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Original Research Article

# A Study on Prevalence of the Adverse Drug Reactions and Dosage Pattern of Anti-Snake Venom.

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**Abstract**

**Background:** Snake bite is a common, neglected and frequently devastating environmental and occupational disease, especially in rural areas of tropical developing countries. Anti-Snake venom (ASV) is the only promising lifesaving treatment for management of snake bite, till date. Adverse Drug reactions (ADR) is defined as "any noxious change which is suspected to be due to a drug, occurs at doses normally used in man, requires treatment or decrease in dose or indicates caution in the future use of the same drug".

**Aims and Objectives:** This study aimed to know prevalence of the Adverse Drug Reactions and dosage patterns of Anti-Snake Venom.

**Material and Methods:** This prospective observational study was conducted in patients admitted with snake bite in Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar during February 2020 to December 2021.

**Results:** Among all 150 victims of snake bite, prevalence of Adverse Drug Reaction was found to be 33%. Patients were administered with ASV I, ASV II and ASV III. Male were dominant over the female in this study. There was a no significant correlation between the various manufacturers and incidence of adverse reactions.

**Conclusion:** Though the incidence of ADR is more troublesome, ASV is the only safe and effective drug in preventing morbidity. Different manufacturers did not show any significant variations in the adverse reactions.

**Keywords:** Anti-Snake Venom, Adverse Drug Reactions, Haemotoxic, Neurotoxic



## Background

Snake bite is a common, neglected and frequently devastating environmental and occupational disease, especially in rural areas of tropical developing countries. It is a major public health problem in India with estimated annual snake bite incidence of about 2,50,000 out of which approximately 20% bites resulted in significant envenoming which required anti-snake venom administration [1]. The snake bite associated morbidity is estimated to be about 1.4-68 per 1 lakh population, mortality about 1.1-2.4 per 1 lakh and case fatality rate of 1.7-20% [2]. It is estimated that between 35,000-50,000 people die of snake bite in India each year [3].

Anti-snake venom (ASV) and its rational use is the only definitive treatment to neutralize venom in circulation and in tissue fluid to save life in snake bite cases. In India only polyvalent ASV is available. The antivenins are produced against 4 most important venomous snakes of India i.e Naja naja (Indian cobra); Bungarus caeruleus (Indian common krait); Daboia russelli (Russell's viper) and Echis carinatus (Saw-scaled viper). Each ml of polyvalent ASV produced in India neutralizes 0.6 mg dried Indian cobra venom, 0.45 mg dried common krait venom, 0.6 mg of dried Russell's viper venom and 0.45 mg of dried Saw-scaled viper venom [4, 5].

Adverse Drug reaction is defined as any noxious change which is suspected to be due to a drug, occurs at doses normally used in man, requires treatment or decrease in dose or indicates caution in the future use of the same drug [6]. The overall approximate hospitalization due to ADRs is estimated to be 5% ranging from 2% to 20%. At least one in 10 to 20% of the hospitalized patients develop ADR [7].

Studies have shown that between 20% and 80% of ADEs and ADRs are preventable with the majority of latter studies showing around 60 - 70% preventability [8]. All the tropical diseases have alternate drugs for their management. But, ASV is the only lifesaving yet dangerous treatment for snake bite. The reactions due to ASV are indeed unpredictable and underreported. The irrationality in its usage is usually due to fear and lack of experience. Moreover the cost and the adverse reactions are mostly taken under consideration. In various parts of the world, there is a continuing crisis in the production, deployment and accessibility of antivenom.

Many of the physicians now-a-days do not rely mainly on the polyvalent ASV in India as they do not cover all the important snake species. Thus, the utilization pattern tends to vary in different regions.

The past decade has seen a wide range of studies on snake bite. But the clarity on the utilization pattern and adverse reactions are still underreported. Also there are very limited manufacturers of ASV in India. Only polyvalent ASV is available in India. There is always a debate on the incidence of adverse reactions due to ASV. Thus in the present study we are going to study about prevalence of adverse reaction and dosage pattern of Anti snake Venom (ASV).

## Materials and methods

A Prospective observational study was conducted on 150 patients admitted during the study period at Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar after getting ethical approval from Institutional ethical committee, during the period of February 2020 to December 2021.

### Inclusion criteria

All patients who were admitted with complaints of snakebite during the study period were considered for the study.

### Exclusion criteria

Cases of unknown bite or which lacked evidence of snake envenomation were excluded.

### Methodology

The relevant details of the study population were collected from our hospital area and demographic, clinical profile, type of envenomation, details of ASV used and its adverse effects, outcome of the patient. Inj. ASV used in this study were from three manufacturers which were depicted in this study as ASV I, ASV II and ASV III. All the patients were monitored for a period of 12 to 24 hours.

Each case of snake bite was admitted and thoroughly examined by the treating doctor. After Securing airway, the patient was subjected to Whole Blood Clotting Test (WBCT).

### Statistical Analysis

Collected data were entered in Microsoft Excel 2016 for further analysis, Qualitative data was expressed in frequency and proportion. Chi-square test was used to see the difference between the proportion. P-value<0.05 was considered as statistically significant. Statistical analysis was done by using SPSS software of version 25.

## Results

In this study, 150 patients were included between age group of 6 to 55 years of age. In the study maximum patients were from the age group of 31 to 55 years. 70.7% of the snake bite victims were male. 72% of the patients were Labourers.

**Table 1: Distribution of Demographic profile of snake bite victims**

| Parameters | Number | Percentage |
|---|---|---|
| **Age** | | |
| >10 Years | 6 | 4 |
| 11 - 30 Years | 11 | 7.33 |
| 31 - 50 Years | 109 | 72.67 |
| >50 Years | 23 | 15.33 |
| **Gender** | | |
| Male | 106 | 70.7 |
| Female | 44 | 29.3 |
| **Profession** | | |
| Labourer | 108 | 72 |
| Farmer | 14 | 9.3 |
| Student | 14 | 9.3 |
| Housewife | 8 | 5.3 |
| Security | 2 | 1.3 |
| Gardner | 2 | 1.3 |
| Others | 2 | 1.3 |

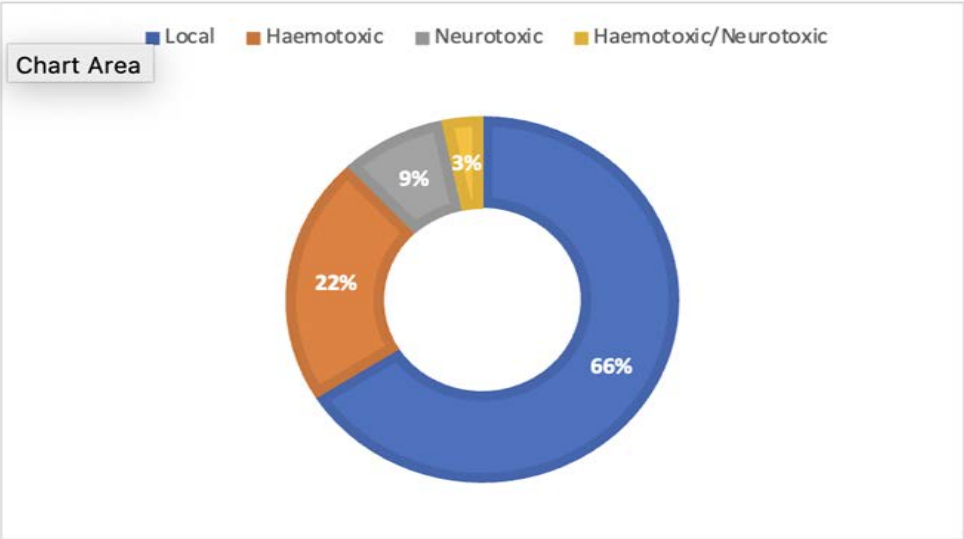


**Figure 1: Distribution of type of envenomation among snake bite victims**

Our study found that 68% of the patients had local envenomation, followed by 23% had hemotoxic envenomation.

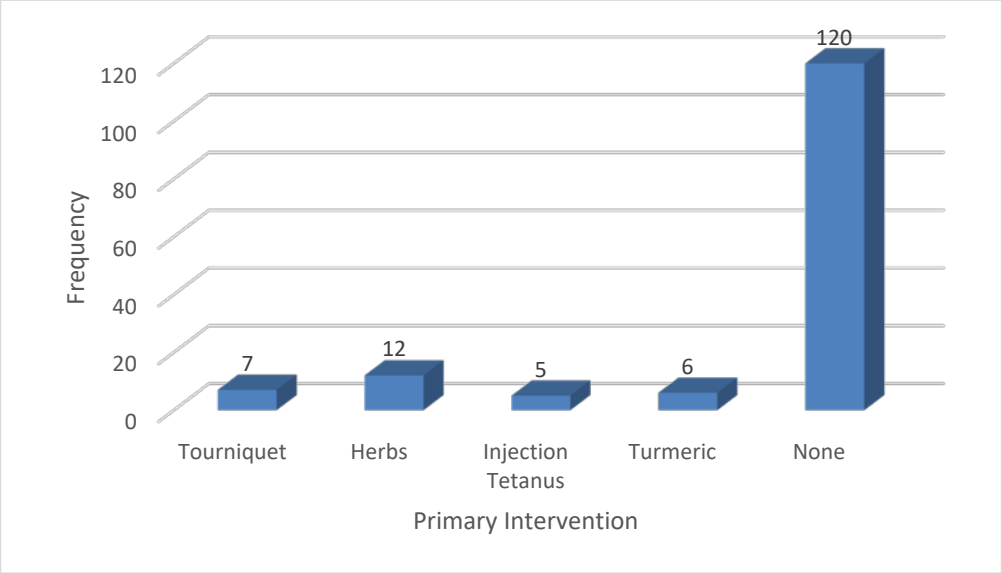


**Figure 2: Distribution of primary intervention among snake bite victims**

**Table 2: Association between Type of Envenomation and ADR**

| Type of Envenomation | Reactions | | Total |
|---|---|---|---|
| | Present (%) | Absent (%) | |
| Local | 5 (3.3%) | 94 (62.7%) | 99 (66.0%) |
| Hemotoxic | 30 (20.0%) | 3 (2.0%) | 33 (22.0%) |
| Neurotoxic | 12 (8%) | 1 (0.7%) | 13 (8.7%) |
| Hemotoxic/Neurotoxic | 2 (1.3%) | 3 (2.0%) | 5 (3.3%) |
| Total | 49 (32.7%) | 101 (67.3%) | 150 (100%) |

ADRs were seen in 20% of the patients who had hemotoxic envenomation followed by 8% who were Neurotoxic and 1.3% with both hemotoxic and Neurotoxic.

**Table 3: Association between ASV Manufacturer and ADR**

| ASV Manufacturer | Adverse Reactions | | Total |
|---|---|---|---|
| | Present | Absent | |
| ASV I | 10 (6.7%) | 25 (16.7%) | 35 (23.3%) |
| ASV II | 31 (20.7%) | 56 (37.3%) | 87 (58.0%) |
| ASV III | 8 (5.3%) | 20 (13.3%) | 28 (18.7%) |
| Total | 49 (32.7%) | 101 (67.3%) | 150 (100%) |

ADRs were seen in 20.7% of the patients who were given ASV II drug followed by ASV I (6.7%) and ASV III (5.3%)

**Table 4: Association between No. of Vials Used and Adverse Reaction**

| No. of vials | Reactions | | Total |
|---|---|---|---|
| | Present (%) | Absent (%) | |
| 01 - 10 Vials | 32 | 48 | 80 |
| 11 - 20 Vials | 10 | 47 | 57 |
| > 20 Vials | 7 | 6 | 13 |
| Total | 49 | 101 | 150 |

Among 150, 32 patients were given1 to 10 vials, followed by 11-20 vials for 10 patients and >20 vials for 7 patients respectively.

**Table 5: Distribution of Adverse effect of ASV among snake bite victims**

| Adverse Reaction | Number | Percentage |
|---|---|---|
| Itching | 20 | 41 |
| Chills & Rigor | 6 | 12 |
| Nausea & Vomiting | 7 | 14 |
| Dyspnoea | 6 | 12 |
| Anaphylaxis | 4 | 8 |
| Urticaria | 4 | 8 |
| Fever | 2 | 4 |
| Total | 49 | 100 |

## Discussion

In the present study, around 150 patients were admitted with snake bite during the study period. Bites were common in the adult age group of 31 to 55 years (88%) with males (70.7%) more affected than females (29.3%) which may be attributed to the fact that men in this age group are physically active and involved in outdoor activities compared to females. In many previous studies also, it was observed that maximum patients affected with snake bite were males compared to females. In the present study, 4% were teenagers. Among them one teenager with the age of 6 years was the victim of snake bite while playing at the farm.

The most common pre hospital intervention in our study was the application of tourniquet (7) and administration of injection tetanus toxoid (5). Six patients used topical application of turmeric and 12 patients used topical application of extract of herbs. In the present study, we found that in majority of cases the exact snake species was not identified, even though fang marks and other symptoms suggestive of venomous bites were present in these cases. As per victims statement, maximum patients had the bite mark on lower limbs compared to upper limbs.

In our study local envenomation was the commonest type of envenomation among all. 66% of the total patients had local envenomation followed by hemotoxic (22%), neurotoxic (8.7%). Both the hemotoxic and neurotoxic (3.3%) envenomation which is more characteristic of Russel‘s viper with both coagulation and neurological manifestations. In one study conducted in Pakistan revealed 84.7% hemotoxic, 8.7% neurotoxic and 6.5% hemotoxic/neurotoxic [9]

All the victims with absolute indications were administered Anti snake venom as the definitive management of ASV from different manufacturers and batch number. ASV from three manufacturers were used in the study designated as ASV I, ASV II and ASV III.

Studies have proven that administration of ASV to victims with established respiratory paralysis does not reverse paralysis [10]. This was one of the important reasons where the lack of restoration of the symptoms had let to administration of excess amount of antivenom. So cautious use of ASV with special concerns about cost and dose is essential for effective management.

Adverse reactions were seen in 49 (33%) patients. Generalized and focal itching were most commonly seen in 20(41%) patients, followed by dyspnoea, nausea and vomiting (14%). Chills & rigor and anaphylaxis were seen among 12% of the patients. To our knowledge, none of the studies in South Asia had reported any death due to adverse reactions and are under-reported. Studies conducted by Mathivani et al, Deshmuhk et al, Sheik et al [11, 12, 13] observed the prevalence of adverse drug reaction was 59.9%, 62% and 23% respectively. Comparing our study with other studies it can be noticed that, difference in the rate of prevalence depends on the various factors mainly like time to reach hospital, geographical area and so on. [14]

The frequency of adverse reactions among various manufactures showed that ASV I, ASV II and ASV III had 10/35, 31/87 and 8/28 reactions respectively. The frequency of the adverse reactions among the three manufacturers was compared using chi-square test and was found to be non significant (P> 0.05). In our study prevalence of adverse reactions are more because of lack of knowledge by the patients or relatives about severity of snake bites and their treatment. Especially in rural area after snake bites, instead of attending the hospital they go for traditional treatment, so the severity increases and leads to the adverse reactions. So for the management of the snake bite victims, social awareness and knowledge about snake bites and their severity among rural as well as urban areas is very important.

Study has some limitations that, the patients were observed only during their admission into hospital and the late reactions which usually occur after a mean of 7 days post treatment were missed. Even after the patients were discharged, the possibilities of the patients returning with complaints of late reactions were rare as the symptoms were often mistaken. No telephonic communication has been made to know the late reactions if any. Readmission details were not available.

## Conclusion

It can be concluded that preventive measures are still underdeveloped for management of snake bite victims. Though the incidence of ADR is more troublesome, ASV is the only safe and effective treatment in preventing morbidity. In the current era where most of medical expenditure is rising up, optimizing the ASV usage becomes one of the important aspects in the treatment. Different manufacturers of ASV did not show any significant variations in the adverse reactions. Premedication had no role in the reduction of adverse reactions. Also batch number should also be periodically checked with response to the incidence of ADRs.

**Acknowledgement:** None

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