

Proteinuria And Thrombocytopenia As Early Predictors Of Acute Kidney Injury In Snake Bite

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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 and thrombocytopenia in venomous snake bites. Hence, this study intends to study proteinuria and thrombocytopenia and assess whether it can serve as a reliable early indicator of acute kidney injury in snake bite.

Objective of the study:

In this study the value of the proteinuria and thrombocytopenia shall be studied as early predictors of acute kidney injury in snake bite.

Methodology:

A prospective clinical study of 35 patients of snake bite was done to know the clinical profile and outcome at SNMC and HSK HOSPITAL BAGALKOT and particularly looked for development of acute renal failure. A detailed clinical examination was conducted on all the patients. A detailed hematological investigation was done, which includes Hb%, TC, DC, BT, CT, and PT. Urine analysis was done for identifying microalbuminuria. Renal function tests were also done. Patients were followed up till discharge or death. They were treated as per protocol. Clinical data was tabulated. Statistical analysis was done.

Results:

Thrombocytopenia and albuminuria, which is to be considered as the major early marker for acute kidney injury among snakebite patients was found to be present in 92% and 100% in our patients with AKI whereas it was only 22% and 61% respectively among the patients without AKI and the difference was found to be statistically significant ($p < .01$). The survival rate was higher among the patients without AKI when compared to the patients with AKI and the difference is statistically significant ($p < .05$).

Interpretation and conclusion-

Cause of AKI in snakebite was multifactorial in origin. Early detection of AKI due to snakebite should be assessed by testing for the platelet count and the urine albumin at the time of admission and appropriate treatment for it would help to reduce the mortality significantly.

Keywords: Snake Bite, AKI, thrombocytopenia, proteinuria.

INTRODUCTION

Snake bite is an important public health concern in developing countries. Most snakebites occur in developing countries with temperate and tropical climates in which populations subsist on agriculture and fishing. Recent estimates indicate that somewhere between 1.2 million and 5.5 million snakebites occur worldwide each year, with 421,000–1,841,000 envenomation and 20,000–94,000 deaths. Such wide-ranging estimates reflect the challenges of collecting accurate data in the regions most affected by venomous snakes; many victims do not seek medical attention, and reporting and record keeping are generally poor. India it is estimated that 45900 deaths occur annually due to snake bite. Uttar Pradesh(8700) Andhra Pradesh(5200) and Bihar(4500) has highest burden of Snake bite.⁽¹⁾ There are various studies on biochemical changes in snake bite patients. The common biochemical and haematological abnormalities that were found are, an increase in serum creatinine, prothombin time, partial thromboplastin time, and whole blood clotting time and decrease in platelet count and fibrinogen.⁽²⁾ Various studies done have shown conflicting views on the importance of proteinuria in venomous snake bites. Hence, this study intends to study intends to study thrombocytopenia and proteinuria and assess whether it can serve as a reliable early indicator of acute kidney injury in snake bite.

OBJECTIVES OF THE STUDY

1. In this study the value of the proteinuria and thrombocytopenia shall be studied as
2. early predictors of acute kidney injury in snake bite

MATERIALS AND METHODS

A prospective clinical study of 35 patients of snake bite was done to know the clinical profile and outcome in SNMC and HSK HOSPITAL BAGALKOT and particularly looked for development of acute renal failure.

A detailed clinical examination was conducted on all the patients. A detailed hematological investigation was done, which includes Hb%, TC, DC, BT, CT, and PT. Urine analysis was done for identifying microalbuminuria. Renal function tests were also done. Patients were followed up till discharge or death. They were treated as per protocol.

Inclusion criteria:

1. A definitive history of snakebite with signs of envenomation.
2. Patients with haemotoxic features and neurotoxic features will be taken.
3. Age more than 15 years

Exclusion criteria

1. The patients with a pre-existent renal disease.
2. Diagnosed cases of hypertension/diabetes.
3. Exposure to nephrotoxic drugs/toxins.

Clinical data was tabulated. Statistical analysis was done.

Statistical Analysis

Qualitative data represented in the form of frequency and percentage. Association between variables was assessed with Chi Square test.

Qualitative variables were represented as mean & Sd. Comparison between variables was done with Unpaired t test.

A P value of <0.05 was considered statistically significant.

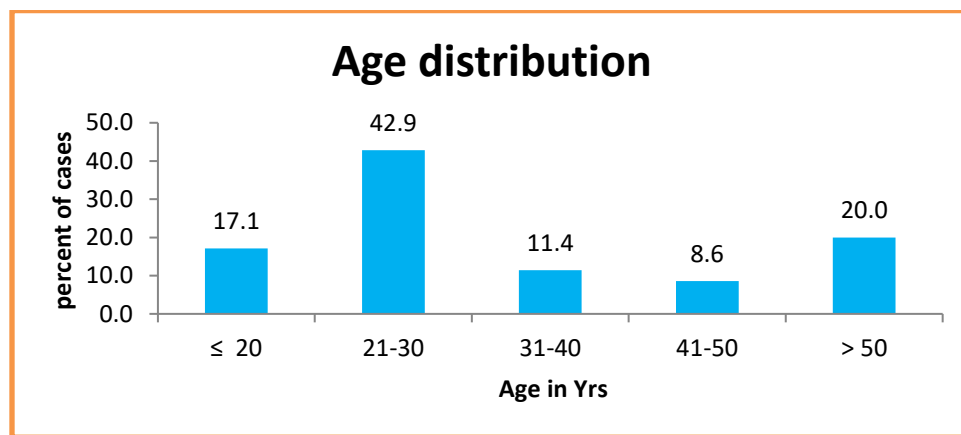
IBM SPSS Version 28 for windows was used to do statistical analysis.

RESULTS

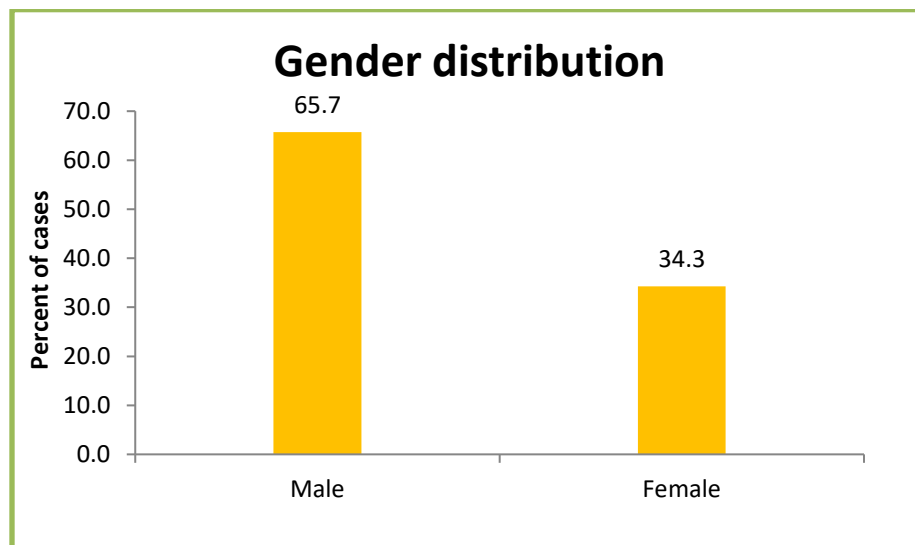
In the present study, 31 cases of snake bite subjects were included. Age and sex wise distribution was done and laboratory & clinical profile were calculated with mean and standard deviation and the results are as follows:

DISTRIBUTION OF AGE IN SNAKE BITE

In our present study, out of 35 patients more cases of snake bite are reported at the age of 21-30 i.e; 15 cases(42%). Less cases reported at the age between 41-50 i.e; 3 cases(8%).



Graph no-1: DISTRIBUTION OF AGE IN SNAKE BITE



Graph no-2: DISTRIBUTION OF GENDER IN SNAKE BITE

In our present study among 35 patients most of the snake bite cases are reported among males with 23 cases(65%). With lesser predominance in females 12 cases(34.3%).

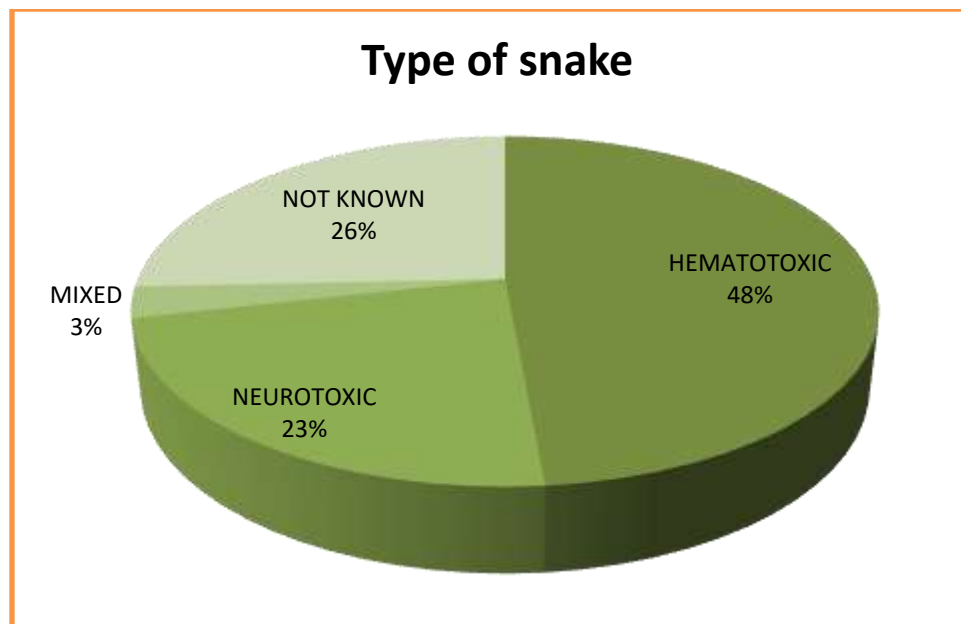
Table no-1: DISTRIBUTION OF DURATION OF HOSPITAL STAY IN SNAKE BITE

DURATION OF STAY (days)	No of cases	Percent
2-4	13	37.1
5-7	18	51.4
8-10	4	11.4
Total	35	100.0

In our study, the maximum duration of stay in the hospital lies between 5-7 days (51.4%).

DISTRIBUTION OF TYPE OF SNAKE IN SNAKE BITE

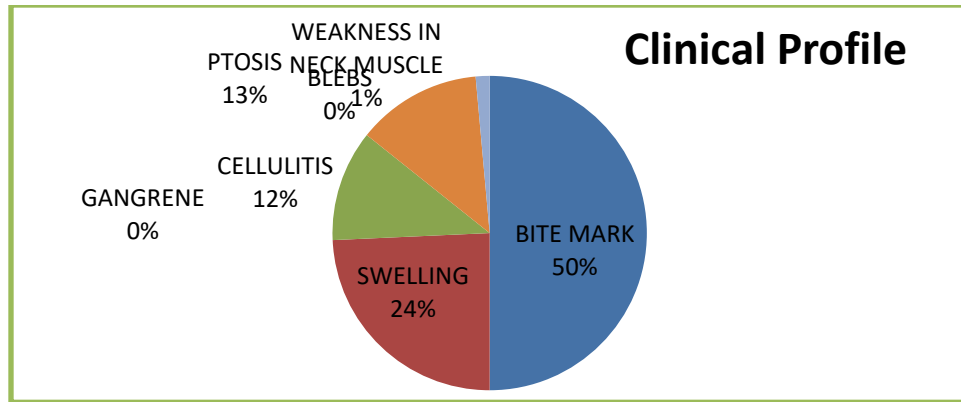
In our study, out of the 35 patients, most cases are hematotoxic snake bite with 17 cases (48.6%). Second most being unknown snake with 9 cases (25.7%). Whereas only one is mixed snake bite (2.9%).



Graph no-3: DISTRIBUTION OF TYPE OF SNAKE IN SNAKE BITE

DISTRIBUTION OF CLINICAL PROFILE IN SNAKE BITE

In our study, all the patients had bite marks. Come with mainly swelling at the bite site with 17 cases (48.6%). Second most being with ptosis, i.e., 9 cases (25.7%). Whereas only one patient comes with weakness of neck muscle (2.9%).



Graph no-4:DISTRIBUTION OF CLINICAL PROFILE IN SNAKE BITE

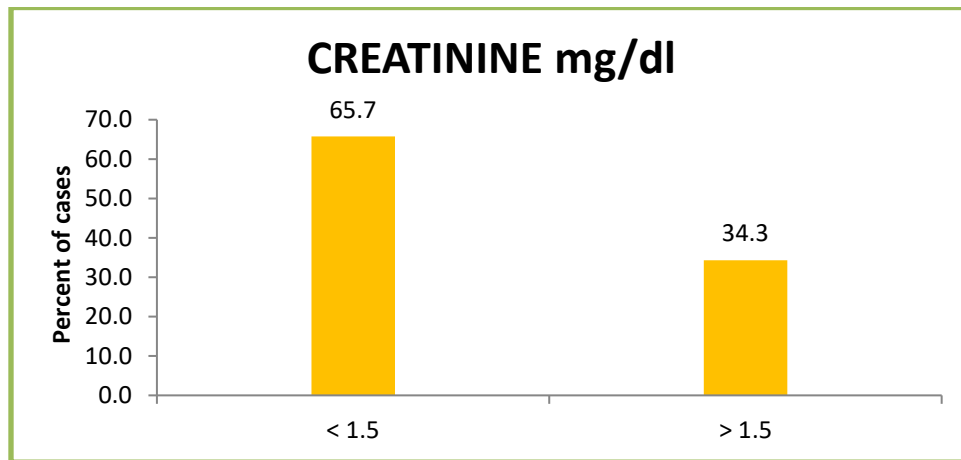
Table no-2 :DISTRIBUTION OF PLATELET IN SNAKE BITE

PLATELETS cells/mm3	No of cases	Percent
< 150000	16	45.7
> 150000	19	54.3
Total	35	100.0

In our study out of 35 patients,most patients have platelets more than 1.5lakh i,e;19 cases (54%). 16 cases(45.7%) have platelet thrombocytopenia(platelet less than 1.5lakh).

DISTRIBUTION OF CREATININE IN SNAKE BITE

In our study out of 35 patients,most of the case creatinine is in normal limit(less than 1.5) i,e;23 cases(65.7%).Where as 12 cases(34.3%) have raised creatinine more than 1.5mg/dl.



Graph no-5:DISTRIBUTION OF CREATININE IN SNAKE BITE

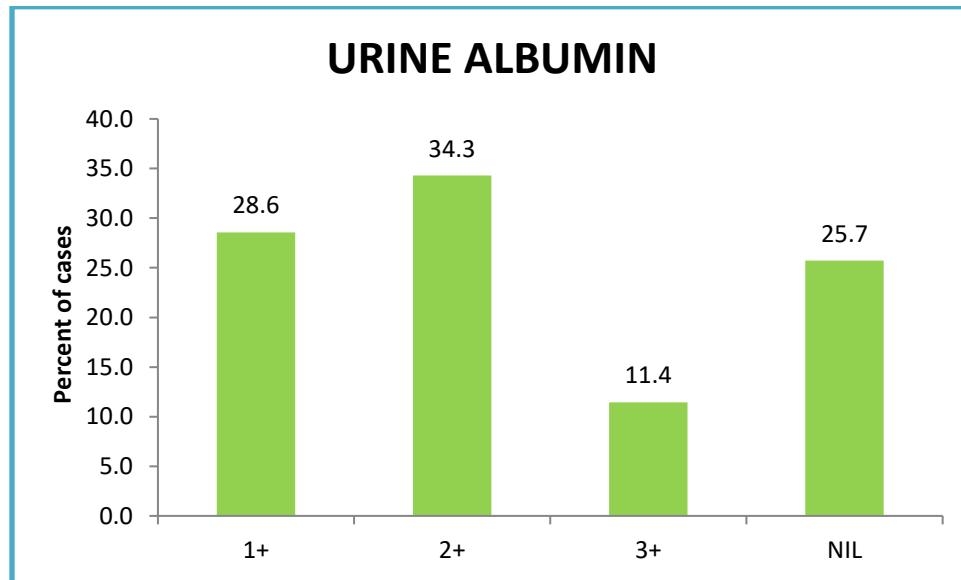
Table no-3: ACUTE KIDNEY INJURY IN SNAKE BITE

OLIGURIA/ANURIA	No of cases	Percent
AKI	11	31.4
No AKI	24	68.6
Total	35	100.0

In our study among 35 patients, 11 cases (31.4%) had gone for acute kidney injury with either oliguria or anuria.

DISTRIBUTION OF URINE ALBUMIN IN SNAKE BITE

In our study among 35 patients, 26 cases (74.3%) had urine albumin positive. Whereas 9 cases (25.7%) are negative for urine albumin.



Graph no-6 : DISTRIBUTION OF URINE ALBUMIN IN SNAKE BITE

Table no-4 : ASSOCIATION OF AGE WITH AKI IN SNAKE BITE

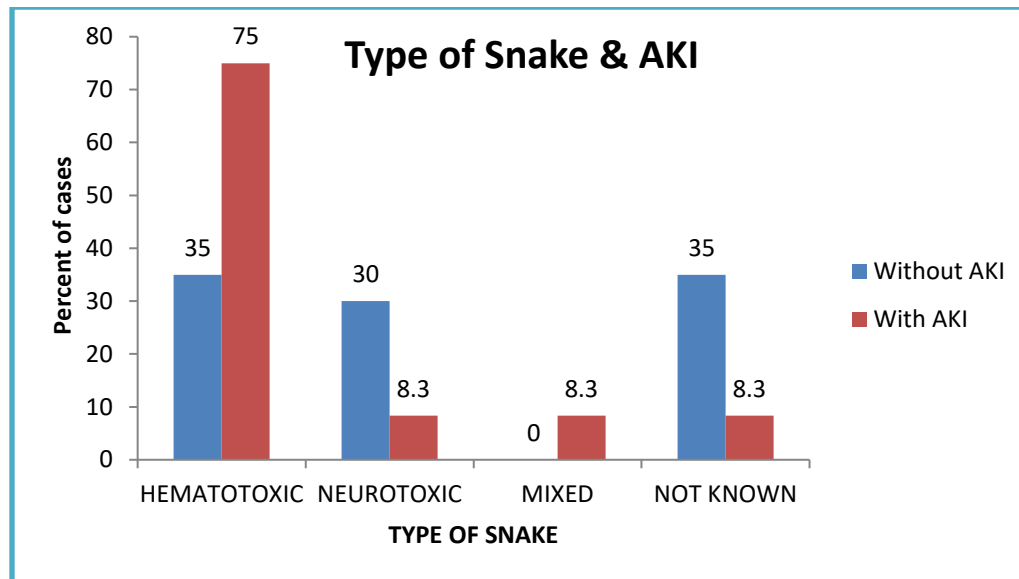
Age	Patients without AKI (n=23)		Patients with AKI (n=12)	
	No	%	No	%
≤ 20	5	22	1	8.3
21-30	11	48	4	33.3
31-40	3	13	1	8.3

41-50	0	0	3	25
> 50	4	17	3	25
Total	23	100	12	100
Chi Square test P<0.119, Not Sig				

In our study among 35 patients, 12 cases progressed to AKI in which age group between 21-30 are more with AKI i.e; 4 cases (33.3%). AKI is less among age group between 31-40 i.e; 1 case (8.3%). P < 0.119 is not significant.

ASSOCIATION OF TYPE OF SNAKE WITH AKI IN SNAKE BITE

In our study, 9 (75%) cases among 12 cases of AKI are hematotoxic snake bite with significant P value < 0.012.



Graph no-7 : ASSOCIATION OF TYPE OF SNAKE WITH AKI IN SNAKE BITE

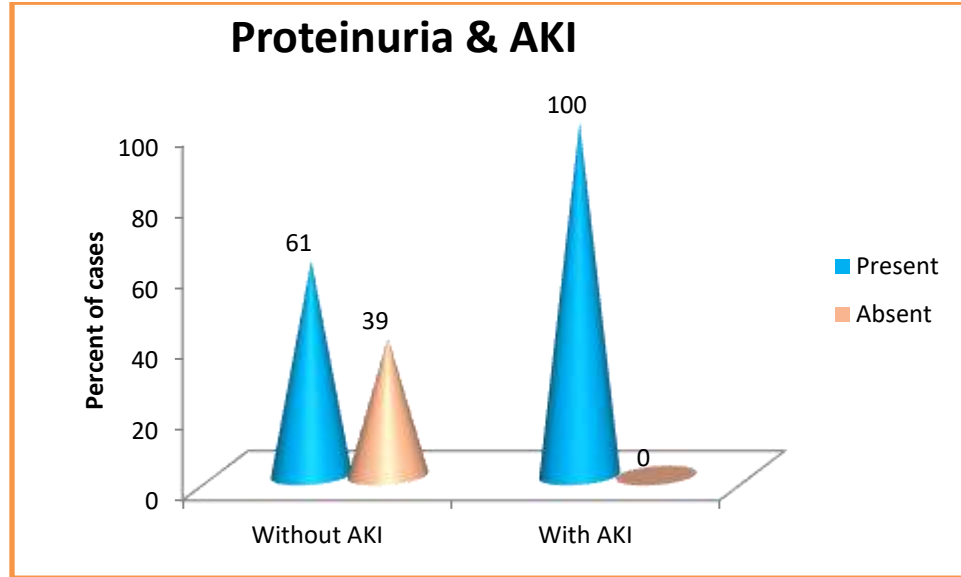
Table no-5 : ASSOCIATION OF THROMBOCYTOPENIA WITH AKI IN SNAKE BITE

Thrombocytopenia	Patients without AKI (n=23)		Patients with AKI (n=12)	
	No	%	No	%
Present	5	22	11	92
Absent	18	78	1	8
Total	23	100	12	100
Chi Square test P<0.001, Highly Sig				

In our study ,11 cases (92%) with thrombocytopenia developed AKI.P<0.001 which is highly significant.

ASSOCIATION OF PROTEINURIA WITH AKI IN SNAKE BITE

In our study 12 cases (100%) who developed AKI had protinuria.P<0.01 significant



Graph no-8:ASSOCIATION OF PROTEINURIA WITH AKI IN SNAKE BITE

Table no-6:ASSOCIATION OF HEMATOLOGICAL PARAMETERS WITH AKI IN SNAKE BITE

Laboratory Parameter	Patients without AKI (n=23)		Patients with AKI (n=12)		Unpaired t Test	
	Mean	Std. Deviation	Mean	Std. Deviation	P value	Significance
Hb%	12.32	1.83	12.83	2.73	0.509	NS
Blood urea (mg/dL)	25.91	6.92	52.23	26.19	0.001	HS
Blood creatinine (mg/dL)	0.93	0.22	2.43	0.58	0.001	HS
Bleeding time (secs.)	2.92	0.38	3.14	0.40	0.118	NS
Clotting time (secs.)	5.70	0.50	5.79	0.52	0.599	NS
Prothrombin time (secs.)	16.37	3.55	26.43	11.67	0.001	HS
PLT	238521.74	82398.63	94000.00	68823.89	0.001	HS
NS=NOT SIG, HS=HIGHLY SIG						

In our study, raised creatinine,urea,prothrombin time and low platelet have higher significance on comparison.

DISCUSSION

Snakebite is a common medical emergency and an occupational hazard, especially in tropical countries like India. Study shown that males are more commonly affected snakebite victims than females, whereas in our study, out of 35 patients, 23 were males and 12 were females and the male:female ratio is 1.9:1, which had shown that male is nearly 2 times predominance than females. Snakebite is more common in the rural setting, primarily because farming is a major occupation in villages and farmers are most vulnerable to exposure to snakes during work.

Clinical features like cellulitis, bleeding tendencies and oliguria was found to be more common among the patients with AKI when compared to the patients without AKI. In the present study, thrombocytopenia found to be independent and early predictor for AKI due to snakebite and similar type of results was also quoted by a study done by Suchitra et al²³ in Kerala and also by certain western studies done by Bucarechi F et al²⁴ and Chen JB et al.²⁵ Platelet count is reduced both due to consumptive coagulopathy and direct toxic effects of snake venom on platelets. Intravascular haemolysis due to phospholipase A₂ is a significant factor in the pathogenesis of snakebite-induced AKI.

The current study had clearly indicated that albuminuria was found to be an early indicator for AKI, as almost all patients with AKI had albuminuria and the similar type of result was also quoted by various studies done by Imitiaz Basha et al,²⁶ Mittal B Y et al,²⁷ Sarangi et al²⁸ and Athappan et al.²⁹ The other renal parameters like urea and creatinine were also elevated among the patients with AKI.

CONCLUSION

From our study, we can conclude that early clinical prediction of AKI development in snakebite patients can be detected by presence of thrombocytopenia and albuminuria and it had also proven that AKI is an important mortality predictor for snakebite victims. So, early detection of AKI by testing for the platelet count and the urine albumin at the time of admission and appropriate treatment for it would help to reduce the mortality significantly.

BIBLIOGRAPHY

1. Simpson ID, Norris RL. Snakes of Medical Importance in India: Is the Concept of the “Big 4” Still Relevant and Useful? *Wilderness Environ Med.*2007;18:2-9.
2. Chippaux JP. Snake bites: Appraisal of the global situation. *Bull WHO.* 1998; 76:515–24.
3. Kasturiratne A, Wickremasinghe AR, de Silva N, Gunawardena NK, Pathmeswaran A, Premaratna R, et al. The global burden of snakebite: a literature analysis and modelling based on regional estimates of envenoming and deaths. *PLoS Med.*2008;5(11):1591-604.
4. Brunda G, Shashidhar R B. Epidemiological Profile of snake Bite Cases from Andhra Pradesh using Immunoanalytical Approach. *Indian J Med.* 2007;125:661-65.
5. Ahmed SM, Nadeem A, Islam MS, Agarwal S, Singh L. Retrospective analysis of snake victims in Northern India admitted in a tertiary level institute. *J Anaesthesiol Clin Pharmacol.* 2012; 28: 45-50.
6. Warrell DA. Snakebite. *Lancet.* 2010; 375: 77-88.
7. Mohapatra B, Warrell DA, Suraweera W, Bhatia P, Dhingra N, Jotkar RM, et al. Million Death Study Collaborators. Snakebite mortality in India: a nationally representative mortality survey. *PLoS Negl Trop Dis* 2011; 5(4): e1018.
8. Warrell DA. Guidelines for the management of snake-bites. 2nd ed. New Delhi. WHO-SEARO;2010. 48
9. Kulkarni ML, Anees S. Snake venom poisoning: experience with 633 cases. *Indian Pediatr.*1994;31(10):1239-43.
10. Warrell DA. Injuries, envenoming, poisoning, and allergic reactions caused by animals. *Oxford Textbook of Medicine.* New York: Oxford University Press. 2010; 5: 1324-60
11. Alirol E, Sharma SK, Bawaskar HS, Kuch U, Chappuis F. Snake bite in South Asia: a review. *PLoS Negl Trop Dis.* 2010; 4: 603-10.
12. 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.

13. National snake bite protocol. New Delhi: Health and Family Welfare Department; 2007. Government of India. <http://164.100.130.11:8091/nationalsnakebitemanagementprotocol.pdf>

14. 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.

15. Than T, Tun T, Pe H, Phillips RE, Lwin M, Swe TN. Development of renal function abnormalities following bites by Russel's vipers (*Daboia russelii*) in Myanmar. Trans R Trop Med Hyg. 1991;85:404-9

16. Swe TN, Tun T, Lwin M, Than T, Pe T, Robertson JJ, et al. Renal ischemia, transient glomerular leak and acute renal tubular damage in patients envenomed by Russell's vipers (*Daboia russelii*) in Myanmar. Trans R Soc Trop Med Hyg. 1993;87:678-81

17. Otero R, Gutierrez J, Mesa MB, Duque E, Rodriguez O, Arango LJ et al. Complication of Bothrops, Porthidium, Bothriechis snakebites in Columbia. A clinical and epidemiological study of 39 cases attended in a university hospital. Toxicon. 2002;40:107-14.

18. Dharod MV, Patil TB, J Deshpande AS, Gulhane RV, Patil MB, Bansod YV. Clinical Predictor of Acute Kidney Injury Following Snake Bite Envenomation. North American Journal of Medical Sciences. 2013;5:594-9.

19. Warrell DA. Venomous bites, stings, and poisoning. Infect Dis Clin North Am. 2012; 26: 207-23.

20. Saul ME, Thomas PA, Dosen PJ, Isbister GK, O'Leary MA, Whyte IM, et al. A pharmacological approach to first aid treatment for snakebite. Nat Med. 2011; 17: 809-11.

21. Cruz LS, Vargas R, Lopes AA. Snakebite envenomation and death in the developing world. Ethn Dis. 2009; 19: 42-6.

22. Swaroop S, Grab B. Snake bite mortality in the world. Bull WHO. 1954;10:35-76.

23. 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(4):200-204.

24. Bucarechi F, Herrera SR, Hyslop S, et al. Snakebites by *Crotalus durissus* ssp in children in Campinas, São Paulo, Brazil. Rev Inst Med Trop São Paulo 2002;44(3):133-138.

25. Chen JB, Leung J, Hsu KT. Acute renal failure after snakebite: a report of four cases. Zhonghua Yi Xue Za Zhi (Taipei) 1997;59(1):65-69.

26. Pasha I, Prabhu SNC, Vardhana HHS et al. Renal parameters as predictors of morbidity and mortality in snakebite patients in a tertiary care hospital in southern India. Global Journal of Medical Research (B) 2014;14(2):21-26.

27. Mittal BV, Kinare SG, Acharya VN. Renal lesions following viper bites --a study of 14 years. Indian J Med Res 1986;83:642-651.

28. Sarangi A, Patnaik BC, Das GC, et al. Renal involvement in viper snakebite. Indian J Med Res 1980;71:918-923.

29. Athappan G, Balaji MV, Navaneethan U, et al. Acute renal failure in snake envenomation: a large prospective study. Saudi J Kidney Dis Transpl 2008;19(3):404-410.