Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/19573
DOI URL: http://dx.doi.org/10.21474/IJAR01/19573

RESEARCH ARTICLE

A STUDY TO DETERMINE IF HEMATURIA IN PATIENTS WITH SNAKE BITE CAN BE USED AS A CRITERIA FOR FORCED ALKALINE DIURESISTO PREVENT AKI

Dr. Chandrashekar S.[1], Dr. Manjunatha B.H[2], Dr. Kallesh Shamanur[3], Dr. Goutham S.V[4], Dr. Vipin Madhukuttan[5] and Dr. Akshay Kuchanur[6]

1. Professor, Department of Emergency Medicine, JJM Medical College, Davangere, Karnataka.
2. Associate Professor, Department of Emergency Medicine, JJM Medical College, Davangere, Karnataka.
3. Associate Professor, Department of Emergency Medicine, JJM Medical College, Davangere, Karnataka.
4. Senior Resident, Department of Emergency Medicine, JJM Medical College, Davangere, Karnataka.
5. Post Graduate, Department of Emergency Medicine, JJM Medical College, Davangere, Karnataka.
6. Post Graduate, Department of Emergency Medicine, JJM Medical College, Davangere, Karnataka.

Manuscript Info

Manuscript History
Received: 30 July 2024
Final Accepted: 31 August 2024
Published: September 2024

Key words:-
Snake Bite, Hematuria, AKI, Anti-Snake Venom, Urine Output, RBCs

Abstract

Hematuria and Acute kidney injury (AKI) are important causes of morbidity and mortality among victims of snake bite. As per Ministry of Health & Family Welfare Government of India, if the patient has oliguria or dipstick positive for blood give a trial of forced alkaline diuresis (FAD) within first 24 hours of the bite to avoid pigment nephropathy leading to acute tubular necrosis (ATN)[19]. In the current study we aim to determine if hematuria can be used as criteria for Forced Alkaline Diuresis in patient who present with hematuria following snake bite who later develop AKI. Results depicted that majority of the study subjects i.e., 88% AKI was not observed. However, urine output in study subjects at 6 hours was not significantly differed with the urine output of study subjects at 12 hours (χ^2 = 0.219) and at 24 hours (χ^2 = 0.066). Microscopic RBCs were present in 40%, 28%, and 24% of study subjects' urine sample at 6 hours,12 hours, and 24 hours respectively. Furthermore, presence of microscopic RBCs in urine samples of study subjects at 6 hours significantly differed with the microscopic RBCs in urine samples of study subjects at 12 hours (χ^2 = 0.000) and at 24 hours (χ^2 = 0.001). In conclusion, patient with snake bite with presence of hematuria do not have AKI as a complication & hence hematuria cannot be used as criteria for Forced Alkaline Diuresis for the treatment of AKI in snake bite.

Copyright, IJAR, 2024,. All rights reserved.

Introduction:-

Snake bite is a significant public health problem causing considerable morbidity and mortality worldwide, particularly in tropics. Snakebite is now recognized as a Neglected Tropical Disease by the World Health Organization (WHO).[1] According to WHO estimates about 5 million people are bitten each year by poisonous snakes which results in 2.5 million envenomation, at least 100000 deaths, and 300000 amputations and other permanent Disabilities.[2] Majority of snakebite induced deaths occur in Asia and Sub-Saharan Africa.[1] The mortality due to venomous snakebite in India is estimated between 35000-50000 per annum, which is the highest in the

Corresponding Author:-Dr.Chandrashekar S.
Address**:-**Professor, Department of Emergency Medicine, JJM Medical College, Davangere, Karnataka.

world.[1,3] The mortality due to venomous snakebite in India continuous to be high due to various social, economic and cultural reasons.[4]
There are 2 important families of venomous snakes in south-East Asia viz.Elapidae and Viperidae. Elapidae have short permanently erect fangs. This family includes the cobras, king cobra, kraits, coral snakes, and the sea snakes. Russel's viper (Daboiarusselli), Cobra (Najanaja), Common Krait (Bungaruscaeruleus) and Saw scaled viper (Echiscarinatus) are medically important snakes of India that occur throughout the country. About 5-29% of the patients will develop acute kidney injury (AKI) following snake bite depending on the species of snake and the severity of envenomation.[5-7]It takes few hours to as late as 4 days to develop AKI after snake bite. AKI generally lasts for 2 to 3 weeks. Main reason for AKI after snake bite is acute tubular necrosis. Acute renal failure is mainly observed following bites by the Viperidae group, sea snakes, and the Colubridae group, but the substantial number of cases result from viper bites.[7]The leading explanation regarding pathogenesis of snakebite induced AKI is elevated oxidative stress and carbonyl stress.[5]

Although bites from all the venomous snakes can cause AKI, a considerable chunk of these patients are victims of viper bites. Other reasons which contribute to AKI are acute interstitial nephritis, cortical necrosis, glomerulonephritis and vasculitis. Haemorrhage is mainly caused by vasoactive mediators, cytokines and direct toxicity of venom. Hypotension, disseminated intravascular coagulation, intravascular haemolysis and rhabdomyolysis enhances renal ischemia which leads to AKI.[8] Forced alkaline diuresis will decrease the passive reabsorption from the proximal renal tubules, thereby increasing the clearance of many nephrotoxic contents such as haemorrhagins, myoglobin's because of rhabdomyolysisfromcellulitis, help in preventing the acute tubular necrosis caused by these agents.
Forced Alkaline Diuresis – If the patient has oliguria or dipstick positive for blood give a trial of forced alkaline diuresis (FAD) within first 24 hours of the bite to avoid pigment nephropathy leading to acute tubular necrosis (ATN). – Delayed FAD has no role. – Sequence of FAD in adults is as follows:
• Inj. Frusemide 40 mg IV stat
• Inj. Normal saline 500 ml + 20 ml of NaHCO3 over 20 minutes
•Inj. Ringer's lactate 500 ml + 20 ml of NaHCO3 over 20 minutes
•Inj. 5% dextrose 500 ml + 10 ml of Potassium Chloride over 90 minutes
•Inj. Mannitol 150 ml over 20 min –

Whole cycle completes in 2 h 30 min and urine output of 3 ml/min is expected.If patient responds to first cycle continue for 3 cycles. FAD converts oliguria into polyuria and avoid ATN and acute kidney injury needing dialysis in more than 75% patients. – If there is no response to furosemide discontinue FAD and proceed with Hemodialysis for the patient[19].

With this scenario the present study was designed to conduct with the main aim to study if hematuria can be used as criteria for forced alkaline diuresis in patient going for AKI following snake bite to prevent AKI.

Methodology:-

A prospective study was started after obtaining clearance from the Institutional Ethical Committee at J. J. M Medical college, Davangere, Karnataka. Study was conducted from March 2023 to March 2024. Study subjects were included based on following inclusion and exclusion criteria.

Inclusion criteria

- Age ≥18 years
- Definitive history of snake bite with normal renal function.

Exclusion criteria

- Age ≤ 18 years
- Pre-existent renal disease or ultrasonographic evidence of bilateral small kidneys or patients with baseline creatinine of >1.5mg or any previous medical records
- Pre-existing AKIs

Treatment

Study subjects were treated with Anti-Snake Venom (ASV)& patients who developed AKI were subjected to FAD

Results:-

Majority of the study subjects i.e., 64% were found to be male followed by female (36%). These findings implied that victims of snake bite were male predominance as compared to female (Table 1).

Table 1:-Demographic characteristics of study subjects.

Demographic profile	Frequency	Percentage
Male	32	64.00
Female	18	36.00
Total	**50**	**100.00**

In majority of the study subjects i.e., 88% AKI was not observed. Whereas, AKI was observed in 12% of the study subjects (Table 2).

Table 2:-Distribution of study subjects based on AKIs.

AKIs	Frequency	Percentage
Present	6	12.00
Absent	44	88.00
Total	**50**	**100.00**

In 20% of study subjects, one and two ASV doses were administered. In 16% and 12% of the study subjects, three and four doses of ASV were administered respectively. Whereas, in majority of the study subjects i.e., 32%, the ASV dose was not administered (Table 3).

Table 3:-Distribution of study subjects based on number of ASV doses administered.

ASV Doses Administered	Frequency	Percentage
0	16	32.00
1	10	20.00
2	10	20.00
3	8	16.00
4	6	12.00
Total	**50**	**100.00**

Microscopic RBCs were present in 40%, 28%, and 24% of study subjects' urine samples at 6 hours, 12 hours, and 24 hours respectively. Whereas, microscopic RBCs were absent in majority of study subjects urine sample i.e., 60%, 72%, and 76% of study subjects urine samples at 6 hours, 12 hours, and 24 hours respectively (Table 4).

Table 4:-Distribution of study subjects based on presence of microscopic RBCs in urine.

RBCs	6 hours		12 hours		24 hours	
	N	%	N	%	N	%
Present	20	40.00	14	28.00	12	24.00
Absent	30	60.00	36	72.00	38	76.00
Total	**50**	**100**	**50**	**100**	**50**	**100.00**

At 6 hours' time interval the urine output in majority of the study subjects i.e., 60% was found to be between 0-250mL followed by 251-500mL and 501-750mL in 28% and 12% study subjects respectively. At 12 hours, in 16% of study subjects the urine output was between 0-250mL and 251-500mL each .Whereas, in majority of study subjects i.e., 48% the urine output was found to be between 751-1000mL followed by 501-750mL in 20% of study subjects. Similarly at 24 hours, in majority of study subjects i.e., 56% the urine output was found to be between 1001-2000mL followed by 751-1000mL, 0-250mL, and 501-750mL in 28%, 12%, and 4% of study subjects respectively (Table 5).

Table 5:-Distribution of study subjects based on urine output.

Urine Output	6 hours		12 hours		24 hours	
	N	%	N	%	N	%
0-250mL	30	60.00	8	16.00	6	12.00
251-500mL	14	28.00	8	16.00	-	-
501-750mL	6	12.00	10	20.00	2	4.00

751-1000mL	-	-	24	48.00	14	28.00
1001-2000mL	-	-	-	-	28	56.00
Total	**50**	**100**	**50**	**100**	**50**	**100.00**

The crosstab results of microscopic RBCs in urine samples of study subjects was represented in Table 6. Results depicted that presence and absence of microscopic RBCs in urine samples of study subjects at 6 hours significantly differed with the microscopic RBCs in urine samples of study subjects at 12 hours (χ^2 = 0.000) and at 24 hours (χ^2 = 0.001).

Table 6:-The crosstab results of microscopic RBCs in urine samples of study subjects.

RBCs		**RBCs at 12 hours**		**RBCs at 24 hours**	
		Present	**Absent**	**Present**	**Absent**
RBCs At 6 hr	Present	14	6	12	8
	Absent	0	30	0	30
	Total	**14**	**36**	**12**	**38**
Chi-square (χ^2)		**0.000**		**0.001**	

The crosstab results of urine output of study subjects were represented in Table 7. Results delineated that urine output of study subjects at 6 hours was not significantly differed with the urine output of study subjects at 12 hours (χ^2 = 0.219) and at 24 hours (χ^2 = 0.066).

Table 7:-The crosstab results of urine output of study subjects.

Urine Output		**Urine Output at 12 hours**				**Urine Output at 12 hours**			
		0-250mL	**251-500mL**	**501-750mL**	**751-1000mL**	**0-250mL**	**501-750mL**	**751-1000mL**	**1001-2000mL**
Urine Output at 6 hr	0-250Ml	8	6	8	8	6	2	6	16
	251-500mL	0	2	2	10	0	0	2	12
	501-750mL	0	0	0	6	0	0	6	0
	Total	**8**	**8**	**10**	**24**	**6**	**2**	**14**	**28**
Chi-square (χ^2)		**0.219**				**0.066**			

In our study, 6 patients who developed AKI, were subjected to FAD, following which there was no improvement in renal functions.

Table 8:- Distribution of study subjects based improvement of AKIs after FAD.

ACUTE KIDNEY INJURY	FREQUENCY	PERCENTAGE
IMPROVED	0	0
NO IMPROVEMENT	6	100
TOTAL	6	100

Discussion:-

Snake bite is an important cause of AKI worldwide and in tropical countries especially like India. It is mainly an occupational hazard. Snake bite AKI and related fatalities mainly seen in monsoon season in India and worldwide.[3] About 5% to 29% of the patients develop AKI following snake bite.[5-7] While some other researchers reported that about 8%-45% adults, and 46% of children develop AKI following snake bite.[5-7,9] A number of factors contribute to the development of AKI, like bleeding, hypotension, circulatory collapse, intravascular haemolysis, disseminated intravascular coagulation, microangiopathichaemolyticanaemia and the direct nephrotoxicity of venom.[10] Hence in the current study we aimed to study on snake bite induced hematuria and AKI. Our study findings revealed that the victims of snake bite were male predominance (64%) as compared to female (36%). These findings were in accordance with the findings reported by Waikhom et al. The increased incidence in males is due to increased exposure.[11]

The kidney, a highly vascularized organ with excretory function, is prone to venom toxicity as an innocent bystander. AKI, the most significant of all the renal manifestations, has been reported with varying frequency in different studies[8] .In our study in majority of the study subjects i.e., 88% AKI was not observed. Similarly,

incidences of 18.1% AKI were noted from another study from India reported by Vikrant et al.[12] However, incidences of AKI in adults were ranged from 8%-45%.[5,7,13-17] However, results of urine output in our study subjects at 6 hours was not significantly differed with the urine output of study subjects at 12 hours (χ^2 = 0.219) and at 24 hours (χ^2 = 0.066). In 20% of our study subjects, one and two ASV doses were administered. In 16% and 12% of the study subjects, three and four doses of ASV were administered respectively. The completion of ASV before the onset of renal failure was associated with greater chance of recovery. As per Harshavardhan et al., delay in the administration of ASV was associated with 4 times increased risk of developing AKI.[18]

In India, most of the snake bites are causes by Russell's viper or Echiscarinatus bites. 5 Snake venom consists of many proteins such as enzymes, polypeptide toxins and non-toxic proteins. Among them, Phospholipase A2 is the important one which damages the mitochondria, red blood corpuscles, white blood corpuscles and platelets. It will hamper the functioning of nerve endings, skeletal muscle, vascular endothelium, and other membranes. It produces presynaptic neurotoxic activity, opiate-like sedative effects which leads to the auto pharmacological release of histamine and anticoagulation. Viper bites are responsible for the most of the systemic symptoms such as coagulopathy; haemolysis; AKI; a generalized increase in capillary permeability; rhabdomyolysis; and neurotoxicity. Haemoglobinuria and myoglobinuria caused by intravascular haemolysis from rhabdomyolysis contribute to the development of AKI after snake bite. Bleeding, hypotension, DIC, intravascular haemolysis, and rhabdomyolysisenhances renal ischemia which leads to acute kidney injury. Enzymatic activities of snake venoms account for direct nephrotoxicity. Immunologic mechanism plays a minor role.[8]

In our study, microscopic RBCs were present in 40%, 28%, and 24% of study subject's urine sample at 6 hours, 12 hours, and 24 hours respectively. Furthermore, presence of microscopic RBCs in urine samples of study subjects at 6 hours was significantly differed with the microscopic RBCs in urine samples of study subjects at 12 hours and at 24 hours. Other studies have quoted thrombocytopenia in 9.7% to 60%.[5,13]The presence of sub conjunctivalhaemorrhage, spontaneous bleeding had poor outcomes among patients. Bleeding tendencies secondary to disseminated intravascular coagulation was a major factor in the development of AKI were common with Viper bites.[16]

Additionally in our study, in 6 patients who developed AKI, were subjected to FAD. Our data showed that no patient showed any improvement in renal functions after FAD, & these 6 patients were subjected to Hemodialysis.

Conclusion:-

In conclusion, a patient with snake bite presenting with hematuria doesn't always suggest AKI, hence hematuria cannot be used as a criteria for Forced Alkaline Diuresis in patient snake bite induced AKI. Also Patients with AKI subjected to FAD didn't show any improvement trends in renal functions.

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 medicine. 2008;5(11):e218.
2. WHO highlights critical need for life-saving antivenoms. [Internet]. Geneva: World Health Organization; 2014. [accessed 2024 April 22]. Available from: URL: 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, Million Death Study Collaborators. Snakebite mortality in India: a nationally representative mortality survey. PLoS neglected tropical diseases. 2011;5(4):e1018.
4. Menon JC, Joseph JK, Kulkarni K. Treatment of snakebites - A Resume. Cobra 2007; 1: 1-21.
5. Chugh KS. Snake-bite-induced acute renal failure in India. Kidney Int. 1989;35(3):891–907.
6. Myint-Lwin DA, Phillips R. Bites by Russell's viper (Viperarussellisiamensis) in Burma: haemostatic, vascular, and renal disturbances and response to treatment. Lancet. 1985;326(8467):1259–64.
7. Pinho FM, Zanetta DM, Burdmann EA. Acute renal failure after Crotalusdurissus snakebite: A prospective survey on 100 patients. Kidney Int. 2005;67(2):659–67.
8. Kanjanabuch T, Sitprija V. Snakebite Nephrotoxicity in Asia. InSeminars in nephrology. 2008;28(4):363–72.
9. Krishnamurthy S, Gunasekaran K, Mahadevan S, Bobby Z, Kumar AP. Russell's viper envenomation-associated acute kidney injury in children in Southern India. Indian pediatrics. 2015;52:583-6.

10. Kohli HS, Sakhuja V. Snake bites and acute renal failure. Saudi Journal of Kidney Diseases and Transplantation. 2003;14(2):165-76.
11. Waikhom R, Sircar D, Patil K, Bennikal M, Gupta SD, Pandey R. Long-term renal outcome of snake bite and acute kidney injury: a single-center experience. Renal failure. 2012;34(3):271-4.
12. Vikrant S, Jaryal A, Parashar A. Clinicopathological spectrum of snake bite-induced acute kidney injury from India. World journal of nephrology. 2017;6(3):150.
13. Athappan G, Balaji MV, Navaneethan U, Thirumalikolundusubramanian P. Acute renal failure in snake envenomation: a large prospective study. Saudi Journal of Kidney Diseases and Transplantation. 2008;19(3):404-10.
14. Danis R, Ozmen S, Celen MK, Akin D, Ayaz C, Yazanel O. Snakebite-induced acute kidney injury: data from Southeast Anatolia. Renal failure. 2008;30(1):51-5.
15. David S, Matathia S, Christopher S. Mortality predictors of snake bite envenomation in southern India—a ten-year retrospective audit of 533 patients. Journal of medical toxicology. 2012; 8:118-23.
16. Dharod MV, Patil TB, Deshpande AS, Gulhane RV, Patil MB, Bansod YV. Clinical predictors of acute kidney injury following snake bite envenomation. North American journal of medical sciences. 2013;5(10):594.
17. Albuquerque PL, Silva Junior GB, Jacinto CN, Lima JB, Lima CB, Amaral YS, Veras MD, Mota RM, Daher EF. Acute kidney injury after snakebite accident treated in a Brazilian tertiary care centre. Nephrology. 2014;19(12):764-70.
18. Harshavardhan L, Lokesh AJ, Tejeshwari HL, Halesha BR, Metri SS. A study on the acute kidney injury in snake bite victims in a tertiary care centre. Journal of Clinical and Diagnostic Research. 2013;7(5):853.
19. STANDARD TREATMENT GUIDELINES-Management of Snake Bite Full Background Document (Draft) January 2016, page 56, available URL:https://nhm.gov.in/images/pdf/guidelines/nrhm-guidelines/stg/Snakebite_Full.pdf