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Evaluate the Clinical Profile and Outcome of Patients of Acute Kidney Injury Due to Hemotoxic Snake Bite Envenomation

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ABSTRACT
In particular in the tropics, snake biting is a serious public health issue that significantly increases morbidity and mortality worldwide. One of the most severe aftereffects of a snake bite and a substantial cause of death is acute kidney damage (AKI). For the best clinical care, the species of snake that bit the patient must be identified. Early anti-snake venom (ASV) administration combined with the right supportive measures can reduce fatalities. Over the course of a year, the aforementioned study was carried out at the GMC JAMMU Postgraduate Department of Medicine. The study comprised 100 adult cases of hemotoxic snakebite-related AKI that were admitted to the medical emergency department. All of these patients received ASV in accordance with the National Snakebite Protocol and patients were followed up on for any changes in ASV dosage needs based on their unique clinical profiles. Majority of subjects were within 30-60 years of age group (59%). In maximum subjects lower limb was having hemotoxic snake bite (83%). The most common clinical presentation was limb swelling/cellulitis (90%). The 48 subjects required Hemodialysis and 4 patients given Peritoneal Dialysis. 88 subjects survived after treatment. A typical systemic outcome of snake envenomation is acute kidney injury (AKI), which can occur directly or indirectly. AKI is early diagnosed with careful fluid balance monitoring and renal function testing. It is expected that SAKI-related mortality and morbidity will decrease if anti-venom medication and supportive care are initiated as soon as possible.

INTRODUCTION

In particular in the tropics, snake biting is a serious public health issue that significantly increases morbidity and mortality worldwide. The World Health Organisation (WHO) now recognises snakebite as a Neglected tropical disease[1]. India has the highest rate of venomous snakebite fatality in the world, with estimates ranging from 35,000 to 50,000 deaths each year[1,2].

Farmers and plantation workers are primarily affected by this occupational ailment. The neurological system, kidneys, heart, lungs, liver, blood coagulation system, vascular endothelium and local effects at the bite site are the main targets of envenomation[3]. One of the most serious aftereffects of a snake bite and a substantial cause of death is acute kidney damage (AKI). A sudden (within 48 hrs) absolute increase in serum creatinine concentration of 0.3 mg dL^{-1} from baseline, a percentage increase in serum creatinine concentration of 50%, or oliguria of 0.5 mL kg^{-1} body wt. hrs^{-1} >6 hrs are all considered signs of acute kidney injury (AKI). For the best clinical care, the species of snake that bit the patient must be identified. Syndrome-species correlation suggests the validity of the main syndromes in identifying the four main venomous snakes i.e., Haemotoxicity without AKI (*Echis carinatus*), haemotoxicity and neurotoxicity with or without renal failure (Daboia russeli), neurotoxicity with local swelling (Naga Naga) and neurotoxicity without local swelling (Bungarus caerulus)[4]. Russell's Viper, saw-scaled Viper, Puff Adder, Pit Viper, Sea snake and Tiger snake" bites are linked to AKI[5-10]. The most common cause of morbidity and fatality in most Indian patients who have been bitten by a Russell's viper is acute renal impairment[11]. Many of the patients who are admitted and have a history of envenomation and poisoning develop acute kidney damage (AKI). The pathophysiology of renal failure in these patients is complicated by a number of factors[12]. AKI is frequently seen following myotoxic or hemotoxic snake attacks. Vasculitis, glomerulonephritis, interstitial nephritis, tubular necrosis and cortical necrosis are among the pathologic changes to the kidneys. Nephropathy is primarily brought on by direct nephrotoxicity, vasoactive mediators and cytokines and hemodynamic changes. AKI is exacerbated by haemorrhage, hypotension, disseminated intravascular coagulation (DIC), intravascular hemolysis and rhabdomyolysis[13]. AKI can start anywhere between a few hours to 96 hrs after the bite. AKI following a snake bite often lasts between two and three weeks. An major pathological correlate of AKI is tubular necrosis. After a snake bite, prolonged AKI with oligoanuria is a sign of cortical necrosis, acute tubular necrosis, interstitial nephritis, or extra capillary glomerulonephritis[13]. By causing catheter-related sepsis and its associated dangers, AKI increases the prevalence of infections in various patient populations. It can extend hospital stays in many patients and add significantly to the cost of healthcare. Anti-snake venom (ASV) administered early and in conjunction with the right supportive measures can reduce fatalities.

Acute kidney damage (AKI) is a significant factor in the death of people who have received a vasculotoxic snake bite. Therefore, in a tertiary care hospital in North India, this study was conducted to assess the clinical profile and prognosis of patients with acute kidney injury caused by hemotoxic snake bite envenomation.

MATERIALS AND METHODS

Study place: Over the course of a year, the aforementioned study was carried out at the GMC JAMMU Postgraduate Department of Medicine.

Study type: Prospective study, observation.

Inclusion criteria: Patients that are at least 18 years old and have snake envenomation clinical parameters, history of clinical features of hemotoxic snake bite envenomation, patients with laboratory investigations findings of hemotoxic snakebite envenomation and those willing to participate.

Exclusion criteria: Pre-existing renal disorders such as chronic glomerulonephritis, T2DM, hypertension, polycystic kidney disease, consumption of nephrotoxic medicines and patients who were unwilling to engage in the study.

Sample size: During the study period, 100 adult instances of AKI due to hemotoxic snakebite admitted to the medical emergency department were taken into account.

Data analysis: With the help of SPSS software version 24, the data was analysed. If a variable's $p<0.05$, it was deemed significant. One-way ANOVA was used to compare three mean values and Tukey's HSD post hoc tests for multiple pairwise comparisons were then done. Independent samples t-test was used to compare two mean values. Chi-Square test was used to compare proportions between the study and control groups. If any anticipated cell frequency was less than five, Fisher's exact test was employed instead.

Ethical considerations: The Institutional ethical Committee granted all necessary clearances. The patients' written informed consent was obtained.

The normal clinical practises and protocols were followed for all routine laboratory tests and patient-related clinical data was documented on the proforma from the time of hospital admission until discharge or

death. Complete blood counts, the 20-minute whole blood clotting time (WBCT), prothrombin time (PT), the international normalised ratio (INR) and abdominal ultrasound (USG) were among the haematology measures measured. The prognosis was determined by noting recovery (improvement in renal parameters and urine output), death morbidity and/or progress to chronic stage. The renal functions were evaluated daily. All of these patients received ASV in accordance with the National Snakebite Protocol and their clinical profiles were used to determine whether their needs for ASV changed over time.

RESULTS

Majority of subjects were within 30-60 years of age group (n = 59, 59%), 28 subjects were between 18-30 years of age and 13 subjects were >60 years of age. (Table 1).

Of the 100 subjects included in study, maximum were males (n = 59, 59%) and rest were females (n = 41,41%). Male to female ratio was 1.44:1. (Table2).

In present study, maximum subject's lower limb was having snake bite (n = 83,83%) and only 17 (17%) subject's upper limb was having snake bite (Table 3).

Majority of subjects were from rural area (n = 75, 75%) and only 25% subjects were residing in urban areas (Table 4).

Sign and symptoms present among study subjects were Oliguria (77%), Hematuria (56%), Limb swelling/cellulitis (90%) and Coagulation defect (88%) (Table 5).

The time interval between snake bite and admission in hospital in maximum subjects was between 2-6 hrs (58%) and in only one subject it was >1 day. 31 subjects were admitted <2 hrs of snake bite, 7 subjects within 6-12 hrs and 3 in >12 hrs (Table 6).

In present study, anti-snake venom (ASV) was given to 98 subjects, Fresh frozen plasma (FFP) was given to 88 subjects, PCV was given in 20 subjects and ICU support was given to only 12 subjects (Table 7).

In present study, 48 subjects required Hemodialysis and 4 patients required Peritoneal Dialysis (Table 8).

Of the total 100 subjects of snake bite 88 subjects survived after treatment and 12 patients died.

In present study, various hematological and biochemical disorders encountered in study subjects were Hb <12 g dL^{-1} (82%), Leukocytosis (73%), Thrombocytopenia (49%), Hyperkalemia (23%), Severe metabolic acidosis (43%), Hepatic dysfunction (40%), Hypoalbuminemia (64%), Hemolysis (87%) and Rhabdomyolysis (63%). (Fig. 2).

Complications encountered in study subjects were Pneumonia/ARDS (10%), Hypertension (8%), Hypotension (4%), Myocarditis (1%), Myocardial infarction (1%), Gastrointestinal bleed (14%), DIC (8%), Seizure/encephalopathy (11%) and multi organ failure (5%) (Fig.3).

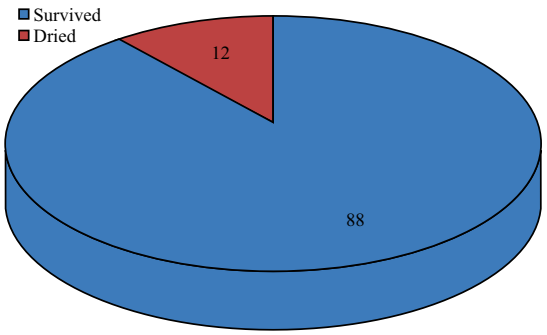

Fig. 1: Outcome among the study subjects

Table 1: Age distribution among the study subjects

Age group (years)	No.	Percentage
18-30	28	28
30-60	59	59
>60	13	13
Total	100	100

Table 2: Gender distribution among the study subjects

Gender	No.	Percentage
Male	59	59
Female	41	41
Total	100	100

Table 3: Site of bite among the study subjects

Site	No.	Percentage
Lower limb	83	83
Upper limb	17	17
Total	100	100

Table 4: Residence distribution among the study subjects

Residence	No.	Percentage
Rural	75	75
Urban	25	25
Total	100	100

Table 5: Sign and symptoms among the study subjects

Sign and symptoms	No.	Percentage
Oliguria	77	77
Hematuria	56	56
Limb swelling/cellulitis	90	90
Coagulation defect	88	88

Table 6: Duration between snake bite and hospital admission

Duration	No.	Percentage
<2 hrs	31	31
2-6 hrs	58	58
6-12 hrs	7	7
>12 hrs	3	3
>1 day	1	1
Total	100	100

Table 7: Treatment given to the study subjects

Variables	No.	Percentage
ASV	98	98
Fresh frozen plasma (FFP)	88	88
PCV	20	20
ICU support	12	12

Table 8: Dialysis therapy and Hemodialys is among the study subjects

Variables	No.	Percentage
Hemodialysis	48	48
Peritoneal dialysis	4	4

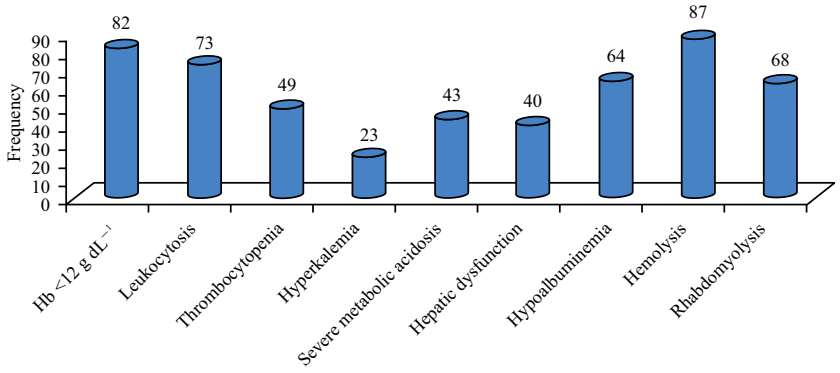

Fig. 2: Frequency of various of hematological and biochemical disorders

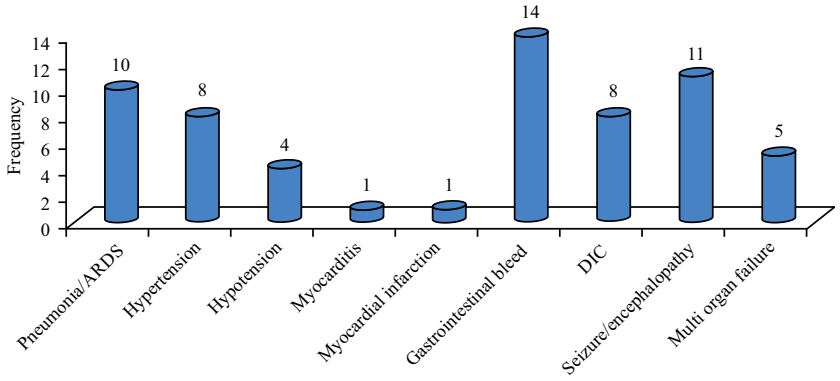

Fig. 3: Complications among the study subjects

DISCUSSIONS

In the current study, 13 subjects were over 60 years of age, 28 subjects were between the ages of 18 and 30 and 59 percent of the subjects fell within the 30 to 60 age range. The included subjects ranged in age from 22 years old to 71 years old. This might be the case since people in their 30s to 60s are typically the breadwinners of the family, going out to work and working in the fields. The majority of the patients in the study by Ramanathan and Vasudevan[4] HS 4 were between the ages of 40 and 60 (51%). 72% of the individuals, it seems, were between the ages of 20 and 60. Ages 30 to 50 were most frequently affected in the study by Arul *et al*.[14].

Of the 100 subjects involved in the study, men made up the majority (59%) while women made up the remaining 41%. The ratio of men to women was 1.44:1. This indicates that there was a minor male predominance among the individuals in the current study, which may be due to the fact that men outnumber women in the population and that men often perform the majority of outdoor activities, farming and field work. Increased incidence in males is due to increased exposure. These findings were similar to results of Abhishek *et al*.[15], who showed that 54% subjects were males and 46% subjects were female in their study. In study done by Ramanathan and Vasudevan[4], 63% subjects were males and 37% were women.

In present study, in maximum subjects' lower limb was having snake bite (n = 83,83%) and in only 17 (17%) subjects' upper limb was having snake bite. This shows that snake bite is common in lower limb as there are chance that people working in fields, or while walking on roads or from grassland encounter them and had snake bite. The dorsum of the foot and ankle were the most often bit locations because the majority of them were field workers who walked about barefoot. Few patients reported being bitten over the dorsum of their hands, over their thighs, or across their shoulders; these patients either worked in seated positions or slept on the ground. These findings were similar to result of Vikrant *et al*.[16], who found that lower limb was affected in 85.2% subjects and upper limb in 14.8% subjects. Almost same were result of Parameswaran *et al*.[17], who found that 87% subjects had snake bite on lower limb, 12 % on upper limb and 1% on chest.

Majority of subjects were from rural area (n = 75, 75%) and only 25% subjects were residing in urban areas. This suggest that chances of encounter with snakes is most common in rural areas and people of

rural areas are more affected as they work in field bare foot and does not have proper facilities during floods, due to which they are more affected by snake bite as compared to people residing in urban areas. These results were almost similar to findings of Arul *et al*.[14], who found that 72% of the subjects were from rural area and 28% were from urban area. The majority of the patients (88%) in the study conducted by Ramanathan and Vasudevan[4] came from rural areas. Oliguria (77%), hematuria (56%), limb swelling/cellulitis (90%) and coagulation malfunction (88%) were signs and symptoms that research participants had. Cellulitis can develop depending on the type of snake that bit you and it is not dependent on the limbs or the venom's potency. However, the effectiveness of the treatment is what determines whether or not cellulitis advances, therefore if the treatment is effective, it won't. 79.5% of people in the study by Vikrant *et al*.[16] had oliguria and 54.5% had a history of hematuria. 13.6% of patients suffered limb edoema or cellulitis, while 5.7% of patients also had neurotoxicity. In 88.6% of patients, a coagulation problem was observed or recorded. According to findings of Ariga *et al*.[17], significant number of cases had extensive cellulitis (84%), thrombocytopenia (83.4%), disseminated intravascular coagulation (34%) and intravascular hemolysis (51.3%).

The time interval between snake bite and admission in hospital in maximum subjects was between 2-6 hrs (58%) and in only one subject it was >1 day. 31% subjects were admitted <2 hrs of snake bite, 7% subjects within 6-12 hours and 3% in >12 hrs. This shows that, as maximum study subjects were from rural areas and they have restricted medical facilities as well as mode of transport and education, because of which time duration between snake bite and admission to hospital increased. And the maximum subjects which were admitted <2 hrs of snake bite were from urban area and few were from rural area, which may be due to access to better medical and transport facilities. In study done by Ramanathan and Vasudevan[4], 92% patients were admitted within 6 hrs of bite, of which 36% came within 2 hours of the bite. Only 1 patient was referred after 5 days for complications of the bite.

In present study, anti-snake venom (ASV) was given to 98% subjects, fresh frozen plasma (FFP) was given to 88 subjects, PCV was given in 20% subjects and ICU support was given to only 12% subjects. These findings were similar to result of Vikrant S et al.[16], who found that ASV given in 96.6%, Blood transfusion 17% and ICU support 11.4%.

In present study, 48% subjects required Hemodialysis and 4% patients required Peritoneal Dialysis. According to Abhishek *et al*.[15], 60% patients required dialysis and remaining 40% patients were treated conservatively. 34% of patients underwent peritoneal dialysis alone and 26% underwent combined peritoneal and hemodialysis. In the Vikrant *et al*.[16] research, 81.8% of patients needed dialysis.

Of the total 100 subjects of snake bite 88 subjects survived after treatment and 12 patients died. Of the maximum subject who died were from rural area and were those who came to hospital after >6hours of snake bite and received ASV >6 hrs after snake bite. As it is shown in study done by Abhishek *et al*.[15], who found that out of total of 64 patients who received ASV early (bite to ASV time <6 hrs), 54 (84.3%) patients survived and 10 patients died. Among those who died 28 (73.6%) of them had got anti-snake venom after 6 hours of snakebite and 10 (26.4%) patients received within 6 hours of snakebite. The association between time of ASV administration and survival was found to be statistically significant.

Hb 12 g dL^{-1} (82%), leukocytosis (73%), thrombocytopenia (49%), hyperkalemia (23%), severe metabolic acidosis (43%), hepatic dysfunction (40%), hypoalbuminemia (64%), hemolysis (87%) and rhabdomyolysis (63%), were among the haematological and biochemical conditions that were observed in the study subjects. AKI has a well-known cause that is rhabdomyolysis Vanholder *et al*.[18]. The most frequent cause of rhabdomyolysis and myoglobinuria is sea snake bites. Many snakes in Australia have myotoxic and hemotoxic effects. In Asia, intravascular hemolysis and rhabdomyolysis can both be brought on by Russell's viper venom depending on the location. Most research on AKI brought on by snake bites has solely examined the haematological and coagulation characteristics[6,13]. In the current investigation, rhabdomyolysis and hemolysis were looked for in all AKI patients[19-21].

Pneumonia/ARDS (10%), Hypertension (8%), Hypotension (4%), Myocarditis (1%), Myocardial infarction (1%), Gastrointestinal bleed (14%), DIC (8%), Seizure/Encephalopathy (11%) and Multi organ failure (5%) were complications the research participants experienced. According to a research by Vikrant *et al*.[16], the most common complications were myocarditis and myocardial infarction (1.1% each), myocarditis with myocardial bleed (12.5%), seizure/encephalopathy (10.2%), hypertension, pneumonia/ARDS and DIC (9.1% each), hypotension and MOF (4.5%).

CONCLUSION

Acute kidney damage (AKI), which can happen directly or indirectly as a result of snake envenomation, is a usual systemic consequence. AKI is

early diagnosed with careful fluid balance monitoring and renal function testing. It is expected that SAKI-related mortality and morbidity will decrease if anti-venom medication and supportive care are initiated as soon as possible. In oligo-anuric AKI, dialysis may be necessary to stabilise fluid overload and electrolyte imbalances. Because some AKI patients develop CKD over time, it is important to regularly evaluate renal function.

LIMITATIONS OF THE STUDY

The study's shortcomings included a small sample size, a lack of investigations such kidney biopsies, snake species identification and an ELISA test to determine snake venom. There were delays in seeking treatment at health facilities and receiving it because ASV was unavailable at peripheral health centres. The majority of patients at our clinic received ASV for the first time. As a result, larger-scale studies with better investigations are needed to validate the current study's conclusions.

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