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Clinical Profile and Outcome of Snake Bite Induced Acute Kidney Injury

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Abstract: *Snake bite is one of the major causes of Acute Kidney Injury in South Tamil Nadu. The outcome in a case of snake bite depends upon multi various factors. Total number of patients admitted for snake bite during the study period was 913 out of which 83 patients who developed AKI following snake bite were included in the study. Among the 83 patients included in the study, 69 (83%) patients received dialysis, 10 (12%) patients died despite treatment, partial recovery seen in 14 patients, renal biopsy was done in 20 patients. Various factors both clinical and laboratory parameters affecting the outcome and their impact were analyzed.*

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I. Introduction

India has the highest estimate of snake bite mortality in the world (15000 to 30000 per annum). The most venomous snakes in India are Cobra, Krait, Russel's Viper, Saw scaled Viper, Hump nosed pit Viper, White lipped pit Viper, Sea snake. More than 100 different types of peptides have been isolated from the snake venoms and not all are toxic to humans. Various mechanisms of toxicity include Endothelial disruption, Activation of Coagulation cascade, Inhibition of platelets, caused by Phospholipases, Serine proteases, Disintegrins, Metalloproteinases, & C type lectins which leads to Coagulopathy. Hemorrhagins cause bleeding by directly injuring the endothelium. Hyaluronidases, Hydrolases, Cytokines contribute to local tissue necrosis. Myotoxic Phospholipase A2 seen in sea snakes is responsible for rhabdomyolysis thereby leading to acute renal failure. AKI is common after hemotoxic or myotoxic snake bites, incidence ranging from 5% to 29% depending on the species and severity of envenomation. The onset is from a few hours to as late as 96 hours after the bite and the duration ranges from 2-3 weeks. Renal biopsy usually reveals Cortical Necrosis or Acute Tubular Necrosis associated with Interstitial nephritis or extra capillary glomerulonephritis. Recovery is usually complete unless cortical necrosis occurs. Mortality in snake bite related AKI ranges from 1-20%

II. Material AndMethods

In this prospective and retrospective study, we selected all cases who developed renal failure after snake bite, admitted to Govt. Rajaji Hospital & Madurai Medical College, for the past 5 years. They were monitored continuously, and the outcome was evaluated. All patients included in the study were subjected to clinical history taking, and complete physical examination. Laboratory investigations included Hemoglobin, Total & Differential WBC count, RBC count, Coagulation profile including Bleeding & Clotting time, Prothrombin time, Activated partial thromboplastin time, and International Normalized Ratio (INR), Urine Microscopy, Urine Albumin, Renal & Liver function tests and Serum Electrolytes. Radiological investigations included X-ray Chest PA view and Ultrasonography of Abdomen. All patients were managed according to Tamil Nadu Health Systems Project guidelines. Anti-Snake Venom protocol strictly followed. The test of significance of each parameter studied was evaluated by Chi Square test. ***Inclusion Criteria:*** All cases of snake bite induced AKI (by RIFLE criteria) were included in the study.***ExclusionCriteria:***Pre-existing renal failure, Features of CKD (as per KDIGO definition), NSAID intake, Usage of drugs interacting with Creatinine estimation.

III. Results

Total number of snake bite admitted was 913, of which 83 (9%)developed acute kidney injury and were categorized by RIFLE criteria. Comparison between the rural (72%) and urban population (28%) regarding the outcome was statistically insignificant (p value 0.30). On analyzing the age factor, the most commonly affected age group was between 30 – 50 years. On determining the severity and outcome of the patients

corresponding to male and female sex, it was found to be of no statistical significance (p value 0.45). 50% of the bites occurred in the early morning 4 am to 10 am, 32% of the bites occurred in the mid night and only 18% of the bites were reported in the day time. Maximum number of deaths i.e. 50% occurred in the early morning bites and it was statistically significant (p value < 0.05).On comparing the initial care, 11 had taken native medications, out of which 3 expired and 7 had to progress to CKD. In the group of 7 patients whose diagnosis is established by the treating physician, all became dialysis dependent, but the mortality was not statistically significant.65% of bites occurred in lower limb, 30% of the bites occurred in upper limb, 5% in trunk

It was found that the severity of renal failure and outcome was statistically significant in those with cellulitis because 57 out of 69 patients with cellulitis needed dialysis.In our study, the presence of lymphadenopathy (present in 46 patients) had no significance, either in the form of severity or outcome.Of the 83 patients, 23 patients had fang marks at the time of presentation out of which 22 were dialysis dependent.Of the 83 patients, 9 (10%) had proteinuria at the time of presentation and all of them were dialysis dependent, of which 5 expired and 2 progressed to CKD. 9 (10%) had thrombocytopenia at the time of presentation, all of them were dialysis dependent, of which 4 expired, 3 progressed to CKD and 2 recovered. 9 (10%) had fragmented RBCs at the time of presentation, all of them were dialysis dependent, of which 4 expired, 3 progressed to CKD and 2 recovered. 15 (18%) patients developed sub conjunctival hemorrhage during illness. These patients were dialysis dependent, of which 4 expired, 8 progressed to CKD, and 3 recovered completely. On comparing these group with the remaining 68 (82%) patients, those who had sub conjunctival hemorrhage at the time of presentation had very poor outcome. (p < 0.04). Spontaneous bleeding was noted in 4 out of 83 patients of which 2 expired and 2 progresses to CKD.12 (14.5%) of 83 patients, had uremic symptoms at the time of presentation and all of them were dialysis dependent, of which 5 expired and 7 progressed to CKD.

In our study 43 (51%) had prolonged PT, APTT. 41 of them were dialysis dependent, 8 (10%) patients expired and 11 (78%) progressed to CKD. Of the 83 patients, 8 (10%) had myoglobinuria. All of them were dialysis dependent, 3 patients expired, and 4 patients progressed to CKD. Whole blood clotting time (WBCT) normalization had high statistical significance in association with the outcome, (p value 0.004) and those with early normalization of WBCT were associated with reduced dialysis requirement and better outcome.27 (32.5%) patients had satisfied the criteria for Hypercatabolic AKI, of which16 were male and 11 were female. They were mostly observed in Viper bite, native medication intake, patients with cellulitis, lymphadenopathy and fang marks. Most of them had renal failure at the time of presentation and associated with DIC.

The time lag for referral in dialysis requiring group was 6.6 hours whereas for those who did not require dialysis was 5.3 hours. The time lag for referral had no significant effect on the severity of renal failure and outcome.The mean time lag for initiating ASV in dialysis requiring group was 9.94 hours and the same for the patients who do not require dialysis was 7.5 hours.Out of the 83 patients 63 patients had completed ASV before the onset of AKI (Group A) and 20 patients had not completed ASV before the onset of renal failure (Group B). On analysis, in Group A 11% of the patients expired 14% of the patients progressed to CKD. In group B 15% of the patients expired and 20% of the patients progressed to CKD. This was statistically significant (p value < 0.005). Time lag for the administration of ASV according to the test for equality of variance was statistically significant with severity of renal failure and outcome. Those who completed ASV before the onset of renal failure were found to have better outcome (p value 0.001). On analysis, there was no significance in dialysis requirement and severity of renal failure in those who completed ASV after 24 hours, but the outcome (death & progression to CKD) was statistically significant.

On analyzing the renal parameters, there was not much difference in presenting serum creatinine, but the average serum peak creatinine, mean time for the onset of renal failure and the mean time for completion of ASV were significantly high.Of the 27 patients who were treated with hemodialysis, jaundice was present in 9 (34%) of the patients. DIC was reported in 11 (42%) Renal failure was present in 13 (50%).On analyzing the histopathology, there was no specific correlation with the type of snake bite, except for 2 cases of TMA in Russel's Viper. Acute Tubular Necrosis(ATN) accounts for 8 cases (40%), AcuteTubulo-Interstitial Nephritis (ATIN) in 3 cases (15%), Thrombotic Micro Angiopathy (TMA) in 2 cases (10%), Acute Cortical Necrosis (CAN) in 6 cases (30%).Total death observed is 10 (12.5%). Cause of death includes DIC in 4 (40%), Sepsis 5 (50%), VAP 2 (20%). The type of snake was Pit Viper in 3 patients, Russel's Viper in 4 patients, Cobra in 1 and Not known in 2 patients. The result was statistically significant. In our study, the mortality associated with snake bite induced AKI was 12%

Chart 1.

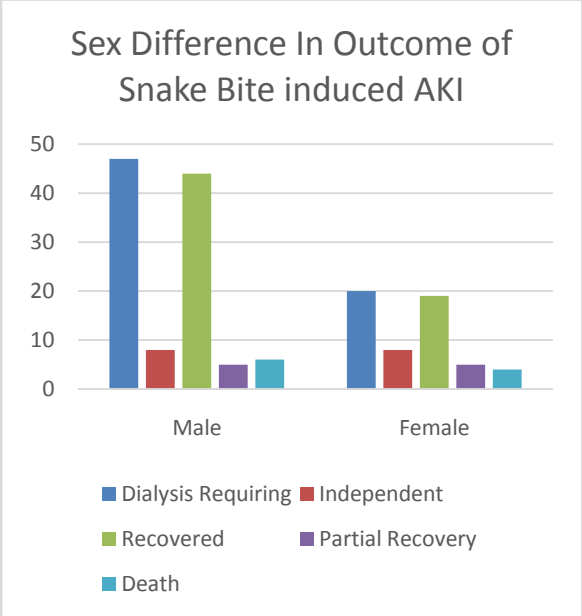


Chart 2.

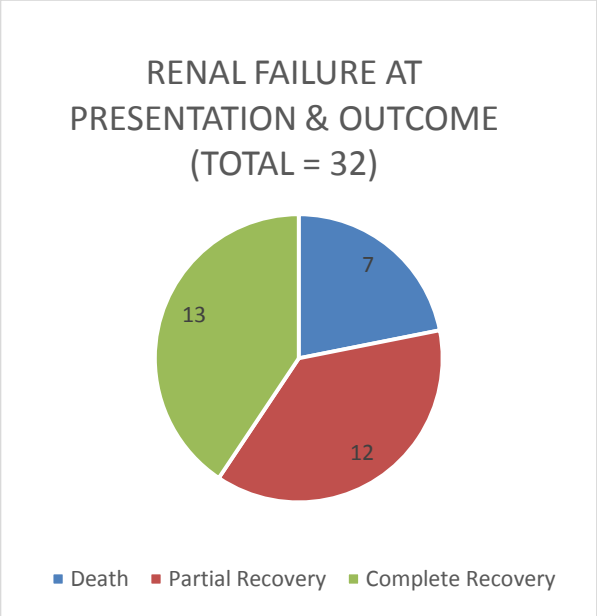


Table 1. Symptom Analysis in Snake Bite patients with AKI

Parameter	Total No. of Patients	Dialysis Dependency	Death	Complete Recovery	Partial Recovery
Edema	72	60	10	51	11
Subconjunctival bleed	15	15	4	3	8
Spontaneous bleed	4	4	2	0	2
Breathlessness	20	19	5	11	4
Uremic symptoms	12	12	5	0	7
Oliguria	22	22	5	9	8

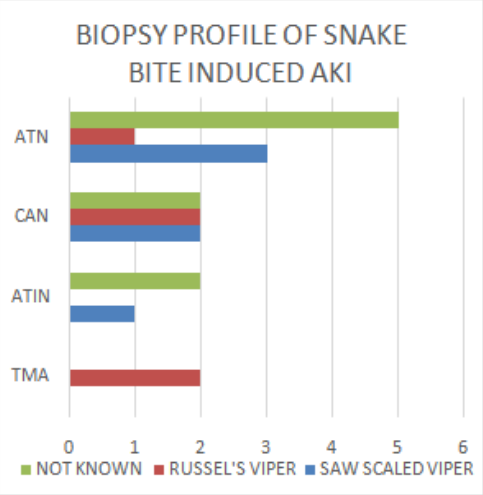
Table 2. Laboratory Parameters in Snake Bite patients with AKI

Parameters	Total	Dialysis Requiring	Complete Recovery	Partial Recovery	Death
Hematuria	13	13	2	7	4
Proteinuria	9	9	2	2	5
Anemia	19	17	6	8	5
Thrombocytopenia	9	9	2	3	4
Fragmented RBC's	9	9	2	3	4
Pt/APTT	43	41	22	11	8
Myoglobin	8	8	1	4	3

Table 3. Requirement of dialysis in Snake Bite induced AKI

PARAMETER	REQUIRING DIALYSIS	NOT REQUIRING DIALYSIS
Presenting Serum Creatinine	2.0377	2.0325
Peak Serum Creatinine	7.3	2.3
Range of Serum Creatinine	0.6 – 9.3	0.7 – 3.4
Hypercatabolic AKI in Snake Bite	27	0
Mean Time of Renal Failure	35.5	43.5
Mean Time for ASV Complication	27.5	43.5
Total Number of Deaths	10	Nil

Chart 3.



IV. Discussion

In an agricultural country like India, snake bite poses a great public health problem. In our study, 9% of the snake bite patients developed AKI. This is in contrast to the study by P. Mukhopadhyay et al [8] as that was predominantly based on Viper bites and timely administration of ASV. The percentage of patients from rural area was 60% when compared to 85.9% as discussed by Tushar B Patil and et al [7], showing increased urbanization. But there was no significance in the outcome. There was a male preponderance among the snake bite cases agreeing with Rajesh Waikhom and et al [4]. Increased incidence in males is due to increased exposure. The commonly affected age group was 30-50 yearssimilar to the study by Mrudul V Dharod and et al [3]. The progression to CKD and death were more in the age group > 50 years. Maximum number of deaths i.e. 50% occurred in the early morning bites (during the farm working hours).It was found that all 3 forms of Viper bite show significant statistical effect on both severity of renal failure and outcome. Incidence was more with Russel's Viper (as stated by VipaThanachartwetand et al [6]) and mortality was more in Pit Viper. On analyzing the severity and outcome, the site of the bite had no statistical significance. But bite at sites with poor vascularity had least toxicity.

In our study 92% of the patients who had cellulitis needed dialysis and the same was pointed out byMrudul V Dharod and et al [3]. Lymphadenopathy was not found to be affecting the outcome. The presence of fang mark indicated furious and deep bites which caused maximum envenomation and was highly significant with relation to dialysis requirement, progression to CKD. Proteinuria at presentation was a risk factor for AKI.Thrombocytopenia was present in 10% of the patients against 17% stated by K S Chugh and was associated with poor outcome. The presence of sub conjunctival hemorrhage, spontaneous bleeding had poor outcomes among patients. Bleeding tendencies secondary to DIC was a major factor in the development of AKI were common with Viper bites as stated by Mrudul V Dharod [3]. Hemorrhage is the major symptom of systemic Viper envenomation. Patients with uremic symptoms at the time of presentation had worse outcome.Prolonged PT, aPTT was found in 51% and was associated with poor outcome. 10% of pateints who had myoglobinuria became dialysis dependent. WBCT normalization time, if lesser was associated with early recovery. Hypercatabolic AKI was seen in 27 (32.5%).

The time lag for referral for dialysis had no significance in the outcome but the time lag for initiating ASV in the dialysis requiring group was significant. The completion of ASV before the onset of renal failure was associated with greater chance of recovery. The delay in the administration of ASV was associated with 4 times increased risk of developing AKI as stated already by Harshavardhan et al [1]. The average peak serum creatinine rather than the serum creatinine at presentation was much useful in assessing the onset of AKI. An increase in serum creatinine concentration of >50% was associated with progress to renal failure. Of the 83 patients, 69 patients needed Hemodialysis. On renal biopsy there was no correlation with the type of snakebite and the biopsy picture except for the 2 cases of Russel's viper bite which showed Thrombotic microangiopathy.In renal biopsy, the predominant lesion noted was acute tubular necrosis. On contrary, Rubina Naqvi [2] stated that acute cortical necrosis was the commonest lesion. This difference is due to the difference in the distribution and the type of snake of our locality. The onset of Acute cortical necrosis leads to irreversible damage and the patient becomes dialysis dependent. In biopsy, the 2 patients had thrombotic microangiopathy which coincided with Viper bites.

V. Conclusion

In snake bite induced AKI, maximum number of deaths were seen in bites that occurred early in the morning, common among the age group of 30-50 years, Viper bite induced AKI showed poor outcome, the time lag for administration of ASV had worse outcomes, those who completed ASV before the onset of renal failure had better prognosis. Cellulitis and regional lymphadenopathy indicated the amount of toxin released and presence of fang marks showed maximum envenomation. Presence of Proteinuria, hematuria, anemia and thrombocytopenia were associated with poor outcomes. Signs of DIC were associated with worse outcomes. WBCT normalization time was associated with the poor outcome and the patients needed dialysis. The overall mortality in Snake bite induced AKI in our study was 12%.

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