

RESEARCH ARTICLE

A STUDY OF CLINICAL PROFILE AND PREDICTORS OF POOR OUTCOME IN SNAKE BITE INDUCED ACUTE KIDNEY INJURY

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Manuscript Info

Abstract

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Acute kidney injury (AKI) is an important cause of morbidity and mortality among victims of snake bite. This study was aimed to assess clinical profile and to identify predictors of poor outcome in snake biteinduced AKI patients. This is a prospective study, conducted among patients who got admitted with snake bite to BAPUJI HOSPITAL. JJM Medical college, Karnataka, from 1/7/021 to 1/9/2022. Detailed history was taken and clinical examination were done for each case. Relevant investigations includingWhole blood clotting time, complete bloodcount, renal function tests, liver function tests, coagulation profile, serum electrolyte analysis, X-ray of the chest, ultrasonography of the abdomen and urine analysis were done. All patients with local toxicity, hematotoxicity and neurotoxicity were treated with Antisnake venom, intravenous antibiotics and other supportive treatment. Demography, clinical profile, course in the hospital, management aspects and outcome were studied indetail. Patients were followed up till they were discharged to determine the recovery of renal function.Results revealed prevalence of AKIamong the victims of snake bite was 19.44%. The mean age of the snake bite induced AKI patients group was 46.5 ± 11.5 and among them 71.42% were male.Common clinical manifestation in AKI group noted were cellulitis in 92.85% of the patients followed by septicaemia(85.71%), regional lymphadenopathy (71%) and gangrene at bite site (64%). Where as in non-AKI group, the cellulitis was noted in 82% followed by regional lymphadenopathy (28%), gangrene at bite site (22%) and septicaemia(13%). In conclusion AKI was found in 19.44% among the victims of snake bite. The common manifestations observed are cellulitis, septicaemia and gangrene at bite site. Delay in administration of ASV, development of coagulopathy, septicaemia, and hypotension were the predictors of poor outcome in snake bite induced acute renal failure. The patients who had visited traditional healers had a higher incidence of developing AKI ,which was supposedly due to delay in receiving ASV. One-third of patients with AKI developed long-term complications like CKD on follow-up. Early recovery from AKI was associated with better preservation of glomerular filtration rate in the long-term.

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Introduction:-

Snake bite is an important cause of morbidity and mortality in tropical countries like India. According to the estimation of WHO, about 5 million people are bitten each year by poisonous snakes which results in 2.5 millionenvenomation, 100000 deaths and 300000 amputations.¹Asia and Sub-Saharan Africa contributes to the majority ofsnake bite induced death.²In India, mortality is estimated between 35000-50000 per annum, and it is highest in the world.^{2,3}500 species are considered to be venomous out of 2500 - 3000 species of snakes.⁴

There are 2 importantgroups (families) of venomous snakes in south-east Asia – Elapidae and Viperidae. Elapidae have short permanently erect fangs. This family includes the cobras, king cobra, kraits, coral snakes, and the sea snakes. Russell's viper (Daboiarusselli), Cobra (Naja naja), Common Krait (Bungarus caeruleus) and Saw scaled viper (Echis carinatus) are medically important snakes of India that are seen throughout the country.Inspite of the wide availability of antisnake venom a number of snakebite victims succumb to complications. This is probably because most snakebite patients resort to traditional remedies or reach medical facilities when it is too late. A number of factors like septicaemia, hypotension, Disseminated intravascular coagulation, direct nephrotoxicity from venom, acute tubular necrosis, acute interstitial nephritis, cortical necrosis are the main causes of AKI in snake bite victims. The AKI which occurs after snakebite is usually reversible, but if acute cortical necrosis occurs, it may lead to an incomplete recovery .Many patients become dialysis dependent. But early hospital care and administration of ASV leads to better clinical outcome.

Considering the prevalence of snakebite and its complications this study was designed with themain purpose to analyse the clinical profile and predictors of poor outcome of AKI in snake bite patients.

Material and Methods:-

In this prospective study, Patients with a definitive history of snake bite attending to the department of Emergency Medicine at J. J. M Medical college, Davangere, Karnataka were enrolled. Meticulous clinical examination was carried out in all cases and patients were segregated into AKI and NON AKIgroup based on the clinical examination and biochemical parameters.

The presence of AKI which is defined as an abrupt (within 48hrs), absolute increase in serum creatinine $\geq 0.3 \text{ mg/dL}$ from baseline value or a percentage increase in serum creatinine concentration of $\geq 50\%$ above the baseline, or oliguria (urine output of less than 400mL/day) or urine output less than 0.5mL/Kg per hour for more than 6 hours, or serum creatinine more than 1.5mg/dL were included for the study.

The patients with a pre-existent renal disease (serum creatinine of >1.5 mg/dL prior to the snake bite or ultrasonography of the abdomen which was suggestive of bilateral shrunken kidneys / loss of the corticomedullary differentiation /obstructive nephropathy/ other renal pathologies), and exposure to nephrotoxic drugs/ toxins were excluded from the study.

Patients were evaluated further using appropriate laboratory investigations individually such as whole blood clotting time, complete blood count, renal function tests, liver function tests, coagulation profile, serum electrolyte analysis, X-ray of the chest, ultrasonography of the abdomen and urinalysis. After admission to ICU, immediately 20 minutes whole blood clotting time test (WBCT)was done for all patients. Those patients with hematotoxicity, and / or neurotoxicity and / or significant local toxicity, Antisnake venom (ASV) was given. 10 vials of polyvalent ASV in 500mL 5% dextrose was given over 1 hour. 20 minutes whole blood clotting time test was repeated after 6 hours. Transfusions of blood products like fresh frozen plasma (FFP) was given to indicated patients. 20 patients required hemodialysis. Patients were followed up till they were discharged.

Results:-

During the study period, a total of 144 patients were admitted for snake bite, of which 116 patients showed signs of envenomation,28 patients were diagnosed to have AKI due to snake bite with an incidence of 19.44% of total snakebite patients. Of the 28 AKI patients included in study, male predominance(71.42%) was observed as compared to females (28.57%). Similarly, of 116 non-AKI patients male predominance was observed (60.34%) as

compared to females (39.65%). The mean age of AKI and non-AKI patients was found to be 46.5 ± 11.5 and 36.0 ± 10.25 respectively (Table 1).

Demographic profile	AKI (28)	Non-AKI cases(116)
Age	46.5 ±11.5	36.0 ± 10.25
Male	20 (71.42%)	70 (60.34%)
Female	8 (28.57%)	46 (39.65%)

Table 1:- Demographic characteristics of study subjects.

The distribution of patients based on the blood parameters is represented in Table 2. Results revealed that leucocytosis was observed in 88% of the patients followed by thrombocytopenia (46%) and hematuria was observed in 14% of the patients.

Table 2:- Distribution of	patients based on Laboratory	Data.
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Blood parameters	Percent
Leucocytosis	88%
Thrombocytopenia	46%
Hematuria	14%

Cellulitis, septicaemia, regional lymphadenopathy and gangrene at bite site, bleeding manifestations were seen in both the groups. In patients of snake bite with AKI Group, cellulitis was noted in 92.85% of the patients followed by septicaemia(85.71%), regional lymphadenopathy (71%) and gangrene at bite site was noted in 64% of patients. Whereasin Non-AKI group, cellulitis was noted in 82% of the patients followed by regional lymphadenopathy (28%), gangrene at bite site (22%) and septicaemia observed in 13% of the patients. Bleeding manifestation was observed in 32.14% and 11% in AKI and non-AKI patients respectively. Hypotension was noted in 21.42% in AKI patients and 2% in non-AKI patients. In this study, Disseminated intravascular coagulation (DIC) (7.14%) and acute respiratory distress syndrome (ARDS) (10.71%) were reported in AKI patients. Bite to needle time -within 6-24 hrs was observed in 22%, between 24 to 72 hrs in 23%, for more than 72 hrs was observed in 55% of the AKI patients. In non-AKI patients, bite to needle time within 24 hrs was observed in 84% of the patients. The study showed, The bite to needle time was significantly more in the patients who developed AKI as compared to that in those who did not develop it.10 vials of ASV were administered in 12 % of the patients, 20 vials in 34% and 30 vials in 54% of AKI patients. In non-AKI patients, 10 vials of ASV were administered in 53%, 20 vials in 32% and 30 vials in 15% of the patients. This shows that the patients who developed AKI had a more severe degree of envenomation and hence they required more number of ASV vials for the treatment, in comparison to those who did not develop AKI. The duration of hospital stay, more than 1 week was noted in 86% of AKI patients and less than 1 week in non-AKI patients. This shows, the patients who developed AKI required more days in the hospital than non-AKI group, which suggested the morbidity which was associated with it.

The incidences of cellulitis, bleeding manifestation, gangrene at bite site (p<0.01), regional lymphadenopathy, hypotension, septicaemia(p<0.001) were significantly more in the AKI group, which was statistically significant as compared to those in the non-AKI group(Table 3).

Characteristics	AKI (n=28)	Non-AKI (n=116)	
Cellulitis	26(92.85%)	95(82%)	p<0.05
Gangrene at bitesite	18(64%)	25(22%)	p<0.01
Regional lymphadenopathy	21(71%)	32(28%)	p<0.001
Bleeding manifestation	9(32.14%)	13(11%)	p<0.05
Hypotension	6(21.42%)	2(2%)	p<0.001
Septicaemia	24(85.71%)	15(13%)	p<0.001
DIC	2(7.14%)	0	
ARDS	3(10.71%)	0	
Bite to needle time	(6-24hrs) 22%	(Within 24hrs)84%	
	24-72hrs : 23%	(24-72hrs):16%	
	(More than 72hrs)	More than 72hrs: nil	

Table 3:- Distribution of patients based on clinical profile.

	55%		
Amount of polyvalent ASV given (in	30 vials 54%	30 vials 15%	NS
vials)	20 vials 34%	20vials 32%	
	10 vials 12%	10 vials 53%	
Duration of hospital stay	More than 1 week	Less than 1 week 100%	NS
	86%		

NS = Non significant

The results showing comparison of outcome of patients in AKI group is represented in Table 4. Results revealed that with regards to AKI patients, the mean age of the patients who survived was found to be 36.5 ± 9.5 and there were 70.83% male patients. The incidence of cellulitis was found to be 91.66% followed by septicaemia (71.42%)regional lymphadenopathy (70.83%), bleeding manifestation (29.2%), hypotension (8.33%) and ARDS (4.1%). The bite to needle time was found to be 16.8 ± 14.3 .

While with regards to AKI patients the mean age of the patients who died was found to be 44.5 ± 10.5 and there were 75 % male patients. The incidence of cellulitis among the patients who died was found to be 100%, hypotension (100%), septicaemia (100%), regional lymphadenopathy (75%), bleeding manifestation (50%), DIC (50%), and ARDS (50%). Bite to needle time was noted as 24 ± 16.1 . The comparison between the AKI patients who survived and those who died showed a significant difference with regard to septicaemia, hypotension,DIC, ARDSand bite to needle time (p<0.05)

Characteristics	Survived (n=24)	Died (n=4)	
Age (yrs)	36.5 ±9.5	44.5 ±10.5	NS
Male (%)	70.83%(17)	75%(3)	p<0.01
Female (%)	29.17%(7)	25%(1)	
Cellulitis	22 (91.66%)	4 (100%)	p<0.01
Regional lymphadenopathy	17 (70.83%)	3(75%)	p<0.001
Bleeding manifestation	07 (29.2%)	02 (50%)	NS
Hypotension	02 (8.33%)	4(100%)	p<0.05
Septicaemia	20 (71.42%)	04(100%)	p<0.05
DIC	0	2 (50%)	NS
ARDS	1(4.1%)	2 (50%)	NS
Bite to needle time	16.8±14.3	24±16.1	p<0.05

Table 4:- Showing comparison of outcome of patients in AKI group.

NS = Non significant

Discussion:-

Snake bite is an important cause of AKI world wide especially in tropical countries like India. It is mainly an occupational hazard. Snake bite causing AKI and related fatalities are mainly seen in monsoon season in India and worldwide.^{3,9,10} About 5% to 29% of the patients develop AKI following snake bite.⁵⁻⁷While some researchers reported that about 8%-45% adults, and 46% of children develop AKI following snake bite.^{5-7,11}A number of factors contribute to the development of AKI, like bleeding, hypotension, intravascular haemolysis, disseminated intravascular coagulation, microangiopathic haemolytic anaemia and the direct nephrotoxicity of venom.¹²An incidence of 18.1% was noted in a study from India.¹³In our study, incidence of AKI was 19.44 % of total snakebite patients.

In this study Males were affected more often than the females since they may constitute the working majority who are actively engaged in farming and other outdoor activities. This study also showed predominantly the younger population were involved (20-40 years of age), probably due to their more ambulant nature.¹⁴⁻¹⁸In accordance with our study findings Bhat et al., had also reported that 80% of the cases occurred in age group of 20-40 years. In our study we have noted SNAKE BITE INDUCED AKI in 13.88% of the males and 5.55% in females. Our findings are in accordance with the findings of Mukhopadhyay et al., Sharma et al., and Patil et al.¹⁹⁻²¹

In our study leucocytosis was observed in 88% of the patients, thrombocytopenia in 46% and hematuria was observed in 14% of the patients. Other studies have quoted thrombocytopenia in 9.7% to 60%.^{5,23}. The earliest symptoms seen in the patients of viper bite are pain and swelling at the bitten part. cellulitis, gangrene at the bite area and regional lymphadenopathy can be bedside indicators of the amount of toxin which is released by the snake bite. Previous studies have noted cellulitis in 39% - 98.7%.²³⁻²⁵ We have observed cellulitis in 92.85% of AKI group which is similar to other studies. DIC plays an important role in development of snake bite-induced cortical necrosis. It is characterized by the presence of microangiopathic hemolytic anaemia, thrombocytopenia and fibrin thrombi in renal microvasculature.^{5,24} In our study, DIC was observed in 7.14% of AKI GROUP patients as compared to 11.1%-43% of patients in other studies.^{5,23}

In our study, 32.14% of the patients among AKI group, developed bleeding manifestations, which was less than the number in the study which was conducted by Chugh (60-65%).⁵We have observed mortality in 4(14.28%)snakebite patients with AKI . Studies in literature reported mortality among snake bite induced AKI patients as 4(9.52%),7 (14.6%),16(15.3%) and none in another study.²⁶ Important reasons which contribute to increased mortality were delay in transport, lack of availability of ASV in peripheral hospitals and inappropriate first-aid measures ^{3,22,27}

Conclusion:-

This study concludes that Acute Kidney Injury occurred in 19.44% victims of snake bite. The Common manifestations of snake bite includes cellulitis, regional lymphadenopathy, bleeding manifestations, gangrene at the bite site. The predictors of poor outcome in snake bite induced acute kidney injury were delay in administration of Anti snake venom, development of coagulopathy, septicaemia and hypotension.

Dialysis and supportive treatment appear to be the mainstay of the therapy in cases which are complicated with Acute kidney injury. One-third of patients with AKI developed long-term complications like CKD and hypertension on follow-up. Early recovery from AKI is associated with better preservation of glomerular filtration rate in the long-term.

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