Anti-snake venom dosage administered to snake bite victims at the National Poisoning Control Center (NPCC) in Karachi, Pakistan.

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ABSTRACT:
Objective: To determine the minimum and maximum doses of ASV provided in various cases of snake bites based on the severity of the bite and the amount of time passed between bite and hospital presentation.
Methodology: Data from 99 snakebite cases between September and December 2023 were examined retrospectively at the National Poison Control Center (NPCC), Jinnah Postgraduate Medical Centre (JPMC), Karachi, focusing on ASV dosage, severity categorization (mild, moderate, severe, and very severe), and time intervals from bite to ASV administration (ranging from very early to extremely late).
Results: The study found a statistically significant relationship between the severity of envenomation and the ASV dosage used, with a moderate to strong level of connection. Mild cases often required lower ASV dosages (50-150ml), but severe cases required highly varied and occasionally extensive dosing of up to 1500ml. Early presenters often got moderate ASV doses (150ml), whereas very late presenters (>72 hours) frequently required greater dosages.
Conclusion: This work adds to the empirical evidence for severity-based ASV dosing techniques and suggests combining real-time data monitoring with the update of worldwide standards to meet the local epidemiological and health-care setting.

Key words: Anti Snake Venom (ASV), Envenomation, Retrospective Study, Public Health.

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Introduction:

Snakebite envenomation is a major public health issue worldwide, particularly in tropical and subtropical regions. It is classed as Class A of "Neglected Tropical Diseases" by the World Health Organization due to its significant morbidity and mortality, as well as global inattention and funding for the disease.[1] Every year, around 5 million people worldwide are bitten by snakes, resulting in 81,000 to 138,000 deaths and approximately 400,000 permanent disabilities due to amputations or disfigurement.[2] These estimates are considered underreported due to a lack of surveillance and the high prevalence of traditional healing techniques in many low-resource communities.[3]

South Asia bears the brunt of snakebite incidences and fatalities, with India, Pakistan, Bangladesh, Nepal, and Sri Lanka accounting for more than 70% of global snakebite mortality.[4] Victims include rural agricultural workers, who are particularly vulnerable to snake bites due to barefoot working and proximity to snake habitats. Out of 300 snake species in the region, approximately 70 are venomous. The "big four" snakes—common krait, Russell's viper, saw-scaled viper, and Indian cobra—cause the majority of venomous bites and deaths. The sickness of these snakes is complex and consists of several venom types (neurotoxins, hemotoxins, nephrotoxins), therefore clinical presentations are diverse.[5]

ASV is the primary treatment for systemic envenomation, and it has been shown to significantly reduce clinical problems associated with snake bites. ASV injection has also been linked to anaphylaxis, and its usage is limited by specific clinical criteria such as fast local swelling, coagulopathy, neurotoxic symptoms, and renal involvement. Furthermore, the costs of ASV are so expensive that it is frequently overused or underused due to a lack of established dose procedures, resulting in increased treatment expenditures and negative effects.[6] The outcomes of ASV treatment are strongly reliant on the time after envenomation when the ASV is provided, the species of snake involved, the quantity of envenomation, and the appropriateness of the ASV dose given.[7] ASV selectively neutralizes circulating venom, which reduces the evolution of suspected symptoms such as neurotoxicity, coagulopathy, acute renal damage, and cardiovascular instability. Several studies have shown that early ASV treatment dramatically lowers mortality and morbidity in snakebite patients.[8]

Snakebite envenomation must be addressed therapeutically according to severity, and classification is necessary. The traditional Snakebite Severity Score (TSSS)[9] is the most commonly used method for categorizing cases as mild, moderate, or severe. This grading method assesses both local and systemic aspects such as edema, discomfort, bleeding disorders, neurotoxicity, and renal impairment.

Classification and intervention are crucial since any delay results in deteriorating clinical state or irreparable effects.[10] However, most healthcare facilities, particularly those with limited resources, lack sufficient classification system training, resulting in empirical treatment. This stresses the need

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of standardized severity scores in optimizing ASV dosage methods and improving patient outcomes.[11]

Based on envenomation symptoms, WHO guidelines recommend starting therapy and re-evaluating for increased dose. Because it is difficult to identify snake species, polyvalent ASVs are widely utilized in South Asia.[12]

However, in Pakistan, ASV is typically used when symptoms such as fast swelling, neurotoxicity, and coagulopathy are present. However, dosage requirements vary greatly due to variable ASV potency and changes in venom composition, even within the same species.[13] Some patients will recover with a low dose, however larger volumes will be required for hemotoxic bites, such as those from Russell's viper. The lack of localized studies presents a significant hurdle to maximizing ASV utilization. However, most current guidelines are based on broad data sets that may not be applicable to the reality of clinical utilities in Pakistan. This underscores the need for region-specific dosage guidelines.[14]

ASV requirements vary by patient, with some requiring only 5-10 vials and others requiring 20 or more in seriously impacted instances. However, there are differences, and no such defined dosage procedure exists, particularly at the regional level.[15] Although snakebites are common in Pakistan, particularly in urban areas like Karachi, there is little locally sourced data on the patterns of giving ASV. No study has systematically assembled the minimum and maximum ASV doses required at various stages of the clinical course to provide dosing guidelines. This opens up opportunities for context-specific research to design standards to which treatment should follow or to increase cost efficiency in resource-constrained environments.[8]

This study assesses snakebite cases from NPCC at Jinnah Postgraduate Medical Center (JPMC) Karachi for the minimal and highest amounts of ASV as a solution to the region's therapeutic gap in snake envenomation care.

Objective:

To determine the minimum and maximum doses of ASV provided in various cases of snake bites based on the severity of the bite and the amount of time passed between bite and hospital presentation.

Methodology:

This retrospective analysis was conducted between September 2023 and December 2023 at the National Poisoning Control Centre NPCC within JPMC, Karachi, after getting approval from the Institutional Review Board (IRB). Record of 99 cases was retrieve using non-probability consecutive sampling. The patients were classified according to Traditional snakebite severity scale (TSSS) based on local wound ranging from 0 (no envenomation) to IV (very severe) showing blisters, blebs, swelling and ecchymosis9 (Table I). The patients were treated with the standard protocol of 50ml ASV stat on arrival followed by 50 ml ASV twice daily till INR was normalized and symptoms had improved. polyvalent ASV was obtained via government supplied stock with well-maintained cold chain.

Patients of either gender, aged above 12 years with history of snake bite incident and details of any treatment taken were included. However, those with degenerative age-related brain disorders, cancers, chronic diseases, and genetic and familial diseases were excluded in anticipation that these may act as confounder. Data collected on customized, structured form including demographics, clinical presentation, ASV dosages given, and patient outcome.

All collected data were analyzed using SPSS software version 25.0. Descriptive statistics such as means and standard deviations were calculated for continuous variables, while frequencies and percentages were used for categorical data. Inferential analysis was performed using the Chi-square test or Fisher's Exact test, as appropriate, to examine associations between variables. A confidence interval of 95% was used, and p-values less than 0.05 were considered statistically significant.

Table No 1: snakebite severity score[9]

Severity scale (0-IV)	Manifestations
0-No envenomation	Local or systemic signs or symptom absent
I-Minimal	Local swelling, absence of systemic sign, normal laboratory findings
II-Moderate	Swelling extending past bite site (6-12 inch), ≥1 systemic sign or symptom, abnormal laboratory findings
III-Severe	Marked swelling (>12 inch), tissue loss, multiple or severe systemic symptoms, immediate systemic signs, rapid progression of symptoms
IV-Very severe	Rapid development of local reaction, ecchymosis, necrosis, blebs, blisters, swelling severe enough to obstruct venous or arterial flow, swelling may involve ipsilateral trunk

Results:

A total of 99 patients with confirmed snakebite were included in the study. The gender distribution revealed that snakebite incidents occurred mainly in males 73(73.7%), while females were considerably fewer 26(26.3%). Most cases occurred among younger populations, with the highest incidence in the 20-29 years age group 30(30.3%), followed by 10-19 years 26(26.3%) and 30-39 years 25 (25.3%), whereas only 2(2.0%) of patients were aged 60 or above. In terms of geographic origin, 54.5% of patients originated from rural areas, while 35.4% were from urban locations and 10.1% from suburban regions. The anatomical site of the snakebite showed that the lower limbs were the most common location, with equal involvement of the right and left legs 32(32.3%) each. Upper limb bites accounted for 31(31.3%) of cases, with 23(23.2%) affecting the right arm and 8(8.1%) the left. The interval between the bite and presentation to the hospital was classified into six categories. Most patients, 46 (46.5%), sought medical care within the "Early" window. Only 9(9.1%) presented within the first hour. A large majority of the patients 93(93.9%), were vitally stable upon receiving care. Regarding hospital stay, the majority 60(60.6%), were discharged within a single day. About 22(22.2%) required a 2-day stay, while only 3 patients remained hospitalized for more than 3 days.

Swelling at the bite site was the most prevalent symptom, reported in nearly all cases (86 out of 99), indicating its universal presence and clinical significance. Pain was the second most common, followed by active bleeding. Together, these three symptoms accounted for over 80% of all symptom occurrences. Other less frequent symptoms included vomiting, bleeding from the gums, hematuria, dizziness, and diarrhea. Rare systemic manifestations such as difficulty breathing, blister formation, or hematemesis

were reported in isolated cases. Despite their low frequency, these symptoms were clinically important, often associated with severe or very severe envenomation.

Table No 2: Demographic Profile.

		N	%
Age Group	10-19	26	26.3
	20-29	30	30.3
	30-39	25	25.3
	40-49	13	13.1
	50-59	3	3.0
	60+	2	2.0
Gender	Male	73	73.7
	Female	26	26.3
Location	Urban	35	35.4
	Suburban	10	10.1
	Rural	54	54.5
Duration Since the Time of Bite	Very Early (0-1 hour)	9	9.1
	Early (>1-6 hours)	46	46.5
	Moderate (>6-24 hours)	11	11.1
	Late (>24-72 hours)	20	20.2
	Very Late (>72-168 hours)	12	12.1
	Extremely Late (>168 hours)	1	1.0
Site of Bite	Upper Limb - Right	23	23.2
	Upper Limb - Left	8	8.1
	Lower Limb - Right	32	32.3
	Lower Limb - Left	32	32.3
	Multiple/ General Limb	1	1.0
	Head/Neck	3	3.0
Vitally Stable When Received	Yes	93	93.9
	No	6	6.1
Duration of Hospital Stay	1 day	60	60.6
	2 days	22	22.2
	3 days	14	14.1
	1 week	2	2.0
	More than a week	1	1.0

A statistically significant association was found between the severity of envenomation and the dose of ASV administered ($\chi^2 = 57.070$, df = 15, $p < 0.001$). The strength of association was moderate to strong (Cramer's V = 0.427) (Table 4.3). In mild cases (n = 23), the majority received either 150ml (56.5%) or 50ml (30.4%) of ASV. Smaller proportions received 350ml (13.04%), with no cases requiring above this. Among moderate cases (n = 58), 150ml (51.7%) and 250ml (31.0%) were the most common doses administered, with occasional use of 350ml (10.34%). For severe cases (n = 13), the distribution of ASV doses was broader, with nearly equal proportions receiving 150ml, 250ml, and 350ml. A small subset received up to 750 mL. In very severe cases (n = 5), dosing ranged from 50 mL to 1500 mL, with each dose category accounting for 20% of cases. This pattern strongly suggests an individualized, tailored approach, potentially influenced by patient response, venom load, or time to presentation, and highlights the critical and unpredictable nature of very severe snakebites (table III).

Table No 3: Cross tabulation between Severity and Dosage of ASV Administered.

	50ml	150ml	250ml	350ml	750ml	1500ml	Total
Mild	7	13	0	3	0	0	23
	30.43%	56.52%	0.00%	13.04%	0.00%	0.00%	100.00%
Moderate	4	30	18	6	0	0	58
	6.90%	51.72%	31.03%	10.34%	0.00%	0.00%	100.00%
Severe	0	4	4	4	1	0	13
	0.00%	30.77%	30.77%	30.77%	7.69%	0.00%	100.00%
Very Severe	1	1	0	1	1	1	5
	20.00%	20.00%	0.00%	20.00%	20.00%	20.00%	100.00%
Total	12	48	22	14	2	1	99
	12.12%	48.48%	22.22%	14.14%	2.02%	1.01%	100.00%
$\chi^2 = 57.070$; df = 15; Cramer's V = 0.427, p = 0.000							

Table No 4:Cross tabulation between Duration Since the Time of Bite and Dosage of ASV Administered.

	50ml	150ml	250ml	350ml	750ml	1500ml	Total
Very Early (0h–1h)	0	6	2	1	0	0	9
	0.00%	66.67%	22.22%	11.11%	0.00%	0.00%	100.00%
Early (>1h–6h)	8	25	11	2	0	0	46
	17.39%	54.35%	23.91%	4.35%	0.00%	0.00%	100.00%
Moderate (>6h–24h)	2	5	2	1	0	1	11
	18.18%	45.45%	18.18%	9.09%	0.00%	9.09%	100.00%
Late (>24h–7h)	2	8	4	5	1	0	20
	10.00%	40.00%	20.00%	25.00%	5.00%	0.00%	100.00%
Very Late (>72h–168h)	0	3	3	5	1	0	12
	0.00%	25.00%	25.00%	41.67%	8.33%	0.00%	100.00%
Extremely Late (>168h)	0	1	0	0	0	0	1
	0.00%	100.00%	0.00%	0.00%	0.00%	0.00%	100.00%
Total	12	48	22	14	2	1	99
	12.12%	48.48%	22.22%	14.14%	2.02%	1.01%	100.00%
$\chi^2 = 31.961$; df = 25; Cramer's V = 0.254, p = 0.159							

Table IV outlines the relationship between the time elapsed from snakebite to hospital presentation and the ASV dose administered. Although not statistically significant (p = 0.159), a weak to moderate association was observed (Cramer's V = 0.254). Patients presenting early (>1-6 hours post-bite) predominantly received 150ml (54.4%), with some receiving 50ml or 250ml. In the very early group (0-1 hour), most received 150ml (66.7%), with a few receiving 250ml or 350ml. For those presenting at moderate time window (>6-24 hours), the most commonly administered dose remains 150ml (45.45%), but other doses (50ml, 250ml, and 350ml) were also used. In the "Very Late" category (72-168 hours), 41.7% received 350ml, and others received 150ml, 250ml, or up to 750ml, while the single "Extremely Late" case (>168 hours) was treated with 150ml of ASV.

Discussion:

This study investigated the demographic profile, symptom pattern, and association between the severity of snakebite

envenomation and Anti Snake Venom (ASV) administration at a prominent poison control center in Karachi, Pakistan. The findings reveal numerous significant patterns with clinical and public health consequences. Our study discovered that the majority of snakebite victims were young males from rural areas, which is consistent with earlier studies that imply that earning members of a family, as well as occupational and environmental exposure, lead to significant hazards.16-18 Other studies have found that the majority of bites occur in the lower limbs.[4,16] This highlights the need of educating vulnerable people about preventive actions. Swelling, discomfort, and active bleeding were the most common clinical signs, accounting for more than 80% of reported symptoms, as illustrated by the Pareto chart. This is consistent with the recognized effects of snake envenomation, which often begins with local discomfort and erythema, progresses to bulla development, and eventually leads to coagulopathy and hemorrhagic signs such as bleeding.[19-21] While uncommon, systemic symptoms such as hematuria, hematemesis, and respiratory distress were seen in a tiny proportion of patients, frequently associated with increased envenomation severity.[22] These findings emphasize the variety of clinical appearances and the significance of a thorough examination. The typical practice at the poisoning center was to administer 50ml of anti-snake venom upon arrival, followed by 50ml twice daily until an improvement in INR was documented and sustained. This equates to a total dose of 150ml on the first day. There was a substantial correlation ($p < 0.001$) between envenomation severity and ASV dosage, with higher doses resulting in greater clinical severity. Mild instances were typically treated with 50-150ml, however significant envenomation showed more variation in dose, with 150ml remaining the most commonly utilized, followed by 250ml. This pattern of dosage escalation in response to symptom intensity is consistent with the findings of Agarwal R, al.[23],and Kumar [24] who discovered a tiered ASV administration technique in Indian and Brazilian hospitals based on symptom presentation and progression. In contrast, severe and extremely severe patients necessitated greater and more varied dosing, with one case topping 750ml. Alvitigala et al.[25] propose a personalized therapeutic method affected by clinical judgment and symptom progression, such as coagulopathy, neurotoxicity, or organ malfunction. Interestingly, whereas one might predict a delayed presentation to correspond with higher ASV dosages, the data revealed no statistically significant connection ($p = 0.159$). However, the tendency points to a clinical preference for greater ASV dosages with delayed presentation. The Early group (>1h-6h) accounts for the majority of cases, with 150ml being the predominant dosage; in the Moderate group (>6h-24h), 150ml remained the primary dose, accompanied by a wider distribution of dosages, indicating that an adaptive clinical approach is required, as suggested by Daswani et al.[16] and Gopal et al.[26], who emphasize modified dosing strategies in such scenarios. In the Late (>24h-72h) and Very Late (>72h-168h) groups, there is a distinct movement toward greater doses, which is presumably due to attempts to manage long-term venom effects. The vast majority of patients were critically stable upon admission and recovered within 1-2 days of hospitalization, indicating a good prognosis for snakebite, as reported in other research.[16] None of the patients died, and the dosing approach used by NPCC, Karachi had positive results for all patients. However, the appearance of a few serious cases necessitating protracted hospitalization and high ASV doses highlights the unpredictable nature of envenomation.

Conclusion:

Based on our findings, we advocate developing standardized, severity-based ASV dosing procedures that include clinical criteria for hemotoxic and neurotoxic manifestations. The dosing strategy used at NPCC, Karachi of 50ml as the first dose upon arrival, followed by 50ml twice daily and continuing this regimen for additional days in severe cases resulted in the survival of all patients in cost-effective settings and can be implemented in other poisoning centers across the country. Training programs for emergency and rural health staff should include red flag detection, dosing algorithms, and early referral protocols. Public awareness campaigns are required in snakebite-prone areas to encourage early hospital presentation. Furthermore, centralized ASV registries and real-time usage tracking should be developed to improve practice and inventory planning. These processes can help with clinical decision-making, reduce dosage variability, and improve results, particularly in resource-constrained situations.

Limitation:

The retrospective nature of this investigation, which depended on the accuracy and completeness of existing medical information, limited its scope. Furthermore, the study was conducted in a single tertiary care hospital, which limits the findings' applicability to other locations or healthcare settings. The tiny sample size may not reflect the entire range of ASV usage patterns. Prospective, multicenter investigations are recommended to confirm and expand on these findings.

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Authors' Contribution	
Muhammad Ashar Khan	• conception and design of the study • data acquisition and manuscript drafting, critically revised the manuscript for important intellectual content. • approved the final version for publication.
Muhammad Inam Khan	• conception and design of the study, • reviewed and revised the manuscript for important intellectual content • approved the final version for publication.
Attaullah Abban	• Drafting the manuscript, • critically revised the content for intellectual accuracy • approved the final version for publication.
Muhammad Omer Sultan	• Reviewed and revised the manuscript for important intellectual content • provided critical input for improvement approved the final version for publication.
Desaar Zehra	• Data collection analysis and interpretation. • critically revised the manuscript for intellectual content. • approved the final version for publication.