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

General Medicine

Dr. R. Kaverikannan MD, Professor, Department of General Medicine, Kanyakumari Government Medical College, Kanyakumari

Dr. Vishnu S Post Graduate, Department of General Medicine, Kanyakumari Government Medical College, Kanyakumari

ABSTRACT

Background: Snake bite is an important public health concern in developing countries. In India it is estimated that 45900 deaths occur annually due to snake bite.Various studies done 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 bite. **Aims and Objectives:** 1.To study the prevalence of proteinuria in snakebite patients 2.To study the correlation of proteinuria in patients with sytemic envenomation **Methodology:** Patients above 18 years presenting with alleged history of snake bite were included in the study. Urine for proteinuria was tested by using dipstick method and followed up at 0, 6, 12, 18 and 24hours. **Results:** In present study it is observed that out of 39 patients who had features of systemic envenomation, 37 had proteinuria and 32 showed proteinuria at 0 hour. Out of 39 patients who had features of systemic envenomation, 35 had clotting defects, 4 had neurological involvement and 32 had proteinuria and coagulopathy . Hence with our study proteinuria can be considered as an early indicator of systemic envenomation. **Interpretation and Conclusion:** In the present study it is evident that proteinuria was seen in patients with prolonged WBCT and deranged PT/INR and it is observed that proteinuria appeared even before a clotting defect was detectable. Hence it would be paramount importance to consider proteinuria as an indicator of systemic envenomation in snake bite.

KEYWORDS

Snake Bite, systemic envenomation, proteinuria

INTRODUCTION

In the tropics, particularly in India, clinical toxicology from natural toxins is a major public health issue. Tropical areas are rich in animals, plants, microbes, and their toxins due to biological diversity and a favourable environment. Snake bites, animal bites, and stings are common, with snake bites accounting for the majority of animal toxin poisoning. Snake bite is an important environmental and occupational hazard. The poor health care infrastructure and lack of disease registries in areas where this problem is frequently seen prevents an assessment of true burden[1]. Each year, about 5 million people are bitten by poisonous snakes, resulting in 2.5 million envenomations, at least 100,000 deaths, and 300,000 amputations and other permanent disabilities, according to WHO estimates[2]. The mortality due to venomous snakebite in India is estimated between 35000-50000 per annum, which is the highest in the world[1,3]. The mortality due to venomous snakebite in India continuous to be high due to various social, economic and cultural reasons[3].

REVIEW OF LITERATURE

There are over 3000 species of snakes in the world, with about 600 of them being venomous. In Southeast Asia, there are two major groups (families) of venomous snakes. Elapidae snakes have short, permanently erect fangs. Cobras, king cobras, kraits, coral snakes, and sea snakes are all members of this family. Viperidae have long fangs that are normally folded against the upper jaw but are erect when the snake strikes. The typical vipers (Viperinae) and the pit vipers (Crotalinae) are the two subgroups[4]. The so-called "Big 4" snakes of India are Russel's viper (Daboia russelli), Cobra (Naja naja), Common Krait (Bungarus caeruleus), and Saw scaled viper (Echis carinatus), which can be found all over the country. In some geographical areas, pit viper species such as the Malabar, green, and hump-nosed, sea snakes, and others such as the king cobra (Ophiophagus hannah), monocle cobra (Naja Kaouthia), Banded Krait (Bungarus fasciatus), and Echis sochureki are important causes.

Medically Important Venomous Snakes In India

VIPERIDAE
Russel's viper (Daboia russelii)
Saw scaled viper (Echis carinatus)
Hump nosed pit viper (Hypnale hypnale)
White lipped pit viper (Trimeresurus albolabris)
ELAPIDAE
Indian or speculated cobra (Naja naja)
Common krait (Bungarus caeruleus)
King cobra (Ophiophagus hannah)
HYDROPHIDAE

It's a common misconception that snake bites always result in envenomation.

Non-venomous snake bites, on the other hand, are quite common.
"Dry bites" are venomous snake bites in which the fangs pierce the skin but do not envenom the victim. This could be due to mechanical inefficiency of the venom apparatus striking at an unnatural angle (or through clothing), or it could be due to the snake's voluntary retention of venom. When envenoming occurs, it can be fatal very quickly.

The Following Are The Clinical Characteristics:

Local Symptoms And Signs In The Bitten Part:

Fang marks
Local pain
Local bleeding
Swelling
Bruising
Lymphangitis
Lymph node enlargement
Blistering
Local infection, abscess formation
Necrosis

Systemic Symptoms

General

Nausea, vomiting, malaise, abdominal pain, weakness, drowsiness, prostration.

Cardiovascular

Dizziness, shock, hypotension, cardiac arrhythmias, pulmonary edema.

Bleeding and clotting disorders Traumatic bleeding from recent wounds -Prolonged bleeding from the fang marks and from old partly-healed wounds Spontaneous systemic bleeding: From gums, epistaxis, bleeding into the ears, intracranial haemorrhage , haemoptysis , haematemesis, rectal bleeding or melaena, haematuria, vaginal bleeding, ante-partum haemorrhage in pregnant women, bleeding into the mucosae and skin (petechiae, purpura and ecchymoses) and retina.

Neurological

Drowsiness, paresthesia, abnormalities of taste and smell, ptosis, external ophthalmoplegia, paralysis of facial muscles and other muscles innervated by the cranial nerves, regurgitation through the nose, and difficulty in swallowing. Limb weakness and loss of deep tendon reflexes may follow. The hallmark of paralysis seen in elapid bites is a progressive and descending paralysis. Once paralysis reaches

diaphragm and intercostals muscles patients usually die of respiratory paralysis unless they are adequately ventilated.

Although many clinical signs and symptoms of neurotoxic envenoming by cobra and krait are similar with both genera being able to cause respiratory failure in 30 minutes, Krait bite causes very minimal local reaction and it is also associated with delayed onset and prolonged period of total paralysis. This prolonged period of paralysis is related to its powerful presynaptic toxins like beta-bungarotoxins that destroy nerve terminals.(5)

Renal

Loin pain, proteinuria, haematuria, haemoglobinuria, myoglobinuria, oliguria/anuria, uraemia.

Endocrine

Acute pituitary /adrenal insufficiency from infarction of the anterior pituitary; especially seen with Russell's viper bite.

Acute phase: Shock, hypoglycaemia
Chronic phase (months to years after the bite): Generalized weakness, loss of secondary sexual hair, loss of libido, amenorrhoea, testicular atrophy and hypothyroidism.

Late onset envenomation
Species like hump nosed pit viper and Krait are known for delayed envenomation. It can take 6-12 hours for the symptoms and signs to manifest (6) . Hence it is necessary to keep a patient under observation for at least 24 hours when there are no obvious signs of envenomation in the initial hours .(7)

Death from snakebite can occur as rapidly as within minutes in case of elapid bites and can be delayed for several days in viperine bites. Local swelling at bite site occurs immediately within 2-4 hours while its resolution can sometimes take months especially in the elderly. Deaths occurring from neurotoxic envenoming are caused by airway obstruction or respiratory paralysis. Late deaths, more than 5 days after the bite, are usually the result of acute kidney injury. Risk factors for poor outcome include capillary leak syndrome, respiratory paralysis and intracerebral hemorrhage.(8)Proteinuria, haematuria and acute renal failure are among the common clinical renal manifestations in snakebite.

Proteinuria can occur after a snake bite. In rats, proteinuria has been observed after intrarenal injection of cobra venom.[9] The incidence of proteinuria after a snakebite varies depending on the type of snake involved, as well as geographical differences. Proteinuria was found in 4% of 400 tropical snakebite patients in a study.[10] Proteinuria is usually less than 500 mg/24 h and is a transient finding that disappears when the patient recovers. In Myanmar, however, 50 percent of Russell's viper bite patients had significant proteinuria over 1 g/24 h, suggesting that geographical variation can affect the venom composition of the same species of snake.[11]

Due to haemorrhagic diatheses, patients bitten by haemotoxic snakes, either viperid or crotalid snakes, frequently develop haematuria, which can be microscopic or gross, depending on the severity of envenomation. It's possible that up to 35% of people are affected.[10]Nephritic syndrome has been described in viper bites with pathological changes of diffuse proliferative and crescentic glomerulonephritis, despite the fact that it is not common.[12],[13]. Renal function has deteriorated to some extent.The clinical outcome is usually favourable; however, renal failure can be severe if there is associated tubular necrosis.

In viperid and crotalid snake bites, intravascular haemolysis is common.

As a result, haemoglobinuria is common in these haemotoxic snake bites. The rise in haematocrit precedes haemolysis, which is preceded by erythrocyte swelling[14],[15].

Calcium chelation by citrate reduces erythrocyte swelling and raises the intravascular haemolysis threshold.[16] Myoglobinuria is caused by rhabdomyolysis caused by phospholipase A2 in myotoxic snake envenoming. In snakebite, both haemoglobinuria and myoglobinuria play a role in the development of acute renal failure. Renal failure has been observed in patients a few hours after snakebite without hypotension, haemorrhage, intravascular haemolysis and rhabdomyolysis. The clinical evidence suggests direct nephrotoxicity of the venom.

AIMS AND OBJECTIVES

1. To study the prevalence of proteinuria in snakebite patients
2. To study the correlation of proteinuria in patients with sytemic envenomation

MATERIALS AND METHODS

Source of Data

Patient admitted to Kanyakumari Governmnet Medical College with alleged history of snake bite were included in the study admitted from July 2021 to June 2022

Method Of Collection Of Data

Study Design-This study was a descriptive study done over a period of 12 months on 60 patients admitted to the Kanyakumari Government Medical College with alleged history of snake bite who were willing to take part in the study and gave a written informed consent and who satisfied the inclusion and exclusion criteria. The study was initiated after obtaining an ethical clearance from the institutions ethical committee.

Inclusion Criteria

- Patients admitted in Kanyakumari Government Medical College Hospital with alleged history of snake bite.
- Age more than 18 years.

Exclusion Criteria

1. Patient with Diabeties and hypertension.
2. Patient with history of chronic kidney disease.
3. Patient with the history of nephrotic syndrome.
4. History of drug intake that can cause proteinuria- NSAIDs, lithium carbonate, Pencillamine.
5. Patient with recent history of urinary tract infection.

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 0,6,12,18,24 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, WBCT, APTT, PT/INR

Data And Statistical Analysis

The collected data was analyzed 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

Demographic Data

Table 1: Gender Distribution

Males	Females
36	24

In present study when we evaluated the gender distribution of cases, males were seen more with snake bite.

Table 2: Age Distribution

Age in years	Frequency	Percentage
18-25	10	16.6
26-60	28	46.7
Above 60	22	36.7
Total	60	100

Most of our patients were in the age group of less than 60 years (63.3%). The mean age of the patients was 39±2 years.

Table 3: Systemic Envenomation

Systemic envenomation	Number	Percentage
Present	39	65
Absent	21	35

In our study out of 60 patients 39 patients (65%) had systemic envenomation in the form of hematological involvement including WBCT >20minutes, haematuria, bleeding from the gums, etc.and neurological involvement.

Table 4: Number of vials of ASV given

No of vials of ASV	Frequnecy	Percentage
None	21	35
1-10	11	18.3
11-30	28	46.7

Most patients 65 % of the cases received ASV, in which 18.3% upto 10 vials and 46.7% received 11 to 30 vials of ASV

Table 5: Proteinuria in Systemic Envenomation

Proteinuria	Systemic envenomation		Total
	Present	Absent	
Present	37	3	40
Absent	2	18	20
Total	39	21	60

In our study out of 39 patients who had systemic envenomation, 37 patients showed urine protein being positive and out of 21 patients who had no systemic envenomation, 3 of them had proteinuria.

Table 6: Comparison of use of ASV vials in Snakebite with Proteinuria

No of vials of ASV	Proteinuria	
	Present	Absent
None	1	20
1-10	7	4
11-30	28	0

In our study it was found that proteinuria was seen in 100 percent of patient who received more than 10 vials of ASV and out of 21 patients who did not receive ASV 20 patients urine protein was negative.

Table 7: Proteinuria and Coagulopathy

Proteinuria	Bleeding parameter(PT/INR)	
	Normal (<1.1)	Deranged (>1.1)
Present	8	32
Absent	17	3
Total	25	35

In present study it was found that out of 35 patients in whom INR was abnormal 32 patients showed proteinuria and there was significant correlation between INR and proteinuria. Out of 39 systemic envenomation, 35 had clotting defects and 4 had other systemic envenomations in the form of neurological involvement.

Table 8: Proteinuria and Renal Involvement

Proteinuria	S.Creatinine	
	Normal (<1.3)	Deranged (>1.3)
Present	14	25
Absent	21	0
Total	35	25

In our study it was found that proteinuria was seen in all the cases with deranged s.creatinine level. 25 out of 25 cases (100%) in whom S.creatinine was abnormal, proteinuria was present.

Table 9: Serial Urine Analysis for Proteinuria at 0,6,12,18,24hrs

Proteinuria	0 hr	at 6hrs	at 12hrs	at 18hrs	at 24hrs	Total
Systemic envenomation (Hematological & Neurological involvement)	32	3	2	0	0	37

In present study it was found that out of 39 patients who had features of systemic envenomation, 37 patients had proteinuria, 32 showed at 0 hour, 3 at 6 hours and 2 at 12 hours.

DISCUSSION

In present study it is observed that out of 39 patients who had features of systemic envenomation, 37 had proteinuria and 32 showed proteinuria at 0 hours. Out of 39 patients who had features of systemic envenomation, 35 had clotting defects, 4 had neurological involvement and 32 had proteinuria and coagulopathy. Hence with our study proteinuria can be considered as an early indicator of systemic envenomation.

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 anti venom treatment.

SUMMARY

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

1. Maximum number of patients was in the age group of 18-60years, with mean age 39±2 years.
2. Males were seen more with snake bite.
3. Majority of our patient present with coagulopathy (haemotoxic envenomation).
4. In present study 46.7% of patients received more than 10 vials of ASV.
5. Proteinuria had significant correlation with deranged INR, prolonged WBCT, systemic envenomation, and abnormal creatinine values.
6. Proteinuria were also found in patient who received more than 10 vials of ASV (100%).
7. Proteinuria was seen even before clotting defect was detectable.

CONCLUSION

In the present study it is evident that proteinuria was seen in patient with prolonged WBCT and deranged PT/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 paramount importance to consider proteinuria as an indicator of systemic envenomation in snake bite.

Limitations Of The Study

1. The study was conducted at a medical college hospital which is a tertiary center and the cases may not be representative of the population of the region.
2. The short duration of study and the small number of cases are the limitations of this study.
3. Study for local reactions was not done.

REFERENCES

1. Kasturiratne A, Wickremasinghe AR, de Silva N, Gunawardena NK, Pathmeswaran A, Premaratna R, Savioli L, Lalloo DG, de Silva HJ. The global burden of snakebite: a literature analysis and modelling based on regional estimates of envenoming and deaths. PLoS Med. 2008;5:e218.
2. WHO highlights critical need for life-saving antivenoms. [Internet] Geneva: World Health Organization; 2014. [accessed; 2014. p. Mar 14]. Available from: http://www.who.int/ mediacentre/news/notes /2010/antivenoms_ 20100504/en/
3. Mohapatra B, Warrell DA, Suraweera W, Bhatia P, Dhingra N, Jotkar RM, Rodriguez PS, Mishra K, Whitaker R, Jha P. Snakebite mortality in India: a nationally representative mortality survey. PLoS Negl Trop Dis. 2011;5:e1018.
4. Warrel DA. World Health Organisation; WHO Library Cataloguing-in-Publication data (NLM classification: WD 410);; 2010. Guidelines for the management of snake-bites; pp. 1–150.
5. Alirol E, Sharma SK, Bawaskar HS, Kuch U, Chappuis F. Snake bite in South Asia: a review. PLoSNegl Trop Dis. 2010; 4: 603-10.
6. Acikalin A, Gokel Y, Kuvandik G, Duru M, Koseoglu Z, Satar S. The efficacy of low-dose antivenom therapy on morbidity and mortality in snakebite cases. Am J Emerg Med. 2008; 26: 402-7.
7. National snake bite protocol. New Delhi: Health and Family Welfare Department; 2007. Government of India. http:// 164.100.130.11:8091/ national snake bite manage-ment protocol.pdf
8. Suchithra N, Pappachan JM, Sujathan P. Snakebite envenoming in Kerala, South India: clinical profile and factors involved in adverse outcomes. Emerg Med J 2008; 25: 200-4
9. Rehan A, Wiggins RC, Kunkel RG, Till GO, Johnson KJ. Glomerular injury and proteinuria in rats after intrarenal injection of cobra venom factor. Evidence of the role of neutrophil-derived oxygen free radicals. Am. J. Pathol. 1986; 123: 57– 66. CASPubMedWeb of Science®Google Scholar
10. Sitprija V. Renal deseases in snakebite. In: D Baker, T Wadstrom (eds). Natural Toxins. Oxford, UK: Pergamon Press, 1980; 43– 8.
11. Swe TN, Tan T, Lwin M et al. Renal ischaemia, transient glomerular leak and acute renal tubular damage in patients envenomated by Russell's vipers (Daboia russellii siamensis) in Myanmar. Trans. R. Soc. Trop. Med. Hyg. 1993; 87: 678– 81. CrossrefPubMedWeb of Science®Google Scholar
12. Seedat YK, Reddy J, Edington DA. Acute renal failure due to proliferative nephritis from snake bite poisoning. Nephron 1974; 13: 455– 63.
13. Sitprija V, Boonpucknavig V. Glomerular changes in tropical viper bite in man. Toxicon 1983; 21 (Suppl 3): 401– 3. CrossrefGoogle Scholar
14. Chisari A, Spinedi E, Voirol MJ, Giovambattista A, Gaillard RC. A phospholipase A2-related snake venom (from Crotalus durissus terrificus) stimulates neuroeudocrine and immune functions determination of different sites of action. Endocrinology 1998; 139: 617– 25. CrossrefCASPubMedWeb of Science®Google Scholar
15. Moura-da-silva AM, Laing GD, Paine MJ et al. Processing of pro-tumor necrosis factor-alpha by venom metalloproteinases: A hypothesis explaining local tissue damage following snake bite. Eur. J. Immunol. 1996; 26: 2000– 2005. Wiley Online LibraryCASPubMedWeb of Science®Google Scholar
16. Avila-Aguero ML, Paris MM, Hu S et al., Snakebite Study Group. Systemic cytokine response in children bitten by snakes in Costa Rica. Pediatr. Emerg. Care 2001; 17: 425– 9.