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INCIDENCE AND SAFETY PROFILE OF POLYVALENT ANTIVENOM IN HEMOTOXIC AND NEUROTOXIC SNAKEBITE VICTIMS: A TERTIARY CARE EXPERIENCE

Deva kumar.K[1], Sumetha suga.D[2*], Selvalaxmi .G[3], Sri devi S.A[4]

[1]Assistant professor, Department of Pharmacology, A.C.S medical college and hospital, affiliated to Dr.M.G.R educational and research institute, Chennai, Tamilnadu, India.
[2*]Associate professor, Department of Microbiology, A.C.S medical college and hospital, affiliated to Dr.M.G.R educational and research institute. Chennai, Tamilnadu, India.
[3]Associate professor, Department of Pharmacology, Bhaarath Medical College and Hospital, Bharath institute of higher education and research. Chennai, Tamilnadu, India
[4]Professor, Department of Pharmacology, A.C.S medical college and hospital, affiliated to Dr.M.G.R educational and research institute. Chennai, Tamilnadu, India.

***Corresponding Author:** Sumetha suga.D
*Mail ID: smilesumetha@gmail.com

Abstract

Snakebite envenoming remains a significant public health concern, particularly in tropical and subtropical regions. Hemotoxic and neurotoxic envenomation present unique clinical challenges, with anti-snake venom (ASV) being the primary treatment. However, adverse drug reactions (ADRs) to ASV, though rare, can range from mild allergic responses to severe complications such as anaphylaxis and renal failure. Underreporting of ADRs further complicates pharmacovigilance efforts, particularly in India. This study aims to estimate the incidence of ADRs in ASV-treated patients with hemotoxic and neurotoxic envenomation, compare the frequency and spectrum of ADRs between envenomation types, and assess ASV safety profiles across three manufacturers. This study is a prospective, observational, multicentre study which was conducted from January 2023 to December 2024 across two government secondary care centers (Perambalur and Ariyalur) and a private hospital in Erode. Data collection included demographics, envenomation classification, ASV details (manufacturer, batch number, dosing), and ADR documentation. The results among the 476 snakebite cases, Perambalur accounted for 77.73%, highlighting a localized risk factor. Laborers were the predominant victims (71.9%), with peak incidence observed between August and November. Of 206 ASV-treated patients, 55 (26.7%) experienced ADRs, with haemotoxic envenomation cases showing the highest incidence (27.08%). Notably, females exhibited a higher ADR rate (31.1%). Lack of pre-hospital intervention was associated with a significant increase in ADRs (28.4%). Patients requiring higher ASV doses (11–20 vials) had a greater likelihood of adverse events, particularly in haemotoxic (40.7%) and neurotoxic (55%) envenomation cases. The conclusion of the study is to underscores the necessity for enhanced pharmacovigilance, early intervention, and optimized ASV administration to mitigate ADR risks. Geographic variations, envenomation types, and manufacturer differences necessitate further investigation to refine treatment protocols and improve patient outcomes.

Key words: snake bite, Adverse drug reaction, anti-snake venom, haemotoxic envenomation, neurotoxic envenomation

Introduction

Snakebite envenoming remains a major public health concern in many parts of the world, especially in tropical and subtropical regions.[1] Among various manifestations of envenoming, hemotoxic and neurotoxic bites present distinct challenges for management due to the differences in the venom's effects on the body. Hemotoxic venom primarily affects the blood and tissues, leading to haemorrhagic disorders, coagulopathy, and tissue necrosis, while neurotoxic venom affects nervous system, leading to general paralysis and respiratory failure.[1,2] The administration of anti-snake venom (ASV) is the cornerstone of treatment for snakebites. However, despite its life-saving effect, the use of ASV also has some adverse effects. Adverse drug reactions (ADRs) to ASV, even though it is rare, it can range from mild to severe allergic reactions like anaphylaxis, serum sickness, and even end up renal failure.[3] These ADRs can complicate the clinical management of snakebite envenoming and require prompt recognition and intervention.[4]

Adverse Drug Reactions (ADRs) pose a significant burden on healthcare systems, ranking among the leading causes of death and contributing substantially to hospital costs. While the prevalence of ADRs is well-documented, with 5-10% of hospital expenses attributable to them, underreporting remains a critical challenge.[4] Estimates suggest only a fraction of ADRs are actually reported, leading to a potentially skewed understanding of the true impact. This is particularly concerning in India, where pharmacovigilance reporting rates are significantly lower than global averages.[2,5] The preventable nature of a considerable proportion of ADRs, estimated between 60-70%, underscores the importance of robust pharmacovigilance systems.[6] Implementing effective pharmacovigilance programs represents a cost-effective investment, minimizing patient suffering and alleviating the financial strain on healthcare resources.[7] Prioritizing and strengthening pharmacovigilance infrastructure is therefore crucial for improving patient outcomes and ensuring the sustainability of healthcare systems globally. ASV is the only lifesaving treatment for snakebite; yet carries its own potential risks. The reactions due to ASV are unpredictable and under-reported. Moreover, the cost and the adverse reaction are often the primary factors considered. There is a continuous crisis in the production, deployment and accessibility of antivenom worldwide. As a result. the pattern of utilization pattern tends to vary in across different regions.[8]

Antivenom serum (ASV), derived from the "Big 4" snakes, remains the cornerstone of snakebite treatment.[3,7] The "Big 4" concept, designed for public awareness, highlights the most medically significant snakes in a given region.[9] While ASV efficacy is paramount, the absence of age-adjusted dosing raises concerns about its safety and effectiveness across the diverse patient population, from children to the elderly.[7] Given the high cost of snakebite management (ranging from Rs. 5,000 to Rs. 2,00,000), coupled with the severe physiological impact of snake venom, focusing solely on ASV may be insufficient.[10] A comprehensive approach, prioritizing optimal patient outcomes, necessitates exploring complementary therapies, refined dosing strategies, and cost-effective preventative measures to improve snakebite management overall.

Snakebite envenoming was only recognized as a Neglected Tropical Disease (NTD) by the WHO in 2009, triggering a surge in snakebite research over the past decade.[11] However, a critical gap persists in understanding antivenom (ASV) utilization patterns and associated adverse reactions, particularly in regions like India, where ASV manufacturing is limited and primarily focused on polyvalent formulations.[12] The incidence of ASV-related adverse reactions remains a subject of ongoing debate. This study aims to address this deficiency by analyzing adverse reaction profiles across different ASV manufacturers. Focusing on the previously unstudied regions of Perambalur and Ariyalur, the research will also contribute to the epidemiological understanding of snakebites in these locations. Furthermore, the study will explore differing perceptions regarding the safety and efficacy of ASVs from various manufacturers, providing valuable insights for improving treatment protocols and addressing the challenges associated with snakebite management in the region. Several in-vitro

studies have revealed mixed results regarding different manufactures.[7,13] Therefore, the present study was conducted to analyze the ADR and compare their safety profile of ASV used in three districts of Tamilnadu.

This prospective observational study aims to explore the adverse drug reactions associated with ASV administration in patients suffering from hemotoxic and neurotoxic snakebites. By identifying the types and frequency of these reactions, the study seeks to provide valuable insights into the safety profile of ASV and contribute to improving patient outcomes. Understanding the incidence and nature of ADRs will also help guide clinical decision-making and enhance the management protocols for snakebites.

OBJECTIVES

- To estimate the incidence of adverse reactions to anti-snake venom (ASV) in patients with hemotoxic and neurotoxic envenomation.
- To compare the frequency and spectrum of Adverse drug reactions between hemotoxic and neurotoxic bite.

MATERIALS AND METHODS:

The ethical and logistical groundwork laid for this study was conducted at Dhanalakshmi Srinivasan Medical College and Hospital, Perambalur. Furthermore, the study's scope was broadened through a collaborative approach, involving permission obtained from authorities at two governments secondary care centres in Perambalur and Ariyalur districts, and a private hospital in Erode. This multi-institutional approach likely aimed to enhance the representativeness and generalizability of the findings by capturing data from a diverse patient population across different healthcare settings.

Inclusion criteria:

- All patients admitted with a history of snakebite during the study period at any of the three participating centers (one tertiary-care hospital in Perambalur, two government secondary-care centers in Perambalur and Ariyalur districts, and one private hospital in Erode)
- Clinical and/or laboratory evidence of hemotoxic or neurotoxic envenomation

Exclusion criteria:

- Bites of unknown origin (no clear history or witness account)
- Absence of any clinical, laboratory or imaging evidence to support snake envenomation.

Methodology:

Study Design & Setting: Prospective, observational, multicentre study conducted over a period of one year at Two government secondary care centers (Perambalur and Ariyalur) and a private hospital in Erode.

Data Collection: Demographics & Clinical Profile including systemic envenomation signs (Envenomation Type: classified as hemotoxic or neurotoxic based on standard clinical/laboratory criteria), ASV Details [Manufacturer and coded label (Biovins = ASV I; Biological E Ltd = ASV II; Bharat Serums = ASV III) – Batch number, manufacture date], dosing details and adverse drug reactions (ADRs).

The management of snakebite is as follows:

The management of snakebite patients includes thorough examination and securing airway. WBCT, a quick coagulopathy detecting test done for every patient.

For hemotoxic snakebites, (WBCT >20 mins or bleeding), 1 vial of ASV is administered in normal saline over 15 mins, with 7 more vials if there are no adverse reactions occur. If bleeding persists and

WBCT >20 mins after 6 hours, 5 vials given every 2 hours, and the procedure repeated up to 3 times. Fresh frozen plasma or Packed cells given in required cases.[14]

For neurotoxic signs such as Dysphagia, Diplopia, etc., ASV administered and reassessed every 2 hours with further doses if required. If patient develops respiratory distress, Atropine, Neostigmine (as prescribed doses) and ventilator support are provided. Anaphylactic reactions were treated with Epinephrine, Chlorpheniramine, Ranitidine, Saline and Hydrocortisone (at prescribed doses). All patients were monitored for 12 to 24 hours.[14]

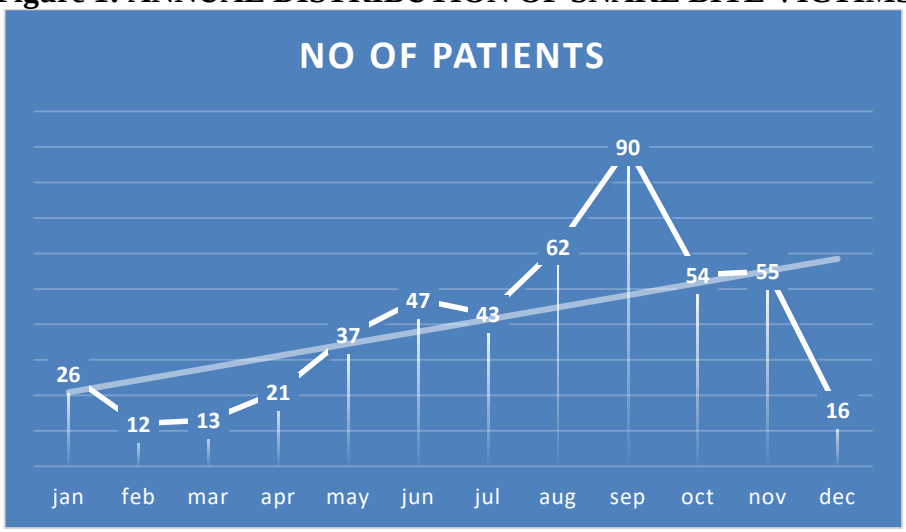
Statistical analysis was done using SPSS software. Descriptive statistics, Percentages were used for analysis.

Results

The study comprised 476 individuals, with the majority—370 participants (77.73%)—residing in Perambalur district. Ariyalur contributed 64 patients (13.44%), while 42 participants (8.82%) were from Erode district.

Significant majority (370 patients) originated from the Perambalur district, which is indicating a localized risk factor. Ariyalur district contributed 13.44% (64 patients), while Erode district accounted for 8.82% (42 patients) of the sample. The adult age group, spanning 20 to 59 years, constituted the largest proportion of participants at 72.5% (345 patients), suggesting heightened exposure within this demographic. Temporal analysis reveals a distinct seasonal pattern, with snakebite incidence peaking in September (19% of cases) as shown in figure 1. Conversely, February exhibited the lowest occurrence. Furthermore, the period between August and November accounted for approximately 55% of all snakebite incidents within the study population, highlighting a specific window of elevated risk. These findings underscore the need for targeted public health interventions focused on the Perambalur district, the adult age group, and the period spanning August to November.

Figure 1: ANNUAL DISTRIBUTION OF SNAKE BITE VICTIMS



A retrospective analysis reveals critical insights into snakebite incidence and management within the affected population. Laborers constituted the majority of victims (71.9%), followed by students (9.03%), indicating a disproportionate occupational hazard. A significant number of incidents (43.9%) occurred during the evening hours (6 pm - 12 am), highlighting a temporal risk factor. Alarmingly, 87% of victims received no first aid, suggesting a critical gap in community knowledge and preparedness. Despite this, some patients resorted to traditional remedies like turmeric application (4.2%) and ingestion of Andrographis paniculata (2.5%). Pain was the predominant symptom reported (85%), with Ptosis, dyspnea, and drowsiness also observed, consistent with neurotoxic envenomation. Furthermore, a Whole Blood Clotting Time (WBCT) exceeding 20 minutes was observed in 34.9% of cases characterized by local envenomation, contrasting with a

mere 2% in cases involving haemotoxic and neurotoxic effects. This data underscores the need for improved education on snakebite prevention, first aid protocols, and appropriate medical intervention to mitigate morbidity and mortality. Further investigation is warranted to identify specific snake species involved and optimize treatment strategies.

This brief analysis of snakebite patients reveals several key trends within the studied population. Local envenomation is the predominant manifestation, with a notably high proportion of cases (61.35%) originating from the Perambalur District. This suggests a potential ecological or occupational risk factor specific to that region that warrants further investigation. Encouragingly, a significant majority (82.5%) sought treatment within one hour of the bite, indicating effective awareness campaigns or accessible healthcare facilities. However, the presence of patients arriving after 12 hours underscores the persistent need to address barriers to timely medical care. The reliance on the availability of Anti-Snake Venom (ASV) from different manufacturers highlights a potential logistical challenge in maintaining a consistent and readily accessible supply. These observations collectively point to a need for targeted interventions, including enhanced preventative measures in Perambalur, continuous efforts to improve timely access to healthcare, and optimized ASV procurement and distribution strategies.

Out of 206 patients with Anti Snake Venom treatment, 55 (26.7%) cases had adverse reactions with 35/143 cases in Perambalur, 5/21 cases in Ariyalur and 15/42 cases in Erode. 39(27.08 %) adverse reactions observed were among patients with Haemotoxic envenomation. 8(29.62 %), 6(23.07%), 2(22.22%) adverse reactions among local, neurotoxic and haemotoxic/neurotoxic envenomation respectively.

Further analysis based on envenomation type indicated that patients with haemotoxic envenomation comprised the largest group experiencing adverse reactions, accounting for 39 cases (27.08%) while the number of reactions within each envenomation category differed, the percentages were relatively consistent. These findings highlight the need for continued investigation into the factors contributing to adverse reactions following ASV administration, with particular attention given to geographical variations and envenomation type. Further research is warranted to optimize ASV protocols and minimize patient morbidity.

Figure 2: ANALYSIS OF SNAKEBITE CASES BASED ON TYPE OF ENVENOMATION

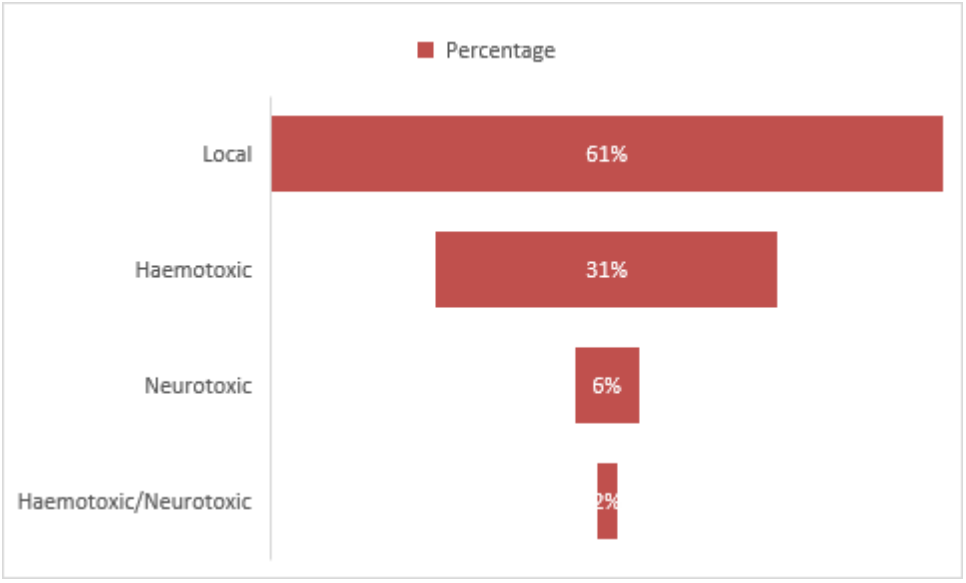


Figure 3: CATEGORICAL ANALYSIS OF ADVERSE DRUG REACTIONS BASED ON SNAKEBITE ENVENOMATION TYPES

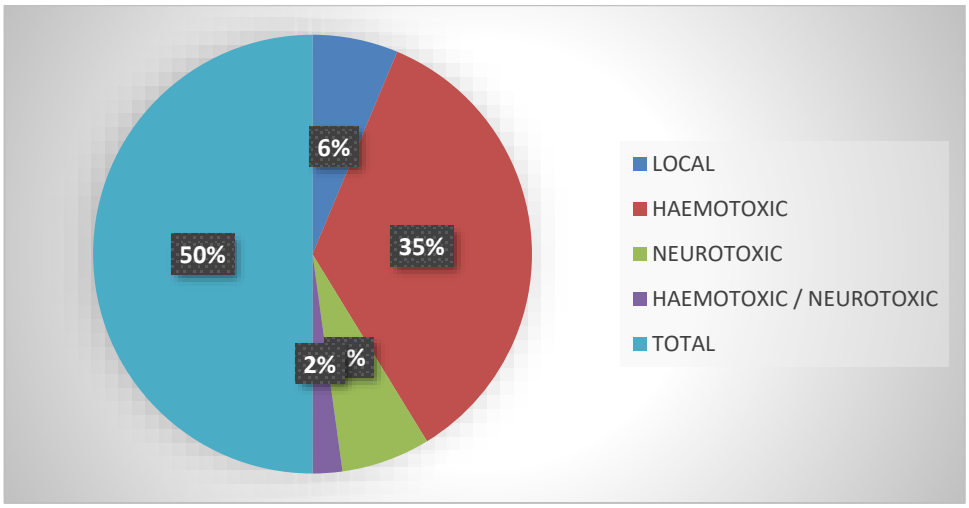


Table 1: DISTRIBUTION PATTERNS OF ANTISNAKE VENOM FOR HEMOTOXIC AND NEUROTOXIC ENVENOMATION

TYPE OF ENVENOMATION	TOTAL ASV VIALS USED	MEAN VIALS USED	RANGE (vials)
HAEMOTOXIC	1634	11.5±5.6	1 to 30
NEUROTOXIC	392	17±6.1	5 to 26

The observed usage of anti-snake venom (ASV) vials in Perambalur district presents a notable case within the context of a larger study. The documented administration of approximately 30 ASV vials in Perambalur, compared to the overall study mean of 11.59 ± 6.38 vials and a total of 2330 vials used, suggests a potential deviation from the average treatment protocol. Further analysis, considering the breakdown of ASV usage in haemotoxic (11.5 ± 5.6 vials) and neurotoxic (17 ± 6.1 vials) snakebite cases, as outlined in Table 1, is crucial. Specifically, the higher-than-average ASV consumption in Perambalur warrants investigation into factors influencing treatment decisions, potentially including the severity of snakebite cases encountered, the availability of resources, or variations in physician practices within the district. Understanding these underlying influences is essential for optimizing ASV usage and improving patient outcomes in future snakebite management strategies.

Figure 4: ADVERSE REACTIONS RELATED TO PRE-HOSPITAL INTERVENTIONS PATTERNS

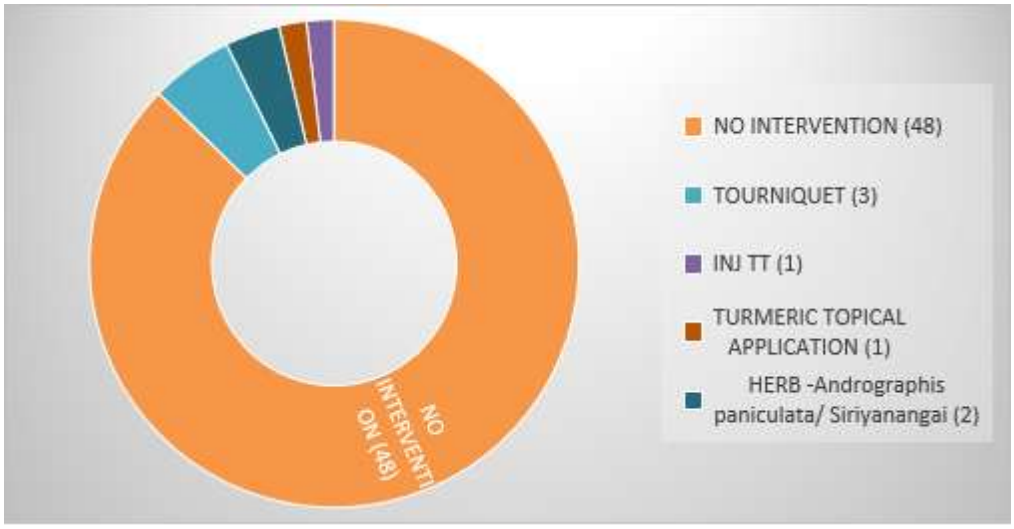


Figure 5: IMPACT OF ANTIVENOM VIAL COUNT ON OCCURRENCE OF ADVERSE REACTIONS

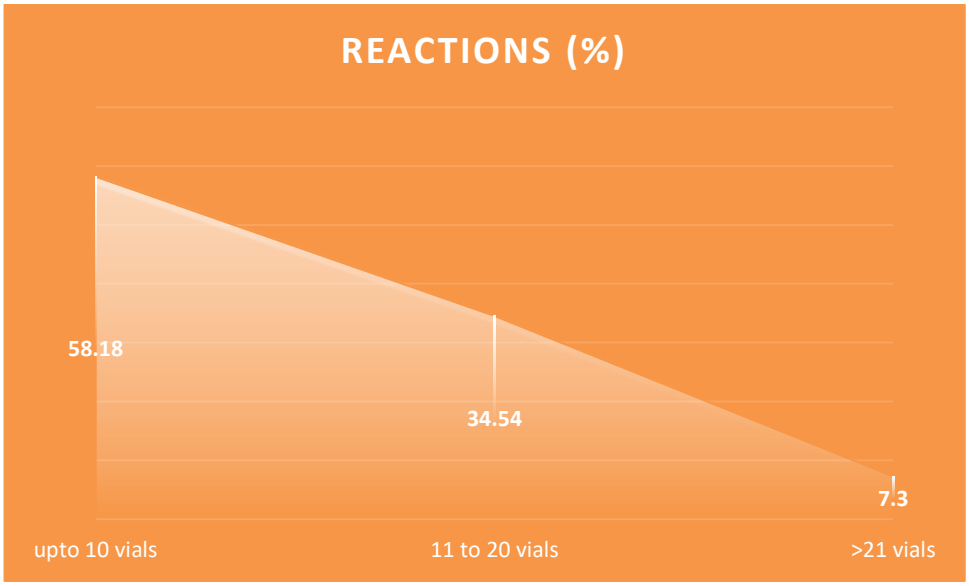
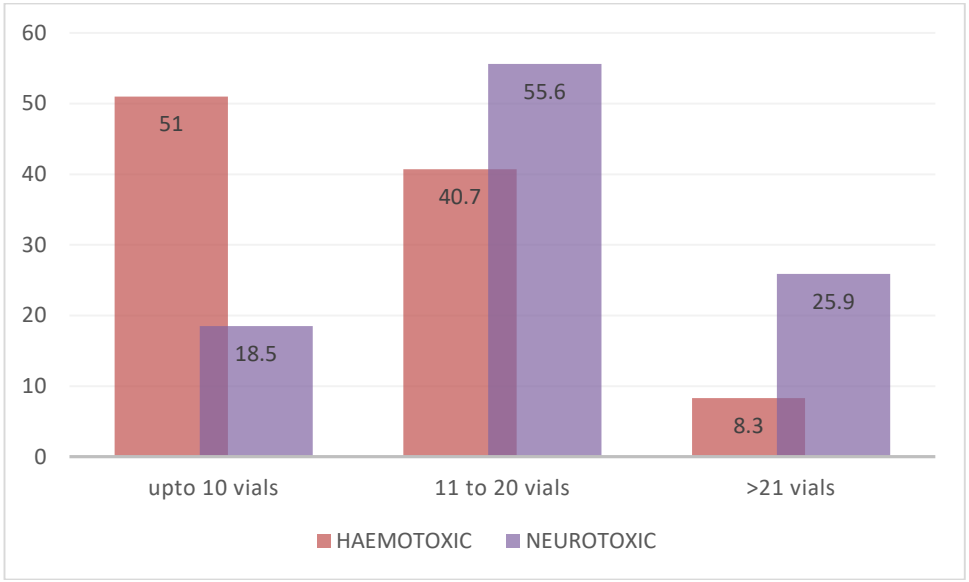


Figure 6: UTILIZATION PATTERNS OF ANTI-SNAKE VENOM IN HEMOTOXIC AND NEUROTOXIC SNAKEBITE CASES



This study elucidates several key aspects of antivenom serum (ASV) use and adverse reactions within the examined population. Notably, females experienced a higher incidence of adverse reactions (31.1%). Furthermore, the lack of pre-hospital intervention was associated with a significant 28.4% of adverse reactions. The data shown in figure 5 suggests a correlation between the number of ASV vials administered and adverse reactions, with patients receiving between 1 and 10 vials exhibiting a higher likelihood of such events. Specifically, a substantial proportion of haemotoxic (40.7%) and neurotoxic (55%) envenomation cases required 11 to 20 vials of ASV as shown in figure 6. The month of October saw a heightened occurrence of adverse reactions among patients receiving a particular batch of ASV (15/20). These findings underscore the importance of careful patient monitoring, particularly in females, those lacking pre-hospital care, and during peak incidence periods, while also suggesting a potential link between ASV dosage and the occurrence of adverse events.

DISCUSSION

A recent large-scale descriptive study conducted across secondary care centers in the Perambalur and Ariyalur districts of Tamil Nadu, India, sheds light on the clinico-epidemiological characteristics and treatment outcomes of snakebite victims in this region.[15] The study, encompassing 476 admitted patients, reveals that adult males aged 19-59 constitute the majority (72.4% and 64.3% respectively) of snakebite cases, a demographic pattern potentially linked to their greater involvement in outdoor economic activities. This finding aligns with existing literature suggesting a lower incidence of snakebite among female patients.[16] Notably, the study also documented a case involving a two-year-old female bitten within her home. This comprehensive analysis, particularly relevant given the acknowledged underreporting of snakebite data in India, provides valuable insights into the local burden and demographics of snakebite, informing targeted public health interventions and resource allocation.[17]

The provided data suggests a complex interplay of factors influencing snakebite treatment choices and reporting rates across Tamil Nadu districts. Perambalur's disproportionately high incidence of snakebite patients (77.7%) compared to Ariyalur (13.4%) warrants further investigation to determine contributing ecological or socio-economic conditions. The strategic placement of the study center in Thalavady, Erode district, near a significant reserved forest area and within a private hospital setting, was likely intended to capture a specific patient demographic, potentially those seeking treatment irrespective of cost. The lower reported snakebite incidence in Erode (42 patients) despite its proximity to the study centre and a substantial forest area highlights the potential influence of cost-effective treatment options. The availability of free antivenom serum (ASV) in government hospitals appears to significantly impact patient preference, leading them to prioritize affordability over potentially perceived benefits of private healthcare. This underscores the critical role of accessible and affordable healthcare in mitigating the impact of snakebites, a neglected tropical disease, and emphasizes the need for further research into the factors driving regional variations in incidence and treatment seeking behavior.[18]

The temporal distribution of snakebite incidents is demonstrably uneven across the year, exhibiting a peak in September, accounting for 19% of cases. While numerous studies implicate heavy rainfall and the resultant habitat disruption as primary drivers of increased human-snake interaction, leading to elevated snakebite incidence, anomalies exist. [19] The areas covered in the study are characterized by a weaker monsoon season and minimal rainfall, presents a notable deviation. Despite the absence of significant habitat disturbance typically associated with monsoonal rains, a substantial 55% of snakebite cases were still reported between August and November, contrasting with the 31% occurring between April and July. This discrepancy suggests that factors beyond rainfall alone, possibly including temperature fluctuations, agricultural practices, or prey availability, may significantly influence the seasonal incidence of snakebites and warrant further investigation.[20]

This study highlights critical gaps in snakebite management within three agricultural districts. The population predominantly consists of labourers (72.4%), and a staggering 87% of snakebite victims receive no pre-hospital intervention due to a lack of awareness regarding WHO-recommended first-aid techniques.[21] counter intuitively, harmful practices like tourniquet application are prevalent. Species identification is also poor, hindering effective treatment protocols. The preponderance of lower limb bites (76.3%) suggests defensive strikes during night time agricultural activities, leading to immediate hospital transport driven by anxiety and obscuring species identification. While pain (85%) and swelling (13%) are common, indicating prompt bites, a significant proportion (34.9%) exhibit prolonged Whole Blood Clotting Time (WBCT), a key indicator of severe envenomation. These findings underscore the urgent need for targeted public health initiatives focused on snakebite prevention, first-aid education, and species identification training within these vulnerable agricultural communities.[22]

Geographical variation in snakebite incidence extends beyond mere frequency and is significantly influenced by the diverse distribution of venomous snake species and their associated toxicological effects.[21,23] This study reveals that while local envenomation predominates (61%),

haemotoxic (31%) and neurotoxic (6%) effects also occur, with a smaller percentage (2%) exhibiting characteristics of Russell's viper envenomation (Figure 2). This contrasts with findings from Pakistan, where haemotoxic envenomation is significantly more prevalent.[34] This discrepancy, attributed to India's diverse landscape and snake species distribution, potentially contributes to a comparatively lower mortality rate despite reports of highly fatal neurotoxic envenomation from the Common Krait. Regional variations within India are also evident, with varying proportions of haemotoxic and neurotoxic envenomation reported in different districts, highlighting the complexity of snakebite epidemiology and the challenges in drawing broad generalizations.[25] Further research focusing on specific species distribution and venom composition within each region is crucial for developing targeted and effective antivenom strategies.

The administration of anti-snake venom (ASV) as definitive management for snakebite victims with absolute indications was documented in 43.3% of a patient cohort (n=206). However, significant variations in ASV administration were observed across different healthcare facilities.[26] In a secondary care government hospital in Perambalur, 144 out of 371 patients received ASV, while in Ariyalur, the rate was 21 out of 64. In contrast, a private hospital in Erode administered ASV to all 42 snakebite patients. These discrepancies likely stem from a confluence of factors. Firstly, the occurrence of non-venomous snakebites and "dry bites" contributes to reduced ASV usage. Secondly, the subtlety of progressing symptoms, particularly in bites from common kraits and hump-nosed pit vipers, can complicate early diagnosis. Further confounding factors include the absence of visible symptoms in ongoing envenomation and the manifestation of non-specific, anxiety-related symptoms that mimic envenoming. These initial symptom ambiguities pose diagnostic challenges for clinicians. Furthermore, geographical accessibility plays a role, with the majority of patients (82.5%) arriving within one hour, while a smaller fraction presented with delayed onset symptoms. This variance highlights the need for improved diagnostic tools and standardized protocols to differentiate between genuine envenomation and other conditions, ultimately optimizing the judicious use of ASV.[27]

The presented data underscores significant regional variation in antivenom (ASV) usage following snakebite envenomation. Initial analysis of 2330 vials administered demonstrates a wide range (0-30 vials) and a mean of 11.59 ± 6.38 vials. Substantial differences exist between districts within Tamil Nadu, with Perambalur exhibiting a higher mean usage (12.76 ± 6.29 vials) compared to Ariyalur (9.81 ± 6.01 vials) and Erode (6.56 ± 4.17 vials). A Rajasthan study further highlights venom-specific variations, showing lower ASV doses for cobra bites compared to unknown snakebites and significantly higher doses for viper bites.[13] The Chandigarh case of a neonatal snakebite requiring 50 vials emphasizes the potential for extreme ASV demands. These discrepancies likely stem from a combination of factors, including regional snake fauna, severity of envenomation, and physician practices. The prevalence of specific venomous species, such as the pit vipers and black cobra found in Himachal Pradesh, coupled with the “Big 4” snakes, may necessitate different treatment protocols compared to regions with less diverse venomous snake populations.[7] This geographical heterogeneity underscores the need for tailored ASV administration guidelines based on local snakebite epidemiology and venom profiles.[14,29]

The utilization of Anti-Snake Venom (ASV) in India reveals intriguing regional variations, suggesting potential differences in venom potency across diverse ecosystems. Rajasthan, a predominantly desert landscape, exhibits higher ASV usage compared to other regions, while Himachal Pradesh, characterized by high altitudes, demonstrates comparatively lower ASV use for haemotoxic envenomation.[31] This observation hints at a possible inverse relationship between venom concentration and altitude, analogous to the varying sweetness levels in fruits across different environments. Factors such as snake age, gender, bite severity, and delay in treatment can significantly impact ASV dosage, with extreme cases requiring up to 30 vials. However, substantial portions (27.4%) of patients were successfully treated with only 8 vials. Furthermore, studies demonstrating patient recovery with just 2 vials, despite a protocol recommending 10, highlight the potential for optimized treatment strategies.[29] These findings underscore the importance of context-specific protocols tailored to local snake populations and patient demographics. While locally

developed protocols have shown promise in reducing ASV usage and mortality rates, the existing practices, particularly high-dosage regimens based on outdated Western guidelines, require critical re-evaluation. Global health organizations, alongside national and state authorities, should prioritize the development and implementation of evidence-based, locally adapted treatment protocols, incorporating the expertise of local healthcare professionals.[30] Currently, the lack of evidence supporting both low-dose and high-dose strategies prevalent in India necessitates rigorous research to establish optimal ASV administration guidelines and improve patient outcomes.

The effectiveness of Anti-Snake Venom (ASV) treatment in India is demonstrably variable, fluctuating across species, regions, and even within the same species. This inconsistency is compounded by inconsistent clinical practice. Studies, such as the one conducted in Manipal, reveal a disparity between the average ASV dose administered (11.1 vials per patient) and the often misguided dosages employed by many hospitals. This is particularly prevalent in severe cases exhibiting coagulopathy, neuroparalysis, and respiratory depression, where clinicians may deviate from established guidelines. Factors like the age and gender of the snake, the duration since the bite, and the bite's severity can further influence treatment decisions, leading to excessive ASV utilization in some instances. Conversely, studies have shown successful patient recovery with significantly lower ASV doses than conventionally recommended, suggesting that standardized protocols might be excessively conservative.[14,22] This underscores the need for tailored treatment strategies that account for regional variations in snake venom composition and patient characteristics. While acknowledging the absence of evidence supporting low-dose ASV regimens in India, the reliance on high-dosage regimens adapted from Western medical literature is equally problematic.[6] To address this variability and optimize patient outcomes, collaborative efforts between the World Health Organization, national, and state-level bodies are crucial. These entities should prioritize the development and promotion of localized ASV treatment protocols, informed by significant input from local experts. Such protocols, tailored to the specific snake species and clinical realities of different regions in India, are essential to ensure the rational and effective utilization of ASV, ultimately reducing mortality rates and improving the overall management of snakebite envenomation.

The management of severe neurotoxic snakebites presents a complex challenge, particularly in resource-limited settings. While a standardized protocol of 200 ml antivenom (ASV), anticholinesterase, and ventilator support can effectively reverse neuroparalysis, the high cost of ASV relative to average wages presents a significant barrier to access.[32, 10] Compounding this issue is the observation that ASV administration alone may be insufficient to reverse respiratory paralysis[33] , potentially leading to the overuse of antivenom in an attempt to achieve a positive outcome. This not only exacerbates the financial burden on patients but also raises the risk of adverse reactions. Therefore, a judicious approach to anti-venom administration is paramount. Careful consideration must be given to dosage, cost-effectiveness, and the potential limitations of ASV in cases of established respiratory compromise. Prioritizing ventilator support and a conservative approach to ASV usage are crucial to optimize patient outcomes while mitigating the financial strain associated with treatment. This careful balancing act is essential for effective and sustainable snakebite management, particularly for vulnerable populations.

The successful management of severe neurotoxic snakebites, particularly in regions with limited resources, demands a multifaceted approach. While a treatment protocol incorporating antivenom (ASV), anticholinesterase, and ventilatory support has demonstrated efficacy, the significant cost of ASV relative to local wages constitutes a substantial impediment to access.[9,24] Furthermore, evidence suggests that ASV administration alone may prove insufficient to reverse established respiratory paralysis, potentially leading to antivenom overuse in a misguided effort to achieve clinical improvement. This overreliance not only amplifies the financial strain on patients but also increases the risk of adverse reactions to the serum.

Therefore, a judicious and nuanced approach to ASV administration is critical. Careful consideration must be afforded to appropriate dosage, cost-effectiveness, and the inherent limitations of ASV in cases already exhibiting respiratory compromise. Prioritizing mechanical ventilation to

address respiratory failure, alongside a conservative approach to ASV utilization, is paramount in optimizing patient outcomes while simultaneously mitigating the economic burden associated with treatment. This deliberate and thoughtful balancing act is essential for ensuring effective and sustainable snakebite management, particularly for vulnerable populations facing significant financial constraints.

A study in Perambalur district examining the outcomes of 84 snakebite patients treated with Anti-Snake Venom (ASV) revealed that 20 experienced adverse reactions. A temporal clustering of these reactions was observed, with 15 occurring in October compared to 5 across other months, and one of the four deaths also occurring in October. This coincides with a change in ASV batch introduced by the Head of Department, suggesting potential batch-to-batch variation influencing reaction incidence. This is supported by previous research in Vellore [34], where variations in ASV batch efficacy led to discontinuation and replacement of a specific batch. The recorded deaths were attributed to respiratory failure (2) and cardiac arrest (2). Despite a majority (82.5%) of patients arriving at the hospital within an hour of the snakebite, contradicting findings in a high-altitude study in Himachal Pradesh where delayed arrival correlated with higher mortality, no correlation between time of bite and ASV administration was found in Perambalur.[29, 31] This is likely due to the rapid presentation to the hospital by most patients. Patient compliance presented a challenge, with 32 (6.7%) absconding from observation, identified as non-venomous bites. This was primarily attributed to the patients being labourers whose daily wages are essential for their families, causing reluctance to remain hospitalized. Preferences for native treatment over allopathic medicine and expectations for advanced care also contributed. Furthermore, financial constraints led to 4 patients being discharged against medical advice from a private hospital in Erode, while 11 were referred for specialized care. The majority (424, 89%) of patients were successfully treated and discharged with follow-up appointments. This data highlights the complexities of snakebite management, including the need to address ASV batch consistency, patient socioeconomic factors, and preferences to improve treatment outcomes.

CONCLUSION

Addressing snakebite envenoming requires a coordinated global response centered on accurate epidemiological data and improved antivenom access. The WHO, working in concert with national and regional health organizations, and public-private partnerships, is ideally positioned to facilitate this collaboration. Well-designed community studies are crucial for understanding the impact and characteristics of snakebite across diverse regions. While preventative measures remain underdeveloped, antivenom (ASV) remains the cornerstone of treatment, despite potential adverse drug reactions (ADRs). Observed in a small percentage (3/10) of snakebite cases, the necessity of ASV for preventing death outweighs the risks. This underscores the importance of optimizing ASV usage, particularly in an environment of increasing medical costs. The present study identified key epidemiological and management variables, demonstrating efficient ASV utilization (average 11.6 vials) compared to established guidelines. Furthermore, the absence of significant differences in ADRs between ASV manufacturers and the ineffectiveness of premedication highlights the need for continued research. Diligent monitoring of ASV batch numbers in response to ADR incidence, as demonstrated in this study, represents a crucial observation. Ultimately, a concerted international effort, focusing on data-driven strategies and optimized ASV management, is essential to minimize the burden of snakebite envenoming globally.

LIMITATIONS OF THE STUDY

- The storage conditions of the ASV vials were outside the investigator's control, which could affect the consistency of the quality and concentration of the ASV, potentially introducing variability in the study results.
- The patients were observed during the inpatient stay, so the late reactions which typically occur around 7 days post treatment were not recorded.

- No follow-up calls were made to know any late reactions that may have occurred.

FUTURE ASPECTS

Snakebite envenomation remains a significant public health challenge, demanding a renewed focus on improving antivenom therapies. The current paradigm needs advancement towards purified, less allergenic, and venom-specific antivenoms offered at affordable prices. This necessitates rigorous improvements in quality testing and assessment procedures alongside active research into specific neutralizing antibodies against individual venom proteins. Promising avenues such as "cocktail antivenoms," "pan-specific antisera," and phage display technology hold potential for enhanced efficacy. The introduction of monovalent antivenoms in regions like India, where they are currently unavailable, could significantly reduce adverse reactions and the volume of antivenom required. Concurrently, leveraging readily accessible communication tools like WhatsApp for expert consultation and antivenom procurement can streamline patient management. Furthermore, empowering the public through snake handling training, spearheaded by forest officials, contributes to snake conservation efforts, minimizing human-wildlife conflict and protecting ecological balance. A holistic strategy integrating improved antivenom development, accessible communication networks, and public education is crucial for mitigating the impact of snakebites globally.

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