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Original Research Article

The Impact of Time Intervals on Snake Bite Treatment Outcomes: Insights from Anti-Snake Venom Administration

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Abstract:

Introduction: Snakebite envenomation represents a persistent health challenge, particularly in regions like India, where it exacts a considerable toll in terms of morbidity and mortality. Despite efforts to address this issue, gaps persist in understanding the treatment patterns and outcomes associated with snakebite incidents. In this study, we aim to investigate the patterns of snakebite envenomation treatment and its outcomes, focusing on factors such as treatment timing, anti-snake venom administration, complications, and mortality rates.

Material and Methods: This prospective observational study, conducted over an eight-month period at a tertiary care center in Mumbai, aimed to investigate the time interval between snake bite incidents and the administration of anti-snake venom (ASV) as a prognostic indicator of patient outcomes in snake bite envenomation cases. Patients presenting with confirmed snake bite envenomation were included, and detailed clinical assessments, including history, physical examination, and laboratory investigations, were conducted. ASV administration and clinical outcomes were closely monitored, with data analyzed to assess the association between treatment timing and patient outcomes. The study underscores the importance of timely intervention in snake bite management to improve patient prognosis.

Results: In our study involving 80 patients treated for snake bite envenomation, significant findings emerged regarding demographics, treatment timing, complications, and outcomes. A notable gender disparity was observed, with males comprising 58.75% of cases, and individuals aged 19-30 years represented 22.5% of the cohort. Kraits were the most common snake species encountered (41.25%), followed by Vipers (25.0%) and Cobras (18.75%), with 15.0% of cases involving unidentified species. Most patients received anti-snake venom within 6 hours of the bite (47.5%), and the distribution of ASV vials varied significantly, with 37.5% receiving 5 vials and 25.0% receiving 20 vials. Complications, predominantly cellulitis (56.25%) and acute kidney injury (37.5%), were observed, alongside an overall mortality rate of 8.75%. Notably, associations were found between treatment timing, vial administration, and mortality rates, emphasizing the critical importance of timely intervention and appropriate management strategies in snake bite cases ($p<0.05$).

Conclusion: Our study highlights key associations in snakebite management, revealing that prompt anti-snake venom administration within 6 hours correlates with increased vial usage and longer hospital stays. Additionally, higher vial usage is linked to higher mortality rates, emphasizing the critical importance of timely intervention in improving patient outcomes.

Keywords: Snake Bite, Envenomation, Anti-Snake Venom, Treatment Timing, Outcomes.

Introduction

Snake bite envenomation is a significant medical emergency that necessitates prompt intervention to prevent severe morbidity and mortality in India. [1] The administration of anti-snake venom (ASV) is the cornerstone of treatment, as it neutralizes the toxins present in snake venom, thereby mitigating the adverse effects. [2] However, the efficacy of ASV is heavily influenced by the timing of its administration. [3] Delays in treatment can lead to increased severity of envenomation symptoms and

poorer patient outcomes. [4] Consequently, the time interval between the snake bite and ASV administration has emerged as a critical prognostic indicator in the management of snake bite cases. [5,6] The period immediately following a snake bite is crucial, as venom components rapidly disseminate through the circulatory system, causing systemic toxicity. [7] Early administration of ASV can significantly reduce the burden of venom on the body, limit tissue damage, and improve overall recovery rates. [8] Conversely, prolonged intervals before ASV administration allow for greater venom absorption and distribution, leading to more extensive tissue damage and systemic complications. Therefore, understanding and optimizing the time frame for ASV administration is essential for improving clinical outcomes and guiding treatment protocols in snake bite envenomation. [9]

Research indicates that shorter time intervals between snake bite and ASV administration are associated with better prognoses and reduced complication rates. [3,5] Studies [4,7] have demonstrated that patients receiving ASV within the first few hours of a snake bite exhibit fewer severe symptoms and complications compared to those treated after a prolonged delay.

This relationship underscores the importance of rapid medical response and efficient healthcare systems in areas prone to snake bites. [10,11] By focusing on minimizing the delay in ASV administration, healthcare providers can enhance the effectiveness of snake bite management and improve survival rates among affected individuals.

Material and Methods

This prospective observational study was conducted at a tertiary care center in Mumbai over an eight-month period from April 2023 to September 2023. The study aimed to investigate the time interval between snake bite incidents and the administration of anti-snake venom (ASV) as a prognostic indicator of patient outcomes in snake bite envenomation cases. Patients of all ages who presented with confirmed snake bite envenomation were eligible for inclusion in the study. Confirmation of envenomation was based on clinical signs and symptoms, patient history, and, when available, identification of the snake species.

Patients who received pre-hospital ASV administration were excluded to maintain consistency in the evaluation of hospital-based intervention times. Additionally, individuals with incomplete medical records or those who left against medical advice before the completion of treatment were excluded from the study. A total of 80 patients were included in the study after fulfilling the inclusion and exclusion criteria. After obtaining informed consent from the patients to participate in the study, a detailed history and physical examination were conducted.

The history included the time since the snake bite, the site of the bite, the species of snake, and the symptoms at presentation, such as level of consciousness, pain at the bite site, cellulitis, vomiting, abdominal pain, ptosis, respiratory failure, oliguria, and bleeding manifestations. A thorough physical examination of the cardiovascular system (CVS), respiratory system (RS), abdomen, and central nervous system (CNS) was performed. Investigations such as whole blood clotting time (WBCT), complete blood count (CBC), renal function tests (RFT), liver function tests (LFT), coagulation profile, and urine analysis were conducted. ASV was administered according to the existing institutional protocol. The "Bite to Needle Time," which is the time interval between the snake bite and ASV administration, was recorded. The total number of ASV vials administered was also noted. Patients were categorized based on the time interval between the snake bite and ASV administration: within 1 hour, 1-3 hours, 3-6 hours, and more than 6 hours.

The primary outcome measured was the severity of envenomation, classified using a standardized grading system that considered local and systemic manifestations. Secondary outcomes included the duration of hospital stay, need for intensive care unit (ICU) admission, incidence of complications (e.g., coagulopathy, renal failure, neurotoxicity), and overall mortality. Patients were closely monitored for the development of complications until the time of discharge.

Data were analyzed using appropriate statistical methods to compare the outcomes across different time interval groups. Continuous variables were expressed as means and standard deviations, while categorical variables were presented as frequencies and percentages. The association between the time interval to ASV administration and clinical outcomes was assessed using chi-square tests for categorical variables and analysis of variance (ANOVA) for continuous variables. P value less than 0.05 was considered statistically significant for analysis purpose.

Results

Our study, comprising 80 patients receiving treatment for snake bite envenomation, unveiled a notable gender disparity, with males constituting the majority at 58.75%. Furthermore, our analysis revealed a pronounced vulnerability am0ong individuals aged 19-30 years, comprising 22.5% of the cases. (Figure 1) Among the patients treated for envenomation, Kraits were the most common snake species (41.25%), followed by Vipers (25.0%) and Cobras (18.75%). Notably, 15.0% of cases presented with unidentified snake species.

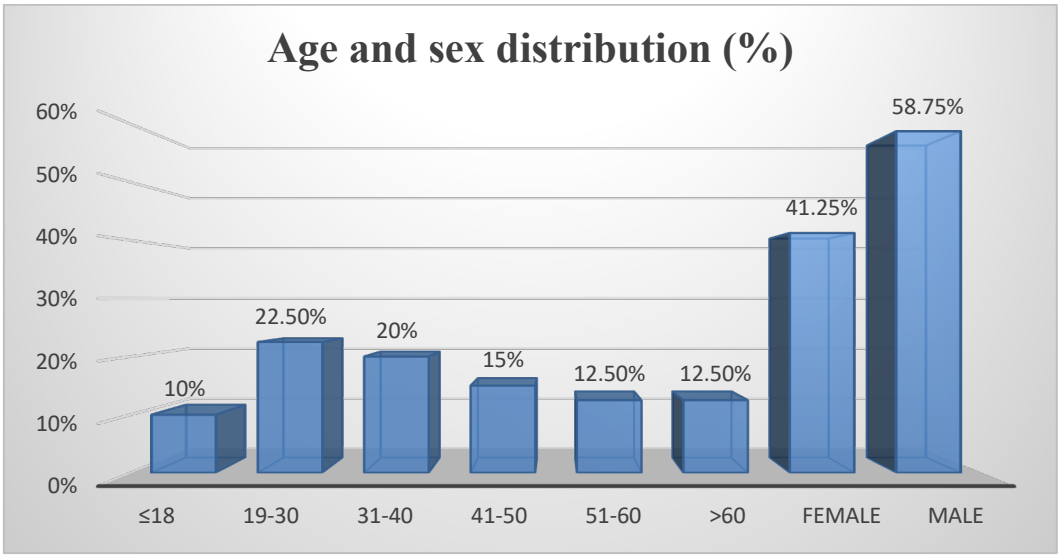

Figure 1: Age and sex distribution (%)

The majority of patients received anti-snake venom within 6 hours of the snake bite (47.5%), followed by those treated between 6-12 hours (27.5%). A smaller proportion received treatment between 12-24 hours (12.5%), while an equal number experienced delays of over 24 hours before receiving treatment (12.5%).

In the treatment of snake bites among 80 patients, the distribution of anti-snake venom (ASV) vials demonstrated significant variation. The majority received 5 vials (37.5%) or 20 vials (25.0%), while 22.5% received 10 vials, and 15.0% received 15 vials. In the assessment of clotting time among 80 patients treated for snake bites, 18.75% exhibited a clotting time of less than 20 minutes, while the majority (81.25%) showed clotting times exceeding 20 minutes.

In our study of snake bite complications among 80 patients, cellulitis was the most prevalent, affecting 56.25% of individuals. This was followed by acute kidney injury (37.5%), respiratory failure (12.5%), septic shock (3.75%), and disseminated intravascular coagulation (DIC) in a smaller proportion (2.5%). (Table 1)

Table 1: Complications Associated with Snake Bite

Complications	Frequency	Percent (%)
Cellulitis	45	56.25
Acute Kidney Injury	30	37.5
DIC	2	2.5
Septic Shock	3	3.75
Respiratory Failure	10	12.5
Total	**80**	**100.0**

The hospitalization duration varied among the 80 patients treated for snake bite envenomation. Approximately 6.25% of patients were discharged in less than 5 days, while 43.75% required hospitalization for 5-10 days, and 50.0% stayed for more than 10 days. Additionally, in our study, mortality was observed in 8.75% of patients, while the majority (91.25%) survived. This table 2 categorizes complications by treatment timing for snake bite patients. It shows significant associations ($p < 0.05$) between treatment delays and varying complication rates, highlighting the importance of prompt anti-snake venom administration.

Table 2: Association between Treatment Timing and Complications

Bite to Needle Time	Cellulitis	Acute Kidney Injury	DIC	Septic Shock	Respiratory Failure	P value
<6	38(84.4%)	23 (76.7%)	1 (50%)	2 (66.7%)	6 (60%)	0.001
6-12	6 (13.3%)	5 (16.7%)	0 (0%)	0 (0%)	2 (20%)	0.011
12-24	1 (2.2%)	2 (6.7%)	1 (50%)	0 (0%)	1 (10%)	0.008
>24	0 (0%)	0 (0%)	0 (0%)	1 (33.3%)	1 (10%)	0.022
Total	45 (100%)	30 (100%)	2(100%)	3 (100%)	10 (100%)	-

In our study, we established a significant link between the number of vials administered and the time from snake bite to treatment ($p < 0.05$). Patients treated within 6 hours tended to receive a higher number of vials. Similarly, a notable correlation was observed between bite-to-needle time and hospital stay duration ($p < 0.05$). Patients with shorter bite-to-needle times had longer hospital stays, with 41% of those treated within 6 hours requiring stays exceeding 10 days.

Furthermore, our findings demonstrated a significant association between the number of anti-snake venom (ASV) vials administered and mortality rates ($p < 0.05$). Patients receiving 30 vials had a mortality rate of 60%, while those receiving 10 or 20 vials had mortality rates of 20% each. Additionally, mortality rates were notably higher in patients with longer hospital stays (>10 days), with a mortality rate of 60%, compared to 40% among those with stays of 5-10 days ($p < 0.05$).

Discussion

Snake bites pose a significant health threat globally, particularly in tropical regions, with India reporting the highest mortality rates attributed to snake bites. Annually, India records approximately 250,000 snake bite incidents, resulting in 50,000 deaths. [12] However, the true extent of mortality and morbidity remains uncertain. Among the 236 snake species in India, most are nonpoisonous, causing minimal harm aside from local injuries. However, among the 13 venomous species, including the common cobra, Russell's viper, saw-scaled viper, and common krait, account for the majority of poisonous bites in the country. [13,14]

Our study, which included 80 patients treated for snake bite envenomation, revealed a notable gender imbalance, with males comprising 58.75% of the cases. Additionally, individuals aged 19-30 years were found to be particularly vulnerable, constituting 22.5% of the cases. These findings align with previous research conducted by Yaqoob and Mufti [15], who analyzed 108 cases over 36 months. Their study reported a male predominance of 57.40% and highlighted a significant proportion of patients aged 10 to 30 years (46.29%). Similarly, Halesha et al. [16] found that the majority of their 180 snake bite cases were aged between 20 and 40 years, suggesting a common trend across studies. Our findings were consistent with previous research. [17,18] This age group's high representation could be attributed to their active lifestyles and occupational exposure in fields. Our study revealed a predominance of snake bites from Russell's viper species (35%), followed by common krait (29%) and cobra (20%). In 16% of cases, the snake species remained unidentified. These findings are in line with the research conducted by Yaqoob and Mufti [15], where 62.96% of snake bites were attributed to vipers, with the remainder from unidentified snakes. Notably, cobras, commonly found in other parts of India, were not reported in our region, consistent with the absence of neurotoxic envenomation cases in our study district. Instead, vipers, known for their haematotoxic venom, were the prevalent poisonous snakes encountered.

In our study, a significant proportion of patients received anti-snake venom within six hours of the snake bite (47.5%), with another notable percentage treated between 6 to 12 hours (27.5%). A smaller group underwent treatment between 12 to 24 hours (12.5%), while an equal number experienced delays exceeding 24 hours before receiving treatment (12.5%). Notably, while previous research has not extensively explored the lag time, select studies by Anil et al. [19], Kularatne et al. [20], and Harsoor et al. [21] have reported time ranges from 0.5 to 10 hours. Yaqoob et al.'s [15] study revealed a reduction in mean time taken by patients to reach the hospital over the years, from 6.3 ± 2.2 hours in 2004 to 4.3 ± 1.3 hours in 2009. Interestingly, we found a significant association between mortality rates and bite-to-needle time ($p < 0.05$), with a higher mortality rate (50%) observed among patients experiencing delays exceeding 24 hours before treatment initiation. While the precise reasons for this decrease in lag time remain uncertain, it is plausible that increased awareness about snake bite treatment options and the availability of such facilities at the Medical College Hospital may have contributed to this positive trend. This shift could signify a move away from ineffective remedies and toward timely medical intervention, potentially saving lives.

In our study, the majority of patients received 5 vials (37.5%) or 20 vials (25.0%), with 22.5% receiving 10 vials and 15.0% receiving 15 vials. Among the 80 patients treated for snake bites, 18.75% exhibited clotting times of less than 20 minutes, while the majority (81.25%) showed clotting times exceeding 20 minutes. This corresponds to findings by Asif et al. [22], who reported a similar mean effective dose of ASV at 120ml. Notably, patients with coagulopathy required a mean ASV of 110ml, while those with neurotoxicity required a mean ASV of 195ml. Additionally, a significant association was found between the number of vials administered and the bite-to-needle time ($p < 0.05$), with higher vial usage observed in patients treated within 6 hours of the bite. Although our study did not record doses according to bite toxicity, Yaqoob et al. [15] reported ASV usage in neurotoxic envenomation parallel to Pramiladevi et al. [23] (180ml) but higher than Bawaskar (150ml). [24] Our mean

ASV dose was 12.3 ± 2.4 vials, differing from Harsoor et al.'s reported mean dose of 146ml, which was notably less than that reported by Agarwal et al. [25] and Sharma et al. [26] These variations could be attributed to differing degrees of envenomation among patients. Furthermore, Ahmed et al. [11] found a highly significant relationship between lag time and total ASV dose, indicating the importance of timely administration in snake bite management.

Yaqoob et al. [27] study, mortality was higher (40%) in patients who developed renal failure with statistically significant (P value 0.005). In various studies, the symptoms of oligoanuria has been reported to be 13.8%-100% [28–31] and hematuria/black colored urine 24.6%-80% [18,28–31] as compared to that of 79.5% and 54.5% respectively in our study. Cellulitis was 39%-98.7% [28–30,32] as compared to that of 13.6% observed in our study, hypotension of 4.5% observed in current study as compared to that of 6.3%-45.2% in other studies [28–31] neurotoxicity of 5.7% as compared to that of 3.2%-100% in other studies [29,31,33].

Bleeding/coagulopathy which is a major symptom of systemic viper poisoning was observed in 88.6% patients as compared to 27.8%-65.8% in other studies of snake bite-induced AKI. [29–31,34] Disseminated intravascular coagulation (DIC) has been one of the major contributors to death in many studies. [35] Though WHO and Indian National Snakebite Protocols 2007 [36] has given recommendation for treatment, in some patients bleeding may continue in spite of giving sufficient doses of ASV.

In such cases ASV should be continued until coagulation abnormalities are restored. In our study, in case of neuroparalysis and acute renal failure, we continued ASV until they responded. In a study conducted by Agrawal et al., [37] ASV was given to patients with neuroparalysis until recovery of neurological manifestations.

Our study revealed significant associations between various factors in snakebite treatment. We found that administering more vials was linked to shorter treatment delays ($p < 0.05$), while shorter treatment delays correlated with longer hospital stays ($p < 0.05$).

Moreover, higher vial usage was associated with increased mortality rates ($p < 0.05$), and longer hospital stays were linked to higher mortality ($p < 0.05$). These findings underscore the importance of prompt treatment and efficient healthcare delivery systems in mitigating the impact of snakebite envenomation. Most of the studies have observed this correlation between bite to hospital time and complications or mortality. [35,38,39] This can be explained by the fact that incidence of complications is directly proportional to the duration of venom in the blood prior to its neutralization by ASV due to late arrival of patient at hospital (Narvencar *et al*.) [40] and as complications occur mortality will increase. This delay can be attributed to lack of awareness of hazards of snake bite, belief in traditional methods of treatment, lack of proper referral systems and transport facilities. [41] Many of the times ASV may not be available at primary health centers (PHCs) and patients may not receive ASV until they reach higher centers. In Yaqoob et al. [27] study, no statistical significance on comparing mortality with age, sex, bite site, use of first aid measures like tourniquet and incision, and hypotension. Mortality was higher (40%) in patients who developed renal failure. [27] Primary care physicians should use Antivenom appropriately when indicated, counsel masses about harm of unscientific methods used by local population after snake bite, and referral to appropriate centers in view of complications. The reason for low mortality in our study is the better availability of ventilatory support and intensive care facilities.

While our study offers valuable insights, its single-center design and retrospective nature may limit the generalizability and introduce biases. Additionally, the relatively small sample size of 80 patients may not fully represent the diversity of snakebite cases. These limitations underscore the need for larger, prospective studies across multiple centers to provide a more robust understanding of snakebite management and outcomes.

Conclusion

Our study elucidates significant correlations between various aspects of snakebite management, revealing pivotal insights into treatment timing, vial administration, and patient outcomes. We found that administering anti-snake venom within 6 hours of the bite was associated with higher vial usage, while shorter treatment delays correlated with longer hospital stays.

Moreover, higher vial usage was linked to increased mortality rates, underscoring the critical importance of timely intervention in mitigating adverse outcomes. These findings emphasize the imperative for efficient healthcare systems and prompt access to anti-snake venom to optimize patient care and outcomes in snakebite envenomation cases.

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