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A STUDY ON HEMOTOXIC SNAKE ENVENOMATION INDUCED ACUTE KIDNEY INJURY AND ITS OUTCOMES: A PROSPECTIVE FOLLOW UP STUDY

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ABSTRACT

Background: Snakebite is a critical public health issue, particularly in rural regions of tropical and subtropical countries, affecting farmers, plantation workers, construction workers, snake charmers, hunters, and migrant populations. Urbanization and deforestation have exacerbated the problem, making snakebite a significant health concern. In India, snakebite-related mortality is alarmingly high, necessitating urgent attention. The World Health Organization (WHO) estimates that 81,000–138,000 deaths occur annually worldwide due to snakebites, with approximately three times as many survivors suffering from amputations and permanent disabilities. The Million Death Study (MDS) in India has documented cause-specific mortality patterns, highlighting the importance of early administration of Anti-Snake Venom (ASV) to reduce mortality and morbidity in envenomation cases.

Methods: This prospective follow-up study focuses on acute kidney injury (AKI) induced by hemotoxic snake envenomation and its long-term outcomes. The study population included patients diagnosed with AKI following snakebite, with an emphasis on evaluating the incidence of chronic kidney disease (CKD) post-recovery. Data were collected on risk factors such as multiple AKI episodes, baseline CKD, and the severity of AKI. Follow-up nephrology care was assessed to determine its impact on long-term renal outcomes.

Results: The study revealed a significant correlation between AKI and CKD, with evidence indicating that even AKI patients with apparent full recovery are at an independent risk for developing CKD later in life. Risk factors such as multiple AKI episodes, pre-existing CKD, and the severity of AKI were identified as reliable predictors of CKD progression.

Conclusion: The findings highlight the long-term renal risks associated with hemotoxic snake envenomation-induced AKI. Even after apparent recovery, AKI survivors are at heightened risk for CKD, emphasizing the need for systematic follow-up nephrology care to mitigate long-term complications.

Key Words: Snakebite, Public Health Concern, Anti-Snake Venom (ASV), WHO, Acute Kidney Injury (AKI), CKD Risk after AKI, Incidence of CKD, Follow-up Nephrology Care.

INTRODUCTION

The World Health Organization (WHO) recognized snakebite as a neglected tropical disease in 2017 and called for global action to reduce mortality and disability.[1] Snakebites affect 1.8 to 2.7 million people worldwide annually, causing an estimated 80,000 to 138,000 deaths.[2] Envenomation occurs when venom is injected into the body through a snakebite, leading to potentially life-threatening complications with long-term physical and psychological consequences.[3] In South Asia, around 70 of the 300 snake species are venomous, with the "big four"-common krait (*Bungarus caeruleus*), binocellate cobra (*Naja naja*), Russell's viper (*Daboia russelii*), and saw-scaled viper (*Echis carinatus*)—being responsible for most fatalities.[4] WHO aims to reduce snakebite-related mortality and disability by 50% before 2030.[5]

Acute kidney injury (AKI) is a frequent complication of snake envenomation, with an incidence ranging from 13% to 25%.[6] Studies in Sri Lanka have shown that Russell's viper and Hump-nosed viper (*Hypnale hypnale*) bites are the most common causes of AKI.[7] The mechanisms of AKI include circulatory collapse, hypotension, hemolysis, disseminated intravascular coagulation, and direct nephrotoxic effects of the venom.[8] The bite-to-needle time, referring to the interval between envenomation and antivenom administration, is a key determinant of AKI severity, as timely intervention can prevent complications.[9]

Previously, AKI was considered a transient condition, but recent studies indicate a risk of long-term renal impairment, including chronic kidney disease (CKD) and end-stage renal disease (ESRD).[10] Severe AKI requiring renal replacement therapy (RRT) is an independent predictor of poor prognosis.[11] Therefore, renal recovery should be a therapeutic priority, and long-term follow-up is crucial to prevent CKD progression.[12]

AIMS AND OBJECTIVES

This study aims to determine the incidence of acute kidney injury (AKI) following hemotoxic snake envenomation and assess its impact on patient outcomes. Hemotoxic envenomation, primarily caused by vipers, leads to systemic complications, including coagulopathy, organ dysfunction, and kidney injury. Understanding the frequency and severity of AKI in these cases will help improve early diagnosis and management strategies.

A crucial objective is to determine the incidence of chronic kidney disease (CKD) in patients who develop AKI due to snake envenomation.

MATERIALS AND METHODS

This study was a single-center prospective follow-up study conducted in the Department of General Medicine at Karnataka Institute of Medical Sciences (KIMS), Hubballi, over a period of two years (August 2022 – July 2024**.** The study included 155 patients who presented with a history of hemotoxic snake envenomation and met the inclusion criteria.

Inclusion Criteria and Exclusion Criteria

Patients included in the study were those aged above 18 years, with confirmed hemotoxic snake envenomation and a diagnosis of acute kidney injury (AKI) based on the Kidney Disease: Improving Global Outcomes (KDIGO) criteria. Patients were excluded if they had neuroparalytic snake envenomation or pre-existing medical conditions such as chronic kidney disease (CKD), chronic liver disease, or coagulation disorders, as determined by medical history and previous records.

Sample Size Calculation

The sample size was calculated using the formula 4PQ/d**2**, where P represents prevalence, Q = (100 – P), and d is the allowable error (5%). Based on this calculation, a total of 155 patients with a history of hemotoxic snakebite and AKI were selected for the study.

Data Analysis

All collected data were entered into Microsoft Excel and analyzed using SPSS software version 17.0**.** Qualitative variables such as age categories, gender, time and place of snakebite, presence of bleeding manifestations, and complications at presentation were presented as frequencies and percentages, with bar diagrams and pie charts used for graphical representation. Statistical analysis was performed using the Chi-square test, and a p-value of less than 0.05 was considered statistically significant at a 95% confidence interval.

Methodology

To assess long-term renal outcomes, all patients were followed for three months, with serum creatinine and urine proteinuria levels monitored at the 1st and 3rd months. Estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI 2021 equation**,** and patients were classified into different stages of chronic kidney disease (CKD) according to KDIGO CKD guidelines**.**

RESULTS

Age Group (Years)	Frequency	Percentage (%)	Gender	Frequency	Percentage (%)
20-30	9	5.8	Male	120	77.4
30-40	35	22.6	Female	35	22.6
40-50	33	21.3			
50-60	35	22.6			
60-70	26	16.8			
70-80	17	11.0			
Total	**155**	**100**	**Total**	**155**	**100**

Table 1: Age and Gender Distribution of Patients

In the table 1 the majority of patients belonged to the 30-40 years (22.6%) and 50-60 years (22.6%) age groups. The male population (77.4%) was significantly higher than females (22.6%).

Time of Snake Bite	Frequency	Percentage (%)	Time of Presentation	Frequency	Percentage (%)
Day	123	79.4	<6 hours	135	87.1
Night	32	20.6	6-12 hours	6	3.9
			12-24 hours	2	1.3
			>24 hours	10	6.45
Total	**155**	**100**	**Total**	**155**	**100**

Table 2: Time of Snake Bite and Time of Hospital Presentation

Table 2 gives the details of patients (79.4%) were bitten during the daytime, and 87.1% reached the hospital within 6 hours, improving treatment outcomes.

Parameter	Frequency	Percentage (%)
Tourniquet Applied	105	67.75
Local Complications	149	96.12
Mild Anemia (10-12 g/dL)	106	68.4
Thrombocytopenia (<1.5 lakh)	77	49.7
Increased PT Time	147	94.8
INR Prolonged	147	94.83
WBCT > 20 min	145	93.5

Table 3: Clinical Features and Laboratory Findings

Table 3 shows: 67.75% of patients applied a tourniquet, which may delay appropriate medical intervention. 96.12% had local complications, emphasizing the severity of envenomation and 49.7% had thrombocytopenia, and 94.8% had increased PT time, indicating coagulopathy.

AKI Stage	Frequency	Percentage (%)
AKI-1	69	44.5
AKI-2	39	25.2
AKI-3	47	30.3
Total	**155**	**100**

Table 4: Severity of Acute Kidney Injury (AKI)

In table 4 - 44.5% had AKI-1, which is the mildest stage and 30.3% had AKI-3, indicating severe kidney injury requiring intensive care.

Treatment	Frequency	Percentage (%)
FFP Transfusion	58	37.41
pRBC Transfusion	30	19.35
Ventilator Support	10	6.5
RRT (Dialysis)	26	16.8
Surgical Intervention	22	14.2
Death	**8**	**5.16**
Improved	**147**	**94.83**

Table 5: Treatment Interventions and Outcomes

According to table 5 16.8% required renal replacement therapy (RRT), showing a high rate of kidney dysfunction and 5.16% mortality rate, meaning most patients (94.83%) showed improvement after treatment.

Parameter	1 Month (%)	3 Months (%)
Normal Serum Creatinine	93.19	85.04
Increased Serum Creatinine	2.72	4.08
Urine Proteinuria (Nil)	76.1	70.06
CKD Stages 1-2	10.88	10.20
CKD Stages 3-5 (Severe)	7.5	8.16

Table 6: Follow-Up after 1 and 3 Months

In table 6 most patients showed improvement, but some progressed to CKD over three months. And in the same way 8.16% developed severe CKD (Stages 3-5), requiring long-term monitoring.

AKI Stage	No CKD (%)	CKD (Stage 1-2) (%)	Severe CKD (%)
AKI-1	67.3	27.5	5.2
AKI-2	35.6	41.0	23.4
AKI-3	15.2	38.1	46.7

Table 7: Association between AKI and CKD Progression

According to table 7 46.7% of patients with AKI-3 developed severe CKD, emphasizing the need for early intervention in AKI patients to prevent long-term kidney damage and patients with AKI-1 had the lowest progression to CKD, reinforcing the importance of early diagnosis and treatment.

DISCUSSION

The present study provides valuable insights into snake bite-induced acute kidney injury and its progression to chronic kidney disease, offering important comparisons with existing literature. Our demographic analysis revealed a clear male predominance (77.4%) with the majority of patients falling in the 30-40 years age group (22.6%). This gender distribution aligns closely with findings from Patil et al., who reported 84.2% male patients in their study [13]. However, it presents an interesting contrast to Vikrant et al.'s research, which found a higher proportion of female victims (57.9%).[14] The male predominance in our study likely reflects occupational exposure patterns, as most victims were from rural areas and were bitten during working hours, with 79.4% of bites occurring during daytime.

A significant finding in our study was the prompt presentation to healthcare facilities, with 87.1% of patients arriving within 6 hours of the bite. This represents a marked improvement compared to the mean arrival time of 3.4 ± 3.7 days reported by Vikrant et al. [14]. This earlier presentation time may be a crucial factor contributing to the better outcomes observed in our study, particularly regarding mortality and complications. The improvement in presentation time could be attributed to better awareness and accessibility of healthcare facilities in our region.

Regarding clinical manifestations, our study found an exceptionally high rate of local complications, with 96.12% of cases showing various degrees of local tissue involvement. All affected patients exhibited swelling and cellulitis, which notably differs from Vikrant et al.'s findings of only 13.6% cases with limb swelling/cellulitis [14]. However, our observations align perfectly with Patil et al.'s study, which reported cellulitis in 100% of cases [13]. This high rate of local complications strongly suggests a predominance of vasculotoxic envenomation in our geographical area. Of particular concern was the high rate of tourniquet application (67.75%) by patients before reaching the hospital, a practice that, while common, can potentially exacerbate local tissue damage and complicate outcomes, as documented in several studies.[1,3].

The laboratory parameters in our study revealed significant coagulation abnormalities, with 49.7% of cases showing thrombocytopenia, 98.7% exhibiting prolonged PT time, 93.50% showing increased WBCT, and 94.8% presenting with elevated INR. These findings indicate a higher prevalence of coagulopathy compared to Patil et al.'s study, which reported coagulation abnormalities in 36.8% of cases.[13] This variation might be attributed to differences in snake species or severity of envenomation across different geographical regions.

Study	AKI (%)	Dialysis Received (%)	Hospital Mortality among AKI Patients (%)
Ali et al (2004)	17	71	25
Athappan et al (2008)	13.5	45.3	22.5
Harshavardhan et al (2013)	14.6	44.4	22.3
Dharod et al (2013)	31	55	39
Mukhopadhyay et al (2016)	44.1	33.7	29.7
Tarun K et al	21	38	6
Present study		16.8%	5.16%

Table 8: Comparison of acute kidney injury (AKI), need for dialysis and mortality rates in different studies *(10,15–19)*

In terms of acute kidney injury progression, our study classified cases into three categories: AKI-1 (mild) at 44.5%, AKI-2 (moderate) at 25.2%, and AKI-3 (severe) at 30.3%. Notably, the requirement for renal replacement therapy in our study (16.8%) was substantially lower than other Indian studies, where dialysis requirements ranged from 33.7% to 71% [15-19]. This reduced need for dialysis could be attributed to our better presentation times and early intervention strategies, highlighting the importance of prompt medical attention in snake bite cases.

The mortality outcomes in our study were particularly encouraging, with an overall mortality rate of 5.16%, significantly lower than other studies reporting mortality rates ranging from 22.3% to 39%

in AKI patients.[15-19] This improved survival rate can be attributed to several factors, including earlier presentation to healthcare facilities, implementation of standardized treatment protocols, availability of renal replacement therapy, and enhanced supportive care measures.

Long-term follow-up results revealed varying degrees of progression to chronic kidney disease. While 70.1% of patients maintained normal renal function (eGFR grade 1), 21.8% developed mild dysfunction (grade 2), and 8.2% progressed to moderate-severe dysfunction (grades 3-5). These findings share similarities with Waikhom et al.'s study, which reported persistent renal abnormalities in 41% of patients at 45 months follow-up.[6] Particularly noteworthy was the progression to severe CKD in AKI-3 patients, where 46.7% developed severe CKD, emphasizing the critical importance of early intervention and consistent long-term monitoring.

The three-month follow-up period may not have been sufficient to capture very long-term outcomes. Additionally, the lack of snake species identification in many cases and limited data on socioeconomic factors affecting outcomes could have impacted our analysis. Future research should focus on extending follow-up periods to better understand CKD progression, analyzing species-specific treatment outcomes, investigating the role of early biomarkers in predicting AKI progression, and evaluating the impact of traditional practices on outcomes.

CONCLUSION

AKI caused by snake envenomation is a common complication. Most middle-aged men from lower socioeconomic classes are affected by this ailment. Most patients will recover with appropriate treatment including anti-snake venom, close monitoring, and timely dialysis. Out of 147 patients followed up one third patients were in different stages of CKD. Furthermore, we noted that the majority of individuals do not require dialysis and do not develop symptomatic renal morbidity. 1.38% (2 patients) had progressed to ESRD. Therefore, further prospective validation is necessary, and hospitals ought to support suitable, intense therapy that has the potential to save lives.

LIMITATIONS

A significant challenge we encountered was the absence of premorbid creatinine values for most patients, which made it impossible to definitively rule out the presence of prior chronic kidney disease (CKD). This limitation creates uncertainty in determining whether the observed kidney dysfunction was entirely attributable to snake envenomation or if there were pre-existing renal conditions that may have influenced the outcomes.

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