

A Study on the Acute Kidney Injury in Snake Bite Victims in A Tertiary Care Centre

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ABSTRACT

Introduction: Snake bite is a common medical emergency and an occupational hazard, more so in tropical India, where farming is a major source of employment. Viper bites are more common than other poisonous snakebites in humans. The World Health Organization has estimated that there are approximately 1,25,000 deaths among 2,50,000 poisonous snake bites worldwide every year, of which India accounts for 10,000 deaths. Acute kidney Injury (AKI) is an important consequence of a snake bite and its proper supportive management after the anti-venom administration is of utmost importance, for a good patient outcome.

Aims and Objectives: 1. To assess the risk factors and the prognostic factors in snake-bite induced Acute Kidney Injury. 2. To determine the outcome of snake bite patients with AKI in a tertiary care centre in Karnataka, India.

Methodology: This prospective study was carried out at Vijaynagar Institute of Medical Sciences, Bellary, Karnataka, India. This institute is a referral government hospital in north Karnataka, India.

Study Design: This was a prospective and descriptive type of study.

Results: A total of 246 cases of venomous snakebite were included in this study, who were admitted in the hospital from

November 2007 to October 2008. Among the AKI and the non-AKI patients, Illiteracy was more among the patients who suffered from AKI (75%). In our study, among all the patients (both AKI and non-AKI patients), viper bite was the commonest and it was seen in 31(91.6%) cases among the AKI patients and in 142 (67.6%) cases among the non-AKI patients. In our study, a majority of the patients who developed AKI had initially visited traditional healers before visiting our hospital, which was found to be statistically significant. In the present study, disseminated intravascular coagulation (DIC) and intravascular haemolysis were found to be predominant among the AKI patients. The "Bite to Needle" time was significantly more in the patients who developed AKI as compared to that in those who developed non-AKI. Out of 36 patients who suffered from AKI, 28 (77.7%) patients survived. Among them, 27(96.7%) patients developed cellulitis, 25(89.5%) had regional lymphadenopathy, 22(81.2%) were bitten at their lower limbs, and 6 (23.8%) patients developed bleeding manifestations.

Conclusion: This study concludes that acute kidney injury occurs in 14.6% of the victims of snake bite. The common manifestations include cellulitis, bleeding manifestations and gangrene at the site of the bite.

Key Words: Acute Kidney Injury, Snake bite, Dialysis

INTRODUCTION

Snake bite is a common medical emergency and an occupational hazard, more so in tropical India, where farming is a major source of employment. Over 2,000 species of snakes are known worldwide, of which around 400 are poisonous. These snakes belong to the families, Elapidae, Viperidae, Hydrophidae and Colubridae [1]. Viper bites are more common than other poisonous snakebites in human beings [2,3]. Of the different varieties of vipers, Russell's viper (*Viperarusselli*) commonly inhabits the south Asian countries, and the Russell's viper's bite is regarded as an occupational hazard for the farming community. The World Health Organization has estimated that nearly 1,25,000 deaths occur among 2,50,000 poisonous snake bites worldwide every year, of which India accounts for 10,000 deaths [4,5]. The involvement of the predominantly young, healthy and the working population in rural areas which are compounded by poverty and the lack of access to health care services in these areas, signify the social and economic impact of this problem.

Acute kidney injury is mainly observed following bites by the snakes which belong to the viperidae group and it is seen less with sea snake bites and the bites of snakes of the Colubridae group. Most of the Indians are victims of Russell's viper or echiscarinatus bites, which cause AKI [6, 7]. Acute kidney injury is an important complication of snake bite and a proper supportive management after the anti-venom administration is of utmost importance for a good patient outcome. Tubular necrosis and cortical necrosis are the main causes of AKI [8]. The AKI which occurs after snake bite is usually reversible, but if acute cortical necrosis occurs, it may lead to an incomplete recovery. The main cause of this "unacceptable incidence" of snake bite fatalities is that people try out all kinds of "bizarre remedies" initially, instead of going to the nearest hospital. Although there are a number of studies on acute kidney injury in snake bite victims from India, there have been no significantly large prospective studies on the risk factors in the development and outcome of AKI in India. This study, therefore, aimed at assessing the risk and the prognostic factors of snake bite induced AKI.

MATERIALS AND METHODS

This prospective study was carried out at Vijaynagar Institute of Medical Sciences, Bellary, Karnataka, India. This institute is a referral government hospital in north Karnataka, India.

Inclusion Criteria

1. A definitive history of snake bite;
2. The clinical picture was consistent with that of a snake bite, such as the presence of fang marks/ cellulitis/ coagulopathy/ neuroparalysis;
3. The presence of an acute kidney injury which is defined as an abrupt (within 48 hours), absolute increase in the serum creatinine concentration of ≥ 0.3 mg/dL from the baseline value which was measured at admission, either in our hospital or elsewhere, after the snake bite, before referral to our hospital, or a percentage increase in the serum creatinine concentration of ≥ 50 percent above the baseline, or oliguria of less than 0.5 mL/kg per hour for more than six hours, or serum creatinine of more than 1.5 mg/dL or oliguria (urine output of less than 400 mL/day) [9].

Exclusion Criteria

1. 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 small kidneys/loss of the corticomedullary differentiation/ obstructive nephropathy/other renal pathologies);
2. Diagnosed cases of hypertension/diabetes mellitus;
3. Exposure to nephrotoxic drugs/toxins.

A clinical history taking and a complete physical examination were done in each case. The laboratory investigations included haemoglobin, total and differential leucocyte counts, platelet counts, red cell counts, bleeding and clotting times, the coagulation profile which included the prothrombin time, the activated partial thromboplastin time and the international normalised ratio (INR), urine microscopy, urine albumin, kidney and liver function tests and serum electrolytes. The radiological investigations included X-ray of the chest and ultrasonography of the abdomen.

All the patients received the tetanus toxoid. We classified the cases of snake bite as mild, moderate and severe. Anti-Snake Venom (ASV) was administered in a dose of 5 vials (50ml) in the mild cases, in a dose of 5-10 vials (50-100ml) in the moderate cases and in a dose of 10-20 vials (100-200ml) as an intravenous infusion in a drip for over 30 minutes. Antibiotics and diuretics were administered, as indicated. Transfusions of blood and blood products were given to the indicated patients. Renal replacement therapy (either peritoneal or haemodialysis, depending upon the availability of the resources), was given to 16 patients. The patients were followed up till they were discharged or till they died.

STATISTICAL METHODS

The patients were classified into two groups according to the presence or absence of AKI. The differences between the two groups were compared by using the Chi square test, the Fisher's exact probability test or the Student's "t" test, wherever applicable.

RESULTS

A total of 246 cases of venomous snakebite cases were included

in this study, who were admitted to the hospital from November 2007 to October 2008. The demographic profiles of the snake bite patients have been provided in [Table/Fig-1]. In our study, the sex wise distribution of the study subjects was classified, based on whether they had AKI or non-AKI, and among males, it was 20(55.5%) (AKI) and 110(52.5%) (non-AKI) respectively. Among females, it was 6(45.5%) (AKI) and 100(47.5%) (non-AKI) respectively. Illiteracy was more among the patients who suffered from AKI (75%). In our study, among all the patients (both AKI and non-AKI patients), viper bite was the commonest and it was seen in 31(91.6%) patients with AKI and in 142 (67.6%) non-AKI patients. In our study, a majority of the patients who developed AKI had initially visited traditional healers before visiting our hospital, which was found to be statistically significant.

Characteristics	ARF (n=36)	Non-ARF (n=210)	
Age (years)	41.2 \pm 12.4	34.4 \pm 10.2	NS
Male	20(55.5%)	110(52.5%)	NS
Educational Status (illiterate)	27 (75%)	41(19.5%)	p<0.001
Type of Snake Bite			
Elapidae	05 (13.8%)	68 (32.3%)	p<0.01
Viper	31 (91.6%)	142 (67.6%)	p<0.01
Visit to traditional healer	30 (83.3%)	40 (19.04%)	p<0.001

[Table/Fig-1]: Demographic profile of snake bite patients

The clinical profiles of the snake bite patients are shown in [Table/Fig-2]. In our study, cellulitis and gangrene at the bite site were significantly more in the AKI patients as compared to those in the non-AKI patients, which was statistically significant. In the present study, the DIC and the intravascular haemolysis were found to be predominant among the AKI patients. 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. 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.

Characteristics	ARF (n=36)	Non-ARF (n=210)	
Cellulitis	33 (91.6%)	155 (73.8%)	p<0.001
Gangrene at the bite area	30 (83.3%)	58 (27.6%)	p<0.001
Regional lymphadenopathy	28 (77.7%)	64 (30.4%)	NS
Bleeding manifestation	14 (38.8%)	22 (10.4%)	p<0.001
Hypotension	12 (33.3%)	10 (4.76%)	p<0.001
Septicemia	09 (25%)	05 (2.3%)	p<0.001
DIC	04 (11.1%)	01 (0.47%)	p<0.01
Intravascular hemolysis	05 (13.8%)	02 (0.95%)	p<0.001
ARDS	03 (8.3%)	0	p<0.01
Time delay (bite to needle time)	21.8 (4-72 hrs)	4.1 (0.2-24hrs)	p<0.001
Amount of ASV units	16.8 (6-44 vials)	12.8 (4-30 vials)	P<0.005
Duration of hospitalization	09 (4-21 days)	01 (1-3 days)	p<0.001

Values expressed as mean (Variation Range), NS = Not Significant.

[Table/Fig-2]: Clinical Profile of snake bite patients

The patients who developed AKI had been admitted for more days in the in-patients department than the non-AKI patients, which suggested the morbidity which was associated with it.

The outcome of the AKI patients has been shown in [Table/Fig-3]. Out of the 36 patients of AKI, 28 (77.7%) patients survived. Among them, 27 (96.7%) developed cellulitis, 25 (89.5%) had regional lymphadenopathy, 6 (23.8%) developed bleeding manifestations and 22 (81.2%) had been bitten at the lower limbs.

Characteristics	Survived (n=28)	Died (n=8)	
Age (yrs)	35.6±11	40.2±12	NS
Male (%)	54.8	58.3	NS
Cellulites	27 (96.7%)	07 (98.9%)	NS
Regional lymphadenopathy	25 (89.5%)	07 (91.7%)	NS
Bite of lower limbs	22 (81.2%)	07 (93.7%)	NS
Bleeding manifestation	06 (23.8%)	04 (61.6%)	NS
Hypotension	02 (9.4%)	05 (63.1%)	p<0.01
Intravascular hemolysis	05 (17.9%)	04 (53.8%)	p<0.01
Serum creatinine mg/dl	2.81±1.3	4.1±2.1	p<0.001
Blood urea	78.4±28.4	108±32.2	p<0.005
Amount of ASV units	15.3±11.6	18.6±10.3	NS
Bite to needle time (hours)	18.7±15.7	26±17.6	p<0.005
ARDS	01	02	NS
DIC	01	03	p<0.01
Septicemia	04	05	p<0.01
Gangrene	26	04	p<0.01

Values expressed as mean (Variation Range), NS = Not Significant.

[Table/Fig-3]: Comparison of outcome of the patients in AKI group

Among the variables which were entered for the univariate analysis, the following were found to predict the development of AKI: age of the patient, his/her educational status, visit to a traditional healer, cellulitis, gangrene at the area of the bite, bleeding manifestations, hypotension, septicaemia, DIC, intravascular haemolysis, acute respiratory distress syndrome (ARDS), time delay (bite to needle time), amount of the ASV units and duration of the hospitalization.

Among the variables which were entered for the univariate analysis to determine the outcome of AKI, the following were found to predict the outcome of AKI: hypotension, DIC, septicaemia, and gangrene, the bite to needle time (hours), blood urea and serum creatinine mg/dl.

DISCUSSION

Snakebites have the highest incidence in Asia and they represent an important health problem. The exact pathogenesis of AKI following snake bites, is not well established. However, a number of factors contribute to it, like bleeding, hypotension, circulatory collapse, intravascular haemolysis, disseminated intravascular coagulation, microangiopathic haemolytic anaemia and the direct nephrotoxicity of venom [10].

Males are affected more often than the females, as they constitute the working majority who are actively engaged in farming and other outdoor activities. Our findings were concurrent with those of earlier studies [11-14]. In our study, predominantly, the younger population was involved (20-40 years of age), probably due to their more ambulant nature [15, 16-19]. A study which was done by Bhat et al., had also noted that 80% of the cases occurred in this age group. In our study, most of the victims who developed were bitten on the lower limbs (81.2%). A similar observation was reported in a study which was done by Viramani et al., [18]. We noticed that 75% of the snake bite victims who developed AKI were illiterate, which may be because those who are illiterate tend to have more superstitious beliefs. This result was comparable to the findings of a study which was done in Nepal [19]. In our study, the prevalence of AKI was 14.6%. In the study which was conducted by Ali et al., [20], AKI was seen in 17% of the snake bite victims, which was comparable to that which was seen our study. We found that a delay in administering the adequate dose of ASV increased the risk of developing AKI to more than 4 times (odds ratio 4.05), as the venom continues to act until it is neutralized [21].

Cellulitis was one of the independent risk factors which was related to the development of AKI in our study. The earliest symptoms which are seen in the patients of viper bite are pain and swelling at the bitten part. Regional lymphadenopathy was another significant independent factor which contributed to the development of AKI. Like 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.

In our study, 38.8% [14] patients who suffered from AKI, developed bleeding manifestations, which was less than the number in the study which was conducted by Chugh K.S (60-65%) [5]. The mortality rate in our study was 22.3 % (8 patients). It was more among the patients who had required and had undergone dialysis. This was less as compared to the estimates of other studies which were conducted in India (22-50%) [22]. The patients who had recovered from AKI had a shorter bite to needle time, as was observed by Sharma et al., [16].

The patients who had visited the traditional healers had a higher incidence of developing AKI, which may be because of two reasons. Firstly, in this context, time had elapsed and the second being, the tying of tourniquets or other treatments which could have affected the patients.

STUDY LIMITATIONS

The limitations of this study were a small sample size, lack of investigations like a renal biopsy, ELISA for the D-dimer and ELISA for the snake venom. In the developing countries, most of the patients consult traditional healers first, instead of seeking treatment at the health centres. Many snakebite cases are treated at the primary healthcare centres and they are not referred to the higher centres, thus leading to an underestimation of the morbidity status in the studies which are being done at the tertiary health care centres.

CONCLUSION

This study concludes that acute kidney injury occurs in 14.6% victims of snake bite. The common manifestations include cellulitis, bleeding manifestations and gangrene at the bite site. The

type of snakebite is an important factor in the development of AKI and the Russell's viper bite is more commonly associated with it. The ASV therapy time, bite to renal insufficiency time and coagulation abnormalities were the major prognostic factors predicting the final outcomes.

Dialysis and a supportive treatment appear to be the mainstay of the therapy in the cases which are complicated by renal failure. The indications for the dialysis in AKI include anuria of more than 48 hours, severe hyperkalaemia which does not respond to the medical therapy, pulmonary oedema, severe acidosis and rising blood urea and serum creatinine.

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