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A STUDY ON PROTEINURIA AS AN EARLY INDICATOR OF SYSTEMIC ENVENOMATION IN SNAKE BITE

General Medicine

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ABSTRACT

Background: Snakebite is an important public health concern in developing countries. In India, it is estimated that 45900 deaths occur annually due to snake bites. Various studies have shown conflicting views on the importance of proteinuria in venomous snake bites. Hence, this study intends to study proteinuria and assess whether it can serve as a reliable early indicator of systemic envenomation in snakebites.
The objective of the study: To study the value of proteinuria as an early indicator of systemic envenomation in snakebite.
Methodology: A Hospital-based Descriptive study was conducted in the Department of General Medicine, Santhiram Medical College, and General Hospital for six months after approval from the Hospital Ethics and Research Committee.
Patients above 18 years presenting with an alleged history of snakebite were included in the study. Urine for proteinuria was tested using the dipstick method and followed up at 0, 6, 12, 18 and 24hours. A total of 60 patients were included in the study.
Results: Out of 60 patients included in the study, the majority (64%) of the patients were in the age group of 18-50 years. The dorsum of the right foot was the most common site of bite amongst the patients. Proteinuria had a significant correlation with deranged bleeding and renal parameters.
Interpretation and conclusion- In the present study, it is evident that proteinuria was seen in patients with prolonged WBCT and deranged PT/APTT/INR, and it is observed that proteinuria appeared even before a clotting defect was detectable. Hence it would be of paramount importance to consider proteinuria as an indicator of systemic envenomation in snake bites.

KEYWORDS

Snake Bite, systemic envenomation, proteinuria

INTRODUCTION

Snakebite is a significant public health concern in developing countries. In India, it is estimated that 45900 deaths occur annually due to snake bites in Uttar Pradesh (8700), Andhra Pradesh (5200), and Bihar (4500) has the highest burden of Snakebite.[1]

There are various studies on biochemical changes in snake bite patients. The common biochemical and haematological abnormalities found are increased serum creatinine, prothrombin time, partial thromboplastin time, whole blood clotting time, and a decrease in platelet count and fibrinogen.[2]

The incidence of proteinuria in snakebite is variable depending on the kind of snakes involved, and there is also geographical variation [3]

Nephrotic syndrome in snakebite has been reported[4], but the cause and effect relationship was not substantiated. Proteinuria may be observed following snakebite. Proteinuria has been noted in rats following intrarenal injection of cobra venom.[5]

The magnitude of proteinuria is less than 500mg/24h, and this is usually a transient finding which completely resolves when the patient recovers. However, significant proteinuria over 1g/24 h has been observed in 50% of Russell's viper bite patients in Myanmar, suggesting that geographical variation can affect the venom composition of the snake of the same species. [6]

A highly vascularised organ, the kidney is prone to venom toxicity. Renal involvement in snakebite varies widely.[7-10]. Acute renal failure is frequently described and is life-threatening. Haematuria and proteinuria are common. There is a broad spectrum of renal pathological changes.[11-14]

Various studies have shown conflicting views on the importance of proteinuria in venomous snake bites. Hence, this study intends to study proteinuria and assess whether it can serve as a reliable early indicator of systemic envenomation in snake bites.

AIMS AND OBJECTIVES

- To study the value of proteinuria as an early indicator of systemic envenomation in snake bites.

MATERIALS AND METHODS

This descriptive study was done over 06 months on 60 patients admitted to the Santhiram Medical College and General hospital with an alleged history of Snakebite who were willing to participate in the study and gave written informed consent who satisfied the inclusion and exclusion criteria. The study was initiated after obtaining Ethical Clearance from the Institution's Ethics Committee.

All patients were subjected to detailed history and clinical examination. Urine Examination for proteinuria was done in all patients as soon as they get admitted into the hospital. Subsequently, urine examination for proteinuria was done at 6,12,18,24 hr following admission.

Following investigation were done in all cases: Haemoglobin, total leucocyte count, differential count, platelet count, blood urea, serum creatinine, bleeding time, Clotting time, prothrombin time, partial thromboplastin time.

Inclusion Criteria

1. Patients admitted to Santhiram Medical College and General Hospital with an alleged history of snakebite.
2. Age more than 18 years.

Exclusion Criteria

1. Patients with Diabetes and hypertension.
2. Patients with a history of chronic kidney disease.
3. Patients with a history of nephrotic syndrome.
4. History of drug intake that can cause proteinuria- NSAIDs, Lithium carbonate, Penicillamine.
5. Patients with a recent history of urinary tract infection.

Data And Statistical Analysis

The collected data were analysed using mean, Mode for demographic data and Frequency percentage for the analysis of the clinical data. Statistical Analysis was Done using SPSS software version 23.0. A 'p-value less than 0.05($p<0.05$) is Considered significant.

RESULTS AND OBSERVATIONS

Bleeding Manifestations

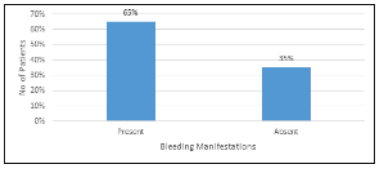

Figure 1; Bleeding Manifestations

- In our study, out of 60 patients, 39 patients (65%) had bleeding manifestation in the form of bleeding from the bite site, haematuria, bleeding from the gums.

Vials of ASV

Table 1: Vials of ASV

Vials of ASV	Frequency	Percent
None	17	28.3
1-10	15	25
Up to 50	28	46.7
Total	60	100

- Most patients 71 % of the cases received ASV, in which 25% received ten vials and 46.7% received 10 to 50 vials of ASV.

Association of bleeding manifestations in snake bite with proteinuria:

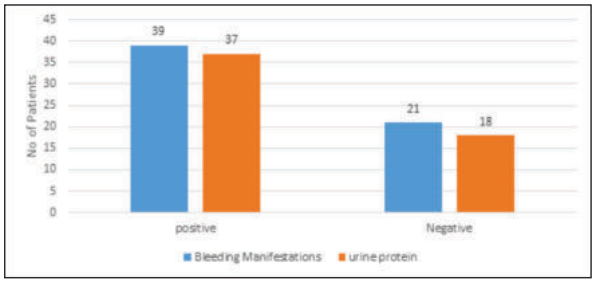

Figure 2: Association of bleeding manifestations in snake bite with proteinuria

- In our study, out of 39 patients who had bleeding manifestation, 37 patients showed positive urine protein, and out of 21 patients who had no bleeding manifestation,3 had proteinuria.

Association of use of ASV vials in snake bite with proteinuria:

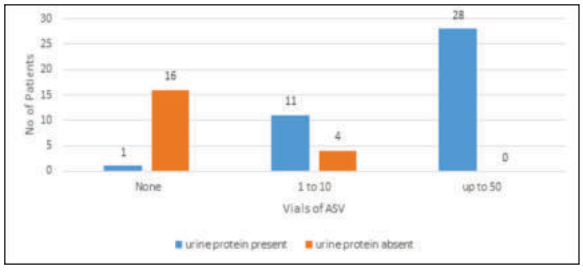

Figure 3: Association of use of ASV vials in snake bite with proteinuria

- In our study, it was found that proteinuria was seen in 100 per cent of the patients who received more than 10 vials of ASV and out of 17 patients who did not receive ASV, 16 patients urine protein was negative.

Association of the value of INR in snake bite with proteinuria:

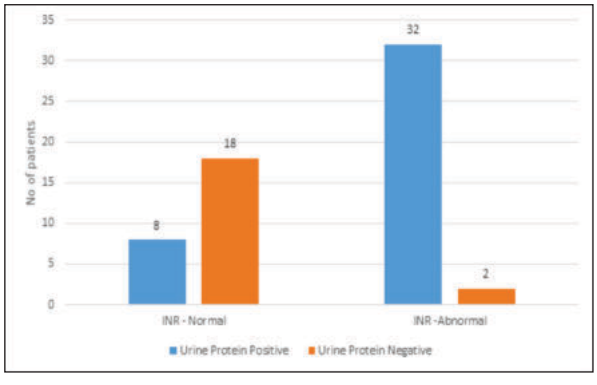

Figure 4: Association of the value of INR in snake bite with proteinuria

In the present study, it was found that out of 34 patients in whom INR was abnormal, 32 Patients showed proteinuria, and there was a significant correlation between INR and Proteinuria. (P-value = 0.001)

Systemic envenomation with Proteinuria and deranged bleeding parameters

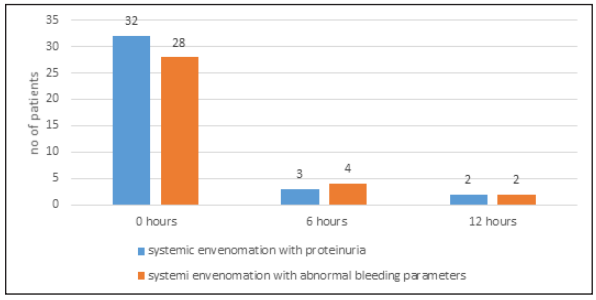

Figure 5: Systemic envenomation with Proteinuria and deranged bleeding parameters at an interval of 0 ,6 and 12 hours

In the present study, it was found that out of 37 patients who had features of systemic

Envenomation with proteinuria 32 showed at 0 hours, 3 at 6 hours and 2 at 12 hours,

However, patients with systemic envenomation with abnormal bleeding parameters

(n=34), 28 showed at 0 hours, 4 at 6 hours and 2 at 12 hours.

Systemic envenomation with the clinical profile.

Symptoms included in the clinical profile are:

1) Nausea, vomiting.
2) Pain abdomen.
3) Tender lymphadenopathy.
4) Spontaneous systemic bleeding.
5) Passage of dark brown urine.

Table 2: Showing patients of systemic envenomation with clinical profile at 0,6,12 hours

	0 hour	Hour	12 hour	Total
Systemic envenomation with clinical profile	36	3	0	39

In the present study, it was found that out of 39 patients who had features of systemic Envenomation 36 showed in 0 hours and 3 at 6 hour

Association of whole blood clotting time (WBCT) >20MIN time in snake bite with Proteinuria

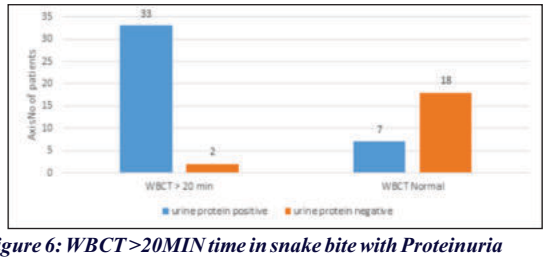

Figure 6: WBCT >20MIN time in snake bite with Proteinuria

In our study, we found that there is a significant (p=0.001) correlation between WBCT and proteinuria. Out of 35 patients of prolonged WBCT, 33 patients showed proteinuria.

Association of s.creatinine in snake bite with Proteinuria

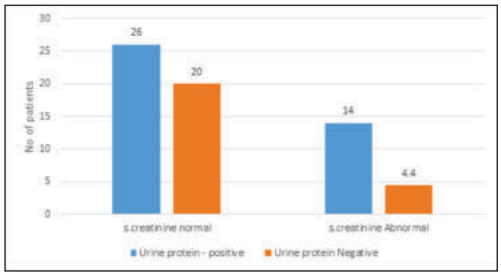

Figure 7; Association of s.creatinine in snake bite with Proteinuria

In our study, it was found that proteinuria was seen in all the cases with deranged s. creatinine level. 14 out of 14 patients (100%) in whom s .creatinine was abnormal Proteinuria was present.

DISCUSSION

Worldwide, there are more than 3000 species of snakes, and only 400 species are venomous. In India, no reliable national statistics are available. It is estimated that between 35,000 and 50,000 people die of snakebite each year among India's population of 980 million.

Association of bleeding manifestations in snake bite with Proteinuria

Table 3: Bleeding manifestations in snake bite with Proteinuria

Bleeding manifestations with proteinuria	Patil TB	Our study
	82.76%	92%

In our study, out of 39 patients who had bleeding manifestation, 37 patients had proteinuria, and out of 21 patients who had no bleeding manifestation, 18 of them urine protein was negative.

In a similar study done by Patil TB, 72 (82.76%) patients had bleeding tendencies with proteinuria, while 15 (17.24%) patients did not have any evidence of bleeding

Dosage of ASV
Comparison of polyvalent ASV in different study

Table 4: Comparison of polyvalent ASV in different studies

Vials of ASV	Harshavardhana HS et al	Present Study
NONE	22%	20%
10 vials	26%	25%
Up to 50 vials	52%	55%

In our study group, most of the patients received more than 10 vials of ASV after admission. In a study done in Maharashtra by Pore SM et al., 40.49 %[15] of the patients received less than 10 vials of ASV, while only 10% received more than 30vials. In a study done in Bangalore by Harshavardhana HS et al., 39.52%[16] of the patients received more than 30 vials of ASV.

The higher dose of ASV administration in our study could be attributed to a larger number of patients with systemic envenomation. There were no standard 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 the majority of patients requiring more than 10 vials of Polyvalent ASV had proteinuria at admission (100%) as compared to those who did not require ASV and those who required lesser than 10 vials (73%).

Comparison Of Haematological Parameters Among Various Studies.

Table 5: Haematological parameters among various study

	Harshavardhana HS et al	Patil TB	Athappan et Al[17]	Present study
PT (>15sec)	56%	37%	27.7%	33%
APTT (>30)	62%	-	-	35%
WBCT (>20MIN)	60%	59.06%	-	58%

PT- prothrombin time APTT- Activated Partial Thromboplastin Time

In our study, among the patients with envenomation, 58% showed prolongation in the WBCT in comparison to 33% and 35% of PT and APTT, respectively. In a study done in Bangalore by Harshavardhana HS et al. [16], 60%, 56% and 48% showed prolongation in the WBCT PT and APTT, respectively. This could be due to a higher number of patients with systemic envenomation in their study group as well as faster presentation to hospital and early initiation of treatment in our study group.

Association of s.creatinine in snake bite with proteinuria

Table 6; Association of s.creatinine in snake bite with proteinuria

	Patil TB	Present study
Proteinuria with deranged renal parameter. (Abnormal S.creatinine)	100%	100%.56

In a study by Patil TB, it was noted that 100% of cases who develop renal dysfunction had proteinuria showing that proteinuria can be a predictor of organ dysfunction in snake bites.

Similarly, in the present study, patients who developed renal dysfunction all cases showed proteinuria.

Proteinuria as an early indicator of systemic envenomation.

In the present study, it is observed that out of 39 patients who had features of systemic envenomation, 32 showed proteinuria at 0 hours.

Out of 39 patients who had features of systemic envenomation, 34 of them had clotting defects. However, it was observed that the remaining 5 patients who had features of systemic envenomation with normal bleeding parameters 3 of them showed proteinuria at 0 hours and 1 at 6 hours. In a similar study done in Myanmar, it was observed that proteinuria appeared even before a clotting defect was detectable, and it was considered as an indicator for Antivenom treatment[18]

Summary

The study was done on proteinuria as an early indicator of systemic envenomation in snake bite

- A majority of our patients present with bleeding manifestation (hemotoxic envenomation)
- In the present study, 71.7% of patients received more than 10 vials of ASV.
- WBCT is the most commonly deranged haematological parameter.
- Proteinuria had a significant correlation with deranged INR, prolonged WBCT, systemic envenomation, and abnormal creatinine values.
- Proteinuria was also found in patients who received more than 10 vials of ASV (100%).
- Proteinuria was seen even before clotting defect was detectable

CONCLUSION

- In the present study, it is evident that proteinuria was seen in patients with prolonged WBCT and deranged PT/APTT/INR.
- In patients with systemic envenomation requiring >10vials of ASV, proteinuria was present in all the patients.
- In the present study, it is observed that proteinuria appeared even before a clotting defect was detectable.
- Hence it would be of paramount importance to consider proteinuria as an indicator of systemic envenomation in snake bites.

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