Clinical profile of acute kidney injury in patients of snake bite

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Abstract

Aims:

Acute kidney injury (AKI) is an important cause of morbidity and mortality in snake bite patients, especially in tropical countries. This study was aimed to describe clinical profile and to identify predictors of poor outcome in snake bite-induced acute kidney injury.

Settings and Design:

This was a retrospective observational study, conducted in a tertiary care hospital.

Materials and Methods:

42 patients of snake bite who were in risk of AKI as per RIFLE criteria were included. Clinical history taking, physical examination, and laboratory evaluation was done. Patients received peritoneal or hemodialysis depending on availability of resources. Two groups were formed based on requirement of renal replacement therapy (RRT). The baseline characteristics of cases were compared amongst the two groups. The Pearson Chi-Square test was used to analyze parametric variables.

Results:

The cases requiring RRT more often presented late, had features of DIC, received low first dose of ASV, and had a higher mean values of INR, blood urea and serum creatinine at the time of presentation. There was statistically significant difference for low dose ASV and mean values of INR, blood urea and serum creatinine at the time of presentation; $P<0.05$. The factors associated with mortality were presence of DIC and extensive cellulitis in patients of AKI

Conclusions:

Early initiation of therapy with the standard high dose of ASV (100ml) as per WHO guidelines can decrease the need of RRT in patients of snake bite with AKI.

Introduction

Snakebite.[1] India accounts for about 30,000 deaths per year due to snake bite.[2] Of the 2500 - 3000 species of snakes, only 500 are considered to be venomous.[3] There are 2 important groups (families) of venomous snakes in south-east Asia - Elapidae -includes the cobras, king cobra, kraits, coral snakes, and the sea snakes and Viperidae - the typical vipers (Viperinae) and the pit vipers (Crotalinae).[4] 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. Tubular necrosis and cortical necrosis are the main causes of ARF.[5]

The objectives of this study were to identify the clinical profile of the snake bite patients who develop acute kidney injury requiring RRT and the predictors of mortality in these patients.

Materials and Methods

This retrospective study included 42 patients of snake bite, who developed acute renal failure, & admitted for renal replacement therapy, from January 2012 to December 2012. The inclusion and exclusion criteria were defined as follows.

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Inclusion criteria

1. Definitive history of snake bite,
2. Clinical picture consistent with snake bite, as presence of flang marks or cellulitis or coagulopathy or neuroparalysis.
3. Presence of acute kidney injury as per RIFLE criteria(table1)[6]

Exclusion Criteria

1. Patients with pre-existent renal disease (serum creatinine > 1.5 mg/dl prior to snake bite or ultrasonography of abdomen suggestive of bilateral small kidneys / loss of corticomedullary differentiation / obstructive nephropathy / other renal pathology)
2. Diagnosed cases of hypertension / diabetes mellitus.
3. Patients with malaria diagnosed on peripheral smear.
4. Exposure to nephrotoxic drugs/toxins.

Clinical history taking and complete physical examination were done in each case. Laboratory investigations included hemoglobin, total and differential leukocyte counts, platelet counts, red cell counts, bleeding and clotting time, coagulation profile and international normalized ratio (INR), urine microscopy, urine albumin, kidney and liver function tests, and serum electrolytes. Radiological investigations included X-ray chest and ultrasonography of abdomen.

All patients received tetanus toxoid. Anti-snake venom (ASV), antibiotics and diuretics were administered as indicated. Blood/ blood products transfusions were given to indicated patients. Renal replacement therapy (either peritoneal / hemodialysis, depending upon availability of resources) was started to 24 patients.

Patients were classified as per outcome in the form of discharge (group A) and death (group B), and various parameters were compared between the 2 groups, which were presence of extensive cellulitis (i.e. cellulitis extending at least 2 joint above the site of bite), features of DIC, mean blood urea, mean serum creatinine, mean bite to needle time, first dose of ASV.

SPSS for Windows version 20.0 was used for statistical analysis. The Pearson Chi-Square test was used to analyze parametric variables. A *P* value of .05 or less was considered statistically significant

RESULTS

During the study period of 12 months from January 2012 to December 2012, 42 patients of snake bite developed acute renal failure as per RIFLE criteria. Among these 42 cases of ARF, 24(57.14%) patients required dialysis. Of these 24 patients, 8 (33.33%) patients expired and 16(66.66%) patients survived. Thus, overall mortality of snake bite-induced ARF is 19.05%.

Of the 42 patients included in study, 30(71.43%) were males and 12 (28.57%) were females. Mean age was 38.77 (± 13.72) years. Rural patients were 35(83.33%), and urban patients were 7 (16.67%). Lower limbs were involved in 33(78.57%) cases.

We studied the clinical profile of patients by comparing between cases requiring RRT (n=24) and those managed conservatively (n=18)

The cases requiring RRT more often presented late, had features of DIC, received low first dose of ASV, and had a higher mean values of INR, blood urea and serum creatinine at the time of presentation. There was statistically significant difference for low dose ASV and mean values of INR, blood urea and serum creatinine at the time of presentation; $P<0.05$.

The cases requiring RRT were grouped to study outcomes, (a) discharge and (b) death. The above same variables were compared. We found significant difference between the groups for extensive cellulitis, features of DIC and mean value of serum creatinine at the time of presentation and on second day; $P<0.05$. (table3)

There were in all nine cases who received lower doses of ASV (<100ml) prior to being referred in our institute for management. All these cases required RRT and three of them succumbed.

Out of 24 cases requiring peritoneal dialysis as first line RRT did not show improvement in renal function and so were shifted for haemodialysis (HD). All of them required prolonged HD for recovery.

DISCUSSION

Snakebites have the highest incidence in Asia and represent an important health problem. In many parts of south-east Asian region, snake bite is a familiar occupational hazard of farmers, plantation workers, and others, resulting in tens of thousands of deaths each year and innumerable cases of chronic physical handicap.[4]

Clinical renal manifestations include proteinuria, hematuria, pigmenturia, and renal failure. Nephropathy usually is caused by bites by snakes with hemotoxic or myotoxic venoms. [7]

The exact pathogenesis of ARF following snake bite is not well-established. However, a number of factors contribute, *viz*, bleeding, hypotension, circulatory collapse, intravascular hemolysis, disseminated intravascular coagulation, microangiopathic hemolytic anemia, and direct nephrotoxicity of venom. [8] Tubular necrosis (53.6%) and cortical necrosis (24.3%) are the main causes of acute renal failure. [5]

Most of the patients were found to be men in working age group, especially from rural population. As expected, the snake bites more commonly involving lower limbs. Therefore, this also shows that use of protective footwear can reduce the snake bites. All of the patients had local cellulitis, indicating the vasculotoxic nature of envenomation.

The overall mortality of snake bite-induced ARF is 19.05% in this study. This is less compared to estimates from other studies from India (22- 50%). [5,9,10] The cases who eventually required RRT more often presented late and received low first dose of ASV supporting the view that mortality can be prevented by an early transfer of the patient to a primary health care facility where ASV should be administered at the earliest.

Furthermore, the comparison between the patients who survived and those who died showed a significant difference with regard to features of DIC, extensive cellulitis and serum creatinine levels at the time of presentation. Patient's fluid status should be optimized with early detection and treatment of coagulopathy. Further, renal replacement therapy should be initiated at the earliest to prevent serious consequences of uremia. The limitations of this study were a smaller sample size, lack of investigations like renal biopsy, ELISA for D-dimer, ELISA for snake venom. Also, renal replacement modality, hemodialysis versus peritoneal dialysis were selected on basis of availability of resources. In conclusions early initiation of therapy with the standard high dose of ASV (100ml) as per WHO guidelines can decrease the need of RRT in patients of snake bite with AKI.

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Table 1. Risk, Injury, Failure, Loss, and End-stage Kidney (RIFLE) Classification

Class	Glomerular filtration rate criteria	Urine output criteria
Risk	Serum creatinine × 1.5	< 0.5 ml/kg/hour × 6 hours
Injury	Serum creatinine × 2	< 0.5 ml/kg/hour × 12 hours
Failure	Serum creatinine × 3, or serum creatinine ≥ 4 mg/dl with an acute rise > 0.5 mg/dl	< 0.3 ml/kg/hour × 24 hours, or anuria × 12 hours
Loss	Persistent acute renal failure = complete loss of kidney function > 4 weeks	
End-stage kidney disease	End-stage kidney disease > 3 months	

Table 2: Baseline characteristics of cases managed conservatively versus those requiring RRT

	RRT required (n=24)	RRT not required (n=18)	P value
Age (Mean)	37.58 ± 12.02	38.94 ± 13.69	0.83
Males (%)	18(75%)	12(66.67%)	0.55
Duration of Bite to ASV Administration (Hours)	**46.83 +/- 58.05**	**16.83 +/- 21.46**	**0.07**
Extensive Cellulitis	13(54.17%)	09(50%)	0.79
Nausea ± Vomiting	17(70.83%)	09(50%)	0.17
Breathlessness	3(12.5%)	0	0.12
Bleeding Manifestation	5(20.83%)	2(11.1%)	0.40
Ptosis / Diplopia	2(8.33%)	1(5.56%)	0.73
DIC	**4(16.67%)**	**0**	**0.07**
WBCT > 20 Min	21(87.5%)	12(66.67%)	0.10
Low dose ASV	**9(37.5%)**	**0**	**0.003**
Hb (Mean)	9.7 +/- 2.47	8.93 +/- 1.06	0.21
TLC	11550 +/- 5312.9	9905.56 +/- 3191.85	0.21
Platelet Count	1.36 +/- 0.610	1.32 +/- 0.57	0.17
INR	**1.65 +/- 0.51**	**1.40 +/- 0.19**	**0.000**
Blood Urea Day1	**96.98 +/- 53.86**	**55.6 +/- 21.67**	**0.003**
Serum Creatinine Day1	**3.03 +/- 1.79**	**1.69 +/- 0.94**	**0.002**
Blood Urea Day2	**146.43 +/- 33.19**	**62.39 +/- 29.4**	**0.000**
Serum Creatinine Day2	**5.3 +/- 2.64**	**1.78 +/- 0.81**	**0.00**

Table 3: Comparison between group (a) and group (b)

	Group (a) DISCHARGE (n=16)	Group (b) DEATH (n=8)	P value
Extensive cellulitis	6	7	0.02
DIC	0	4	0.002
serum creatinine day 1	2.35± 1.20	3.16± 2.01	0.04