of ASV whereas 41% received 10-20 vials while only 10% received more than 30 vials. In a study done in Bangalore by Harshavardhana HS, et al.[12] 52% of the patients received more than 30 vials of ASV. The less dose of ASV administration in our study could be attributed to smaller number of patients with systemic envenomation. Also to be noted was that there was no common criteria between the 3 studies for the administration of ASV and it was purely at the discretion of the treating physician. An observation was made in our study that patients requiring more than 30 vials of Polyvalent ASV had elevated S CRP(90.9%) and LDH(27.27) values at admission.

In our study among the patients with envenomation 75.92% showed prolongation in the WBCT in comparison to 53.77% and 14.81% of PT and INR. In a study done in Bangalore by

Harshavardhana HS et al.[12] 60%, 56% and 48% showed prolongation in the WBCT PT and INR. This could be due to higher number of patients with systemic envenomation in their study group. In our study there was found to be statistically significant difference in Sr.LDH values at the time of admission and 24 hours later **(p value< 0.05)** in the envenomed group. A significant difference was also noted in patients who presented with severe as compared to those with no envenomation. A study done by Bhagwat K, et al[14] in Maharashtra on 50 patients of snakebite showed elevated Sr. LDH recordings at the time of admission and 24 hours later in snake bite victims as compared to the control group (p value < 0.05). However there was found to be no similarity in the values of S.LDH between our study and that of Bhagwat K, et al.[14] A study done by Kandaswamy S, et al.[15] in Tamil Nadu involving 30 snakebite victims showed a statistically significant difference (p value 0.01) between S. LDH values recorded in haemotoxic snakebite victims and control group at admission. S. LDH values done at admission in patients with envenomation were found to be similar between our study and Kandaswamy S, et al.[15] This could be because of the similar profile of patients as well grade of envenomation in our group and that of Kandaswamy S, et al.[15]

The difference between the 2 groups among the grades of envenomation could be attributed to, higher incidence of pit viper bites, differences in study population as well as systemic envenomation in our study group as compaired to theirs.

It was also noted that in our study that 3 patients with no features envenomation were found to have raised S.CRP values. The reason for these raised CRP values in non envenomed cases could not be justified.

CONCLUSION

1. Snakebite commonly affects people in the younger age group who are in the working class. This effects the economy of the concerned family as they are deprived of work for the period of illness.
2. Haemotoxic envenomation is most common manifestation of envenomation observed signifying presence of more number of viperidae in this geographic area.
3. Most of the patients received 10-20 vials of Polyvalent ASV signifying lesser incidence of systemic envenomation in our patients.
4. WBCT was the most commonly deranged haematological parameter in envenomed patients. However most of them did not show similar derangement in PT/INR values.
5. S. CRP were found to be elevated significantly in the severe as compared to those with other grades of envenomation.
6. S. LDH levels demonstrated significant difference in the severely envenomed group as compared to those with other grades of envenomation. And also, all severely envenomed patients had

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raised S. LDH and required 30 vials or more number of ASV signifying the importance of raised S. LDH at the time of presentation.

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