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ADVERSE DRUG REACTION PROFILE OF ANTI-SNAKE VENOM IN A TERTIARY CARE HOSPITAL

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Abstract: Snake envenomation is a major public health issue, particularly in tropical regions like India, where an estimated 250,000 snake bite cases occur annually. The administration of anti-snake venom (ASV) is the primary treatment modality; however, adverse drug reactions (ADRs) associated with ASV pose a significant clinical challenge. This retrospective study aims to evaluate the incidence, severity, and clinical outcomes of ASV-related ADRs in patients treated at a tertiary care hospital. A total of 150 cases from June 2022 to May 2024 were analyzed, documenting demographic distribution, reaction profiles, severity classifications, and management strategies. **Results*:*** Among 150 patients, vascular toxic snakebites were the most common. The 21–30 years age group was predominantly affected, with a male preponderance. ASV-related adverse reactions occurred in 60% (n=90) of cases, with itching (56.7%) being the most frequently reported symptom. Other reactions included chills and rigor (30%), nausea and vomiting (12.2%), and severe respiratory distress (1.1%) requiring intubation. The 20-minute Whole Blood Clotting Test (WBCT) was abnormal in 43.3% of patients. Intradermal ASV sensitivity testing was performed in 54.7% of cases. The majority of patients experienced mild envenomation, with an average hospital stay of 3 days. Recovery was achieved in 81.3%, while 18.7% were referred to higher centers. **Conclusion:** This study highlights the high incidence of ASV-related adverse reactions, emphasizing the need for careful monitoring and pre-medication strategies to mitigate risks.

Keywords: Snakebite, Anti-Snake Venom, Adverse Drug Reactions, Tertiary Care, Envenomation, Vasculotoxic Snakebite.

Introduction

Snakebite envenomation is a major public health problem in many tropical and subtropical countries, particularly affecting agricultural workers, herders, laborers, and individuals residing in rural areas. It is estimated that globally, snakebites cause millions of envenomation cases annually**,** leading to significant morbidity, long-term disability, and mortality. In India alone, approximately 250,000 cases are reported each year, with an estimated 58,000 deaths attributed to snakebite envenomation, making it a neglected tropical disease (NTD) as per the World Health Organization (WHO). Despite the burden of this disease, comprehensive epidemiological data remain limited**,** and access to effective and timely medical intervention is often inadequate**,** especially in remote areas.

The primary treatment for snakebite envenomation is the administration of Anti-Snake Venom (ASV), which is currently the only specific antidote available. In India, only polyvalent ASV is manufactured and used, targeting venom neutralization against the four most medically significant snake species-Russell's viper (Daboia russelii), Indian cobra (Naja naja), Common krait (Bungarus caeruleus), and Saw-scaled viper (Echis carinatus). While ASV plays a critical role in reducing morbidity and mortality, its use is not without risks, as it is associated with a significant incidence of adverse drug reactions (ADRs). Studies indicate that 20-60% of patients who receive ASV experience adverse reactions, which can range from mild hypersensitivity responses to severe and life-threatening complications.

Adverse reactions to ASV are broadly classified into early reactions and late reactions. Early reactions typically occur within minutes to a few hours of ASV infusion and include anaphylaxis, urticaria, bronchospasm, chills, fever, nausea, vomiting, angioedema, hypotension, and even cardiovascular collapse. In contrast, late reactions occur days to weeks after administration, often presenting as serum sickness, characterized by fever, rash, arthralgia, myalgia, and nephritis. The underlying mechanism of ASV-related hypersensitivity is attributed to the presence of foreign proteins in the equine-derived serum, leading to immune complex formation and complement activation. Given the potential severity of these reactions, close monitoring, early recognition, and prompt management are essential to improving patient safety and clinical outcomes.

Some studies suggest pre-medication with antihistamines and corticosteroids to reduce hypersensitivity reactions, but the efficacy of such interventions remains controversial. Furthermore, factors such as the quality of ASV production, storage conditions, patient-related immune responses, and genetic predispositions may influence the occurrence and severity of ADRs. The incidence of reactions also appears to vary geographically, with some regions reporting higher rates of severe anaphylaxis compared to others. This variability underscores the need for hospital-based studies that assess ASV safety profiles in different patient populations.

Given these considerations, the present study aims to evaluate the incidence, severity, and clinical presentation of adverse reactions to ASV in patients admitted with snakebite envenomation at a tertiary care hospital. By analyzing patient demographics, type of envenomation, reaction profiles, and outcomes, this study will provide valuable insights into the safety and efficacy of ASV therapy. Furthermore, a comparative analysis with previous literature will highlight regional differences in ASV reactions and identify potential gaps in clinical management. The findings from this study may contribute to the development of improved ASV administration protocols, enhanced patient monitoring strategies, and evidence-based guidelines for the management of snakebite envenomation in India and similar settings.

Objectives

1. To analyze the incidence and severity of adverse reaction following administration of Anti-snake venom in snake bite cases
2. To estimate the clinical outcomes in Snake bite cases including recovered, referral and mortality

Materials and Methods

Study Design and Setting: A retrospective study was conducted over 24 months (June 2022–May 2024) at the Emergency Department of Bowring and Lady Curzon Hospital, Bengaluru. The study was approved by the Institutional Ethics Committee (IEC Number: SABVMCRI/ IEC/ PG-ARP/24/2024-25).

Inclusion Criteria

- Snake bite cases administered with Anti snake venom
- Patients who received ASV irrespective of them having reactions to it

Exclusion Criteria

- Incomplete or inadequately documented patient records.

Methodology

The study was conducted as a retrospective observational analysis at Bowring and Lady Curzon Hospital, Bangalore**,** a tertiary care center that receives a significant number of snakebite cases. The study included patients admitted with snakebite envenomation from June 2022 to May 2024**,** and medical records were retrieved from the Medical Record Section**.** A structured case record proforma was used to collect demographic data, clinical presentation, type of snakebite, laboratory investigations, ASV administration details, and adverse drug reactions (ADRs) following ASV administration.

The study included patients who received ASV for envenomation and had documented adverse reactions**,** while those with incomplete records or pre-existing allergic conditions that could confound results were excluded. Demographic details**,** including age, gender, and geographic location, were recorded. The type of envenomation (vasculotoxic, neurotoxic, or cytotoxic) was classified based on clinical features. Initial presentation symptoms such as pain, swelling, coagulopathy, bleeding tendencies, or neurotoxic signs were documented. Laboratory investigations included the 20-minute Whole Blood Clotting Test (WBCT-20) for assessing coagulation abnormalities and the intradermal sensitivity test for ASV hypersensitivity in some cases.

The dose, route, and frequency of ASV administration were carefully recorded, along with the total number of vials used per patient**.** ADRs were categorized as mild (itching, urticaria), moderate (fever, chills, hypotension), or severe (anaphylaxis, bronchospasm, cardiovascular collapse)**.** The time of onset of these reactions was also noted, distinguishing between early (within minutes to hours) and late (serum sickness-like reactions after days to weeks)**.** Management strategies, including the use of antihistamines, corticosteroids, and adrenaline**,** were documented to assess the treatment response. The data was filled on suspected adverse drug reactions reporting form by Central Drug Standard Control Organization. The reactions were assessed by seriousness (death, life threatening, hospitalization- initial or prolonged, disability and other medically important) and outcome (recovered, recovering, fatal, recovered with sequalae and not recovered). The outcome of the patients was evaluated, including recovery, complications, need for ICU admission, referral to higher centers, or mortality**.**

Statistical analysis

Data will be recorded in an Excel sheet and will be analyzed using the Statistical Package for the Social Sciences (SPSS) version 22.0. Data will be represented using Descriptive statistics.

Results

A total of 150 snake bite cases treated with anti-snake venom (ASV) were analyzed, focusing on demographic characteristics, monthly incidence trends, toxicity patterns, adverse reaction profiles, severity grading, investigations performed, and clinical outcomes.

Demographic Characteristics (Age and Gender Distribution)

The demographic analysis of 150 snakebite patients who received anti-snake venom (ASV) administration highlights key trends in age and gender distribution. The highest incidence of snakebite cases was observed in the 21–30 years age group, accounting for 35.3% (n=53) of the total cases, followed by the 31–40 years group with 25.3% (n=38). The number of cases gradually declined in older age groups, with 12% (n=18) in the 41–50 years category, 4.7% (n=7) in the 51–60 years category, and 5.3% (n=8) in individuals above 60 years. The lowest incidence was recorded in children aged 0–10 years, comprising only 0.6% (n=1) of cases.

Regarding gender distribution, a significant male predominance was observed, with 80% (n=120) of the cases being males and only 20% (n=30) females. This disparity suggests that men are at a higher risk of snakebites, likely due to increased outdoor activities, occupational exposure in agricultural and rural settings, and behavioral patterns that put them in closer proximity to snake habitats. The data indicate that young adult males are the most vulnerable population for snakebites, underscoring

the need for targeted awareness programs, protective measures, and early intervention strategies in high-risk groups (Fig. 1).

Monthly Incidence of Snake Bite Cases

The monthly incidence of snakebite cases from June 2022 to May 2024 exhibits notable fluctuations, indicating seasonal variations in snakebite occurrences. The number of cases per month ranged from a low of approximately 1–2 cases in certain months to a peak of around 16–17 cases in others. A higher incidence of snakebites was observed during specific months, particularly in June 2023 and September 2023, where cases reached their highest levels.

A trend of increased cases can be noted during the monsoon and post-monsoon seasons, which typically coincide with higher snake activity due to increased humidity, flooding, and human interaction with snake habitats. This trend is evident from the spikes in cases around June–July and September–October in both years. Conversely, the lowest number of cases was reported in certain months, particularly in the winter season (December–February), when snake activity tends to decrease due to lower temperatures and hibernation tendencies.

The data suggest that snakebite cases follow a seasonal pattern, with peaks during monsoon months and a decline during winter. These findings highlight the need for enhanced public awareness, preventive measures, and healthcare preparedness, particularly in high-incidence months, to reduce the burden of snakebite cases and ensure timely management of envenomation (Fig. 2).

Antivenom dosage forms and routes of administration

- Lyophilized antivenom reconstituted with 10 ml water to 10 ml ASV
- ASV diluted in IV fluids and infused intravenously at a constant rate of about one to two hours

Toxicity of Snake Bites

The toxicity profile of snakebite cases (n=150) reveals that the majority of envenomations were vasculotoxic in nature, affecting 58.7% (n=88) of patients. Vasculotoxic envenomation, typically caused by Viperidae species, leads to local tissue damage, coagulopathy, and systemic bleeding tendencies, making it the most frequently encountered form of toxicity in this study.

Neurotoxic envenomation, which is commonly associated with Elapidae species such as cobras and kraits, accounted for 8.7% (n=13) of cases. Neurotoxic bites can result in paralysis, respiratory distress, and neuromuscular blockade, requiring urgent medical intervention.

A significant proportion of cases (32.7%, n=49) were categorized as "Not Mentioned," indicating either incomplete documentation of clinical manifestations or cases where the toxicity type could not be determined. This highlights the importance of accurate and detailed clinical assessment to categorize snakebite cases appropriately.

These findings underscore the predominance of vasculotoxic snakebites in the studied population, emphasizing the need for effective management strategies, early recognition of complications, and appropriate administration of anti-snake venom (ASV) to mitigate morbidity and mortality (Fig. 3).

Frequency Distribution of Adverse Drug Reactions (ADRs) to ASV

The frequency distribution of snakebite sites among 150 patients indicates that the lower limb was the most commonly affected region, accounting for 75% of cases. This finding aligns with the fact that snakebites often occur when individuals walk barefoot or wear inadequate protective footwear, particularly in rural and agricultural settings where encounters with snakes are more frequent.

The upper limb was the second most commonly affected site, comprising 25% of cases. Bites to the upper limb typically occur during activities such as farming, handling objects in snake-prone areas, or accidental contact with snakes in vegetation or storage spaces.

A very small proportion of cases (0.6%) involved snakebites to the neck, which is an uncommon but potentially more dangerous site due to the risk of airway compromise and rapid systemic envenomation.

These findings highlight the importance of preventive measures such as wearing protective footwear, using gloves when working in snake-prone areas, and increasing awareness about snakebite risks and first-aid measures to reduce the incidence and severity of envenomation (Fig. 4).

Investigations:
The investigation findings for 150 snakebite patients provide critical insights into the diagnostic and pre-treatment evaluation processes.

20-Minute Whole Blood Clotting Test (WBCT)
The 20-minute WBCT, a crucial bedside test for detecting coagulopathy in snakebite envenomation, was performed on all patients. The results indicate that 56.7% (n=85) of patients had clotted blood, suggesting either the absence of significant envenomation or a predominance of neurotoxic bites, which typically do not cause coagulopathy. However, 43.3% (n=65) of patients had uncoagulated blood, indicating a coagulopathy suggestive of vasculotoxic envenomation, commonly caused by viper bites. This finding underscores the importance of WBCT as a rapid and effective test in diagnosing hemotoxic envenomation and guiding the decision for anti-snake venom (ASV) administration (Fig. 5).

Intradermal Sensitivity Test for ASV
The intradermal sensitivity test for ASV was conducted in 54.7% (n=82) of cases, while it was not performed in 45.3% (n=68) of patients. Despite historical use, the intradermal ASV sensitivity test is now considered unnecessary and is not recommended by WHO guidelines, as it does not reliably predict hypersensitivity reactions and may delay the timely administration of ASV. The near-equal distribution of patients who underwent this test and those who did not reflects variations in clinical practice, emphasizing the need for adherence to updated treatment protocols to ensure prompt and effective snakebite management (Fig. 5).
These findings highlight the importance of evidence-based diagnostic and treatment approaches in snakebite management, particularly emphasizing the role of WBCT in detecting vasculotoxic envenomation and discouraging unnecessary pre-administration ASV sensitivity testing to optimize patient outcomes.

Age and Gender-Wise Distribution of ASV Reactions
The age- and gender-wise distribution of adverse reactions to anti-snake venom (ASV) among 150 snakebite patients reveals that 60% (n=90) of patients experienced adverse reactions, while 40% (n=60) had no reactions. The highest incidence of ASV reactions was observed in the 21–40 years age group, with 47.8% (n=43) of affected males and 11.1% (n=10) of affected females. This was followed by the ≤20 years age group, where 15.5% (n=14) of males and 1.1% (n=1) of females developed reactions. Among patients aged 41–60 years, 16.7% (n=15) of males and 3.3% (n=3) of females experienced ASV-related reactions. In patients older than 60 years, 4.4% (n=4) of males had reactions, while no reactions were reported among females. The data indicates a higher incidence of ASV-related adverse reactions in males across all age groups, particularly in the younger and middle-aged populations. These findings highlight the need for close monitoring of ASV administration, particularly in male patients of working age, who are more frequently affected by snakebites and ASV-related adverse effects (Table 1).

Antivenom Reaction Presentation
The distribution of antivenom reactions among 90 patients who experienced adverse effects following ASV administration reveals that the most common presentation was generalized itching, reported in 56.7% (n=51) of cases. This was followed by chills and rigor in 30% (n=27) of patients, indicating a systemic hypersensitivity response. Nausea and vomiting were observed in 12.2% (n=11) of cases, reflecting mild to moderate systemic involvement. A severe reaction, breathlessness leading to respiratory failure requiring intubation, was noted in 1.1% (n=1) of patients, highlighting the potential

for life-threatening complications. These findings underscore the importance of premedication strategies and close monitoring of patients receiving ASV to manage and mitigate adverse reactions effectively (Fig. 6).

Reaction Profile According to Snake Type

The reaction profile of snakebite patients according to the type of envenomation reveals that vasculotoxic bites had the highest incidence of adverse reactions to ASV, occurring in 68.9% (n=62) of cases, compared to 40% (n=24) who did not experience a reaction. Neurotoxic envenomation resulted in ASV reactions in 11.1% (n=10) of cases, while 8.3% (n=5) did not develop adverse effects. Among cases where the type of snakebite was not specified, 20% (n=18) had an ASV reaction, whereas 51.7% (n=31) did not. These findings indicate that vasculotoxic envenomation is more commonly associated with ASV-related adverse effects, emphasizing the need for vigilant monitoring and supportive care in this patient group (Table 2).

Severity of Snake Bite Cases

The severity of snakebite cases among 150 patients highlights various complications. Cellulitis was the most common severe manifestation, occurring in 6.7% (n=10) of cases, with six patients requiring fasciotomy. Acute renal failure was observed in 2.7% (n=4) of cases, and one patient required hemodialysis. Additionally, four patients (2.7%) needed fresh frozen plasma due to coagulopathy. The average hospitalization period was three days, and a significant proportion (70–90%) of patients sought medical attention within 2–6 hours post-bite, indicating timely intervention in most cases (Table 3).

Clinical Outcomes

The outcome analysis of 150 snakebite cases shows that the majority of patients, 122 (81.3%), recovered successfully following treatment. However, 28 patients (18.7%) required referral to higher centers, possibly due to complications or the need for specialized care. The high recovery rate suggests effective management at the treating facility, while the referral rate indicates that some cases required advanced medical interventions beyond the available resources. This data underscores the importance of timely treatment and the need for referral pathways in managing severe envenomation cases (Fig. 7).

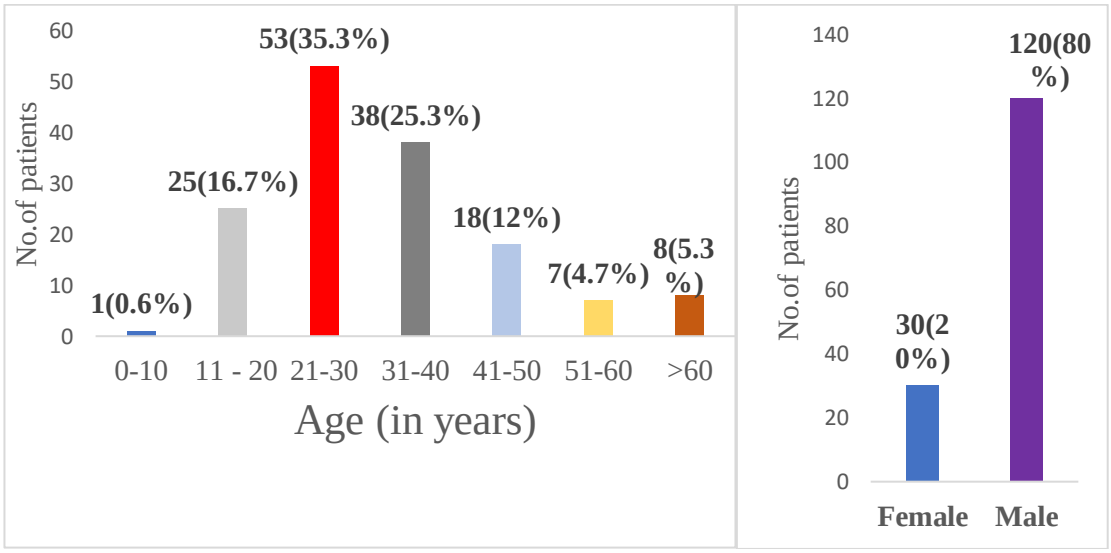

Fig 1. Demographic details(age and gender distribution) of Snake bite patients with ASV administration (n=150)

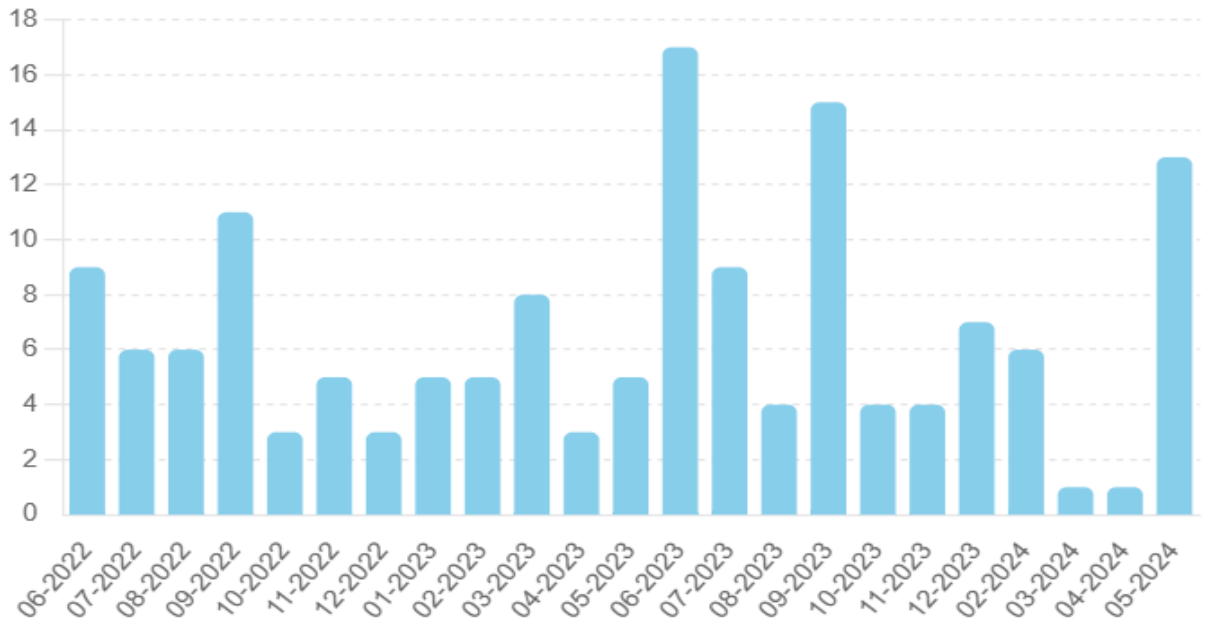

Fig 2. Monthly incidence of Snake bite cases (June 2022- May 2024)

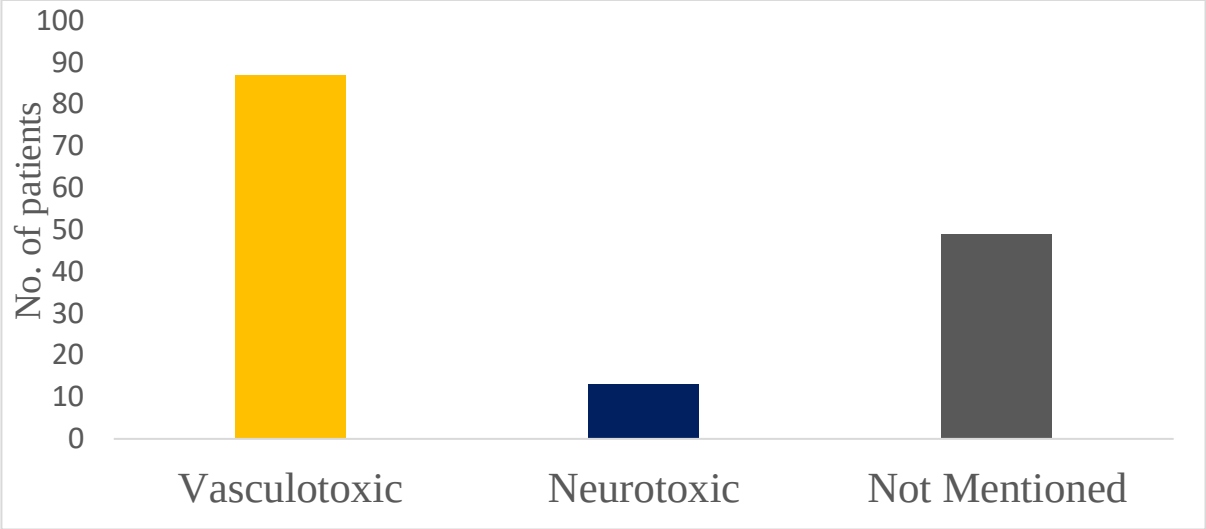

Fig 3. Toxicity of Snake bite (n=150)

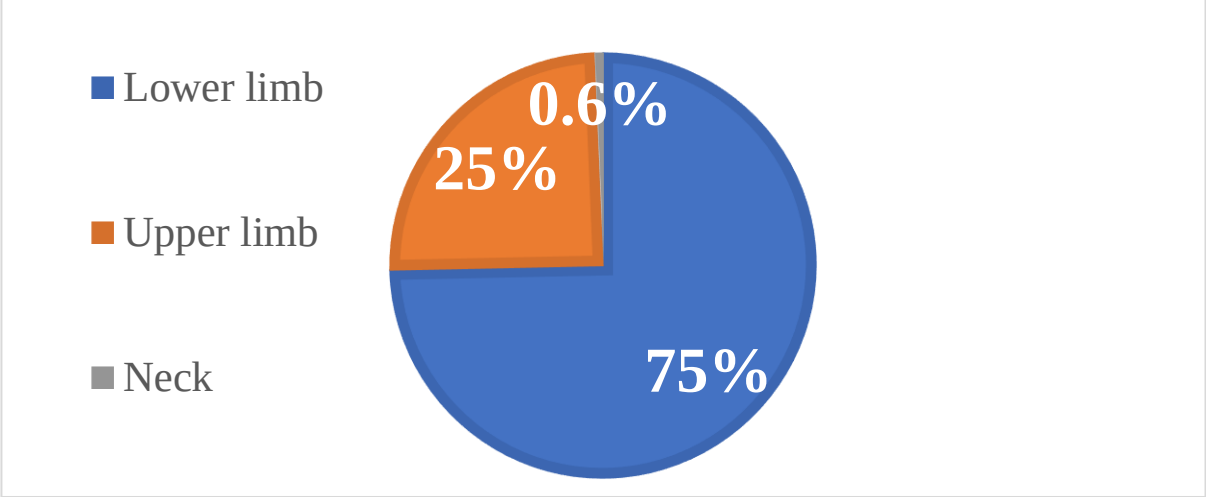

Fig 4. Frequency distribution(n=150)

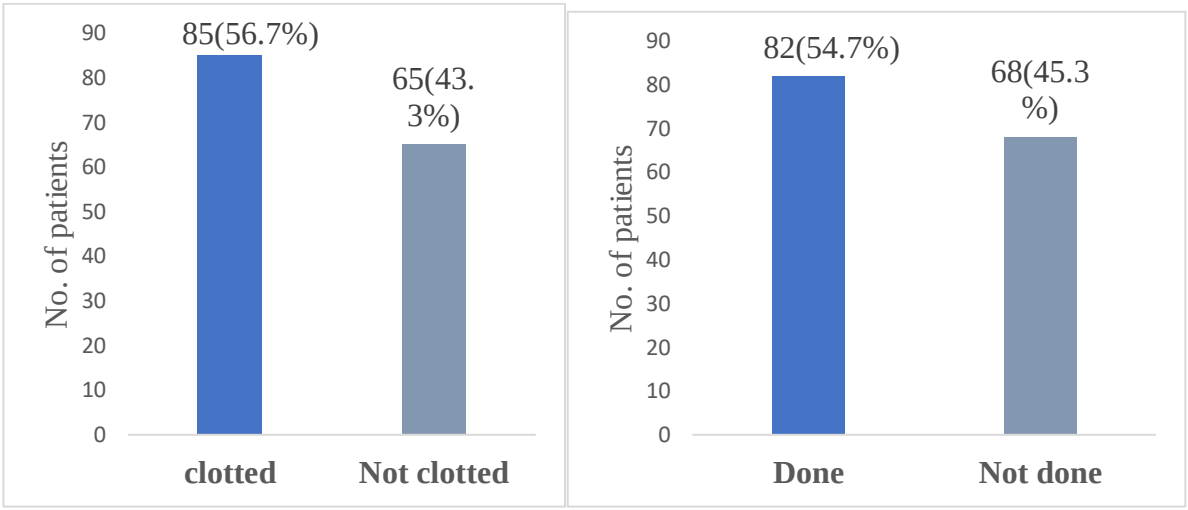

Fig 5. 20 minutes Whole Blood Clotting Test(clotted or not) and Intradermal sensitivity of ASV done or not done(n=150)

Age (Years)	Gender	Reaction occurred		Reaction not occurred	
		Number	%	Number	%
≤ 20	Male	14	15.5	8	13.3
	Female	1	1.1	3	5
21-40	Male	43	47.8	28	46.7
	Female	10	11.1	10	16.7
41-60	Male	15	16.7	5	8.3
	Female	3	3.3	2	3.3
>60	Male	4	4.4	3	5
	Female	0	0	1	1.7
Total		**90**		**60**	

Table 1: Age and gender wise distribution of antivenom reactions (n=150)

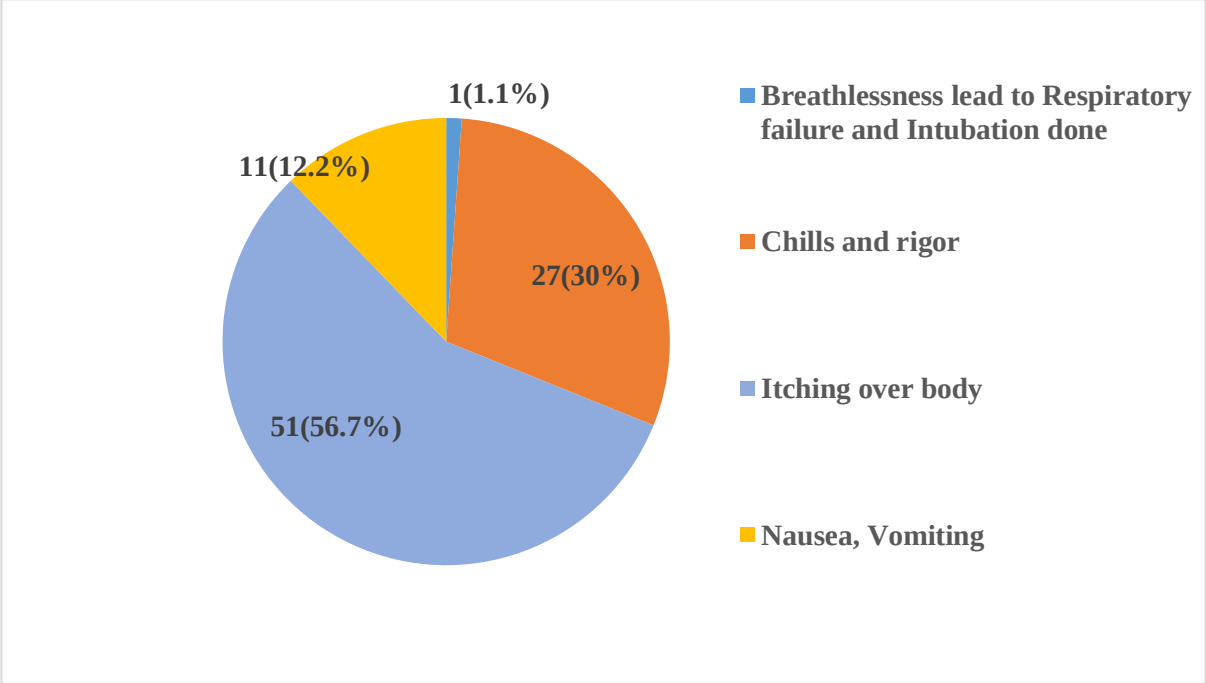

Fig 6. Antivenom reaction presentation(n=90)

Type of snake bite	Reaction to ASV occurred		Reaction to ASV not occurred	
	Number	%	Number	%
Vasculotoxic	62	68.9	24	40
Neuroparalytic	10	11.1	5	8.3
Not mentioned	18	20	31	51.7
Total	90		60	

Table 2. Reaction profile according to types of snake bite(n=150)

Signs and Symptoms	Number of patients and %
Cellulitis	10 (6.7%)
Cellulitis requiring Fasciotomy	6 patients
Acute Renal Failure	4 (2.7%)
Acute Renal Failure with Hemodialysis	1 patients
Need for Fresh Frozen Plasma due to coagulopathy	4 (2.7%)

Table 3. Severity of snake bite cases(n=150)

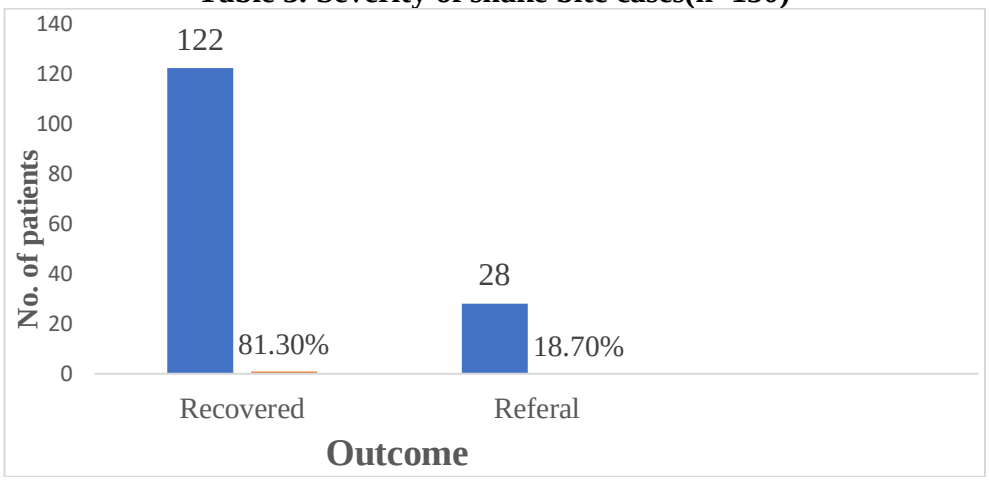

Fig 7. Outcome of Snake bite cases (n=150)

Discussion

The findings of this study highlight the profile of adverse drug reactions (ADRs) associated with anti-snake venom (ASV) therapy in a tertiary care hospital setting. Our data indicate that vasculotoxic snakebites were the most common type encountered, with a significant proportion of patients experiencing ASV-related reactions. The majority of patients (56.7%) had a positive 20-minute Whole Blood Clotting Test (WBCT), reflecting a predominant vasculotoxic envenomation pattern. These findings align with previous studies conducted in India and other tropical regions where Russell's viper and other vasculotoxic snake species are prevalent. [1,2]

Adverse Reactions to ASV

A significant proportion (40%) of patients did not experience any ASV-related reaction; however, 90 patients (60%) developed ADRs, including chills, rigor (30%), itching (56.7%), nausea, vomiting (12.2%), and severe respiratory complications requiring intubation (1.1%). These reactions are consistent with prior studies that reported early anaphylactic and pyrogenic reactions as the most frequent complications of ASV therapy.[3] Studies by Warrell et al. [4] and Alam et al. [5] suggest that immediate hypersensitivity reactions to ASV are largely due to IgE-mediated mechanisms or direct complement activation by non-immunoglobulin factors in ASV preparations.

The overall incidence of ASV-related adverse reactions in our study (60%) is comparable to findings by Das et al. [6] who reported an incidence of 56% in a cohort of 200 patients. However, our results indicate a slightly higher prevalence of systemic reactions requiring intervention. This could be attributed to differences in ASV formulations, batch-to-batch variations, and patient factors such as pre-existing allergies or comorbidities.[7] A meta-analysis by Gutiérrez et al. [8] on snakebite treatment strategies emphasized that premedication with antihistamines or corticosteroids may reduce reaction severity but does not completely prevent ASV-induced anaphylaxis.

Severity and Management of Snakebite Cases

In our study, 6.7% of patients developed cellulitis, with a subset requiring fasciotomy. Additionally, 2.7% of patients experienced acute renal failure, and 2.7% required fresh frozen plasma due to coagulopathy. These findings correlate with previous research indicating that complications such as renal failure and coagulopathies are more frequently associated with vasculotoxic envenomation.[9] Studies from South Asia have reported similar morbidity patterns, emphasizing the need for early intervention to prevent long-term complications.[10]

Clinical Implications and Future Directions

The overall recovery rate in our cohort was 81.3%, with 18.7% requiring referral to higher centers due to severe complications. The high recovery rate underscores the efficacy of early ASV administration and supportive care. However, the referral rate also highlights gaps in resource availability and critical care management at primary and secondary healthcare levels. Future studies should focus on optimizing ASV dosing strategies, improving ASV purification techniques to minimize immunogenicity, and developing alternative therapeutic options such as monoclonal antibodies for snakebite management.[11]

Limitations

This study has certain limitations, including its single-center design and limited sample size. Additionally, batch-wise variations in ASV composition were not analyzed, which may influence reaction rates. Future multicenter studies with larger sample sizes and standardized ASV formulations are needed to validate these findings.

Conclusion

The conclusion emphasizes the necessity of proper documentation of adverse reactions related to anti-snake venom (ASV) treatment, including details on onset, duration, severity, and outcomes. It highlights the role of this study in improving the understanding of current clinical management practices for snakebite cases in tertiary care settings. The findings aim to enhance patient care, treatment strategies, and overall outcomes. Additionally, the study identifies vasculotoxic snakebites as the most common type encountered, underscoring the need for targeted interventions and treatment protocols for such cases.

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