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# Anti Snake Venom Consumption In Symptomatic Snake Bite Patients Attending Tertiary Care Centre In Central India

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**Abstract**

**Introduction**

Snake bite in India is a common medical emergency and an occupational hazard for majority of Indian population especially farmers. This study focuses on evaluating the ASV consumption in various types of snake bites found in our area.

**Material & Methods**

75 patient diagnosed with symptomatic snake bite with fang marks and signs of envenomation were assessed over a period of 1 year. The requirement of ASV, duration of hospital stay, duration of ventilator support, outcomes were assessed and compared.

**Results**

Maximum cases belonged to age group interval of 21-30 years (26.7%). Study revealed male sex predilection with 52% Males and 48% Females. Maximum patients resided in rural areas (78.7%) while rest pertained from urban areas (21.3%). Average dose of ASV was higher for neurotoxic snake bite(61.79) as compared to Hematotoxic snake bite(50.06). Neostigmine, Atropine requirement and duration of ventilator support had significant difference between two snake bites (P-value <0.001, P-value=0.001, P-value=0.004). No significant differences was established for required ASV dose(P-value =0.35), atropine(P-value =0.083), neostigmine(P-value =0.067), and duration of ventilator support(P-value =0.083) with respect to the outcomes.

**Conclusion**

In this study, it was found that high ASV dose was required in neurotoxic snake bites. However, the findings need to be tested in a larger randomized controlled trial for definitive conclusions. Regular public health programmes regarding pre –hospital management and the importance of the early transfer to the hospital should be appreciated.

**Keywords**: Snake bite, Anti-snake venom, Neurotoxic snake-bite, Hematotoxic snake-bite

## Introduction

Snake-bite is an occupational disease of farmers, plantation workers, herdsmen, fishermen, and other food producers. It is therefore a medical problem that has important implications for the nutrition and economy of the countries. It is a serious medical crisis, wherein the spectrum of injury can vary from local tissue damage to involvement of almost all vital organs of the body [1]. According to World Health Organization (WHO), people living in densely populated low altitude agricultural areas in the states of Bihar, Jharkhand, Madhya Pradesh, Odisha, Uttar Pradesh, Andhra Pradesh, Telangana, Rajasthan and Gujarat, suffered 70% of deaths during the period

2001-2014, particularly during the rainy season when encounters between snakes and humans are more frequent at home and outdoors [2].

Snakebite remains an underrated cause of accidental death in modern India. It is even more underestimated as people fail to reach out to modern medicine and fall victim to the handful of quacks using traditional healing methods [3]. India has vegetation involving 250 species and subspecies of snakes, out of which 50 are venomous. Mainly 4 venomous land snakes pose public health problem in India. Among them are elapidae, including cobra (Najanaja) and krait (Bungarus caeruleus) and viperidae Russell's viper (Daboia russelii) and saw scaled viper (Echiscarinatus) [4].

Snake bites are categorized into neurotoxic, hematotoxic, and locally toxic on the basis of toxicity. The toxic effect of snake venom is the result of its protein and the nonprotein component. It is further complicated by the inflammatory response of the victim's body and damages red blood cells, leukocytes, platelets, skeletal muscle, vascular endothelium, peripheral nerve endings, as well as the myoneural junction. Hyaluronidase helps spread of venom through tissues, and proteolytic enzymes are responsible for the local edema, blistering, and necrosis. Alpha- Neurotoxins and beta- neurotoxins lead to a flaccid paralysis of the victim [8]. Kidney related complications and breathing difficulty are common in patients with snake bites admitted in the hospital and is also an important cause of morbidity and mortality [9].

Anti–snake venom (ASV) is immunoglobulin prepared by immunizing horses with the venom of poisonous snakes and subsequently extracting and purifying the horses' serum. Antivenoms may be species specific (monovalent/monospecific) or may be effective against several species (polyvalent/polyspecific) [10]. As per the recommendations of WHO, the most effective treatment for snakebite is the administration of monospecific ASV; however, this therapy is not always available to snakebite victims because of its high cost, frequent lack of availability, and the difficulty in correctly identifying the snake [2].

In India, polyvalent antivenom prepared by Central Research Institute, Kasauli Himachal Pradesh is effective against the most common Indian species. While, Antivenom produced at the Haffkine Corporation, Parel (Maharashtra, Mumbai) is effective against the venom of larger range of species [11]. ASV treatment can be expected to neutralize free circulating venom, prevent progression of envenoming and allow recovery. However, these processes are time taking so, the severely envenomed patient might require life support systems such as treatment of shock, assisted ventilation and renal dialysis until the severely damaged organs and tissues have had time to recover [2].

Since there is no proper reporting system and regular studies in snake bites in snake prone areas are lacking, very reliable data on treatment protocol is not available. Therefore, we focused on objective of evaluating the requirement of ASV in various types of snake bites.

**Material And Methods**

This single centre, hospital based cross-sectional observational study was conducted in department of Medicine at DR. B.R.A.M.H Raipur located in Central India. 75 patients visiting Medicine OPD with snake bite or fang marks along with signs of envenomation for a period of 1 year from October 2020 to September 2021 were included in this study.

Patients with Asymptomatic snake bite, absence of fang mark, cases suffering from pre existing liver disease with coagulopathy, or patients taking anticoagulant or antiplatelet drug therapy were excluded from the study. After explaining the study procedure, written informed consent obtained from all the subjects selected for the study. Data was collected in a predesigned questionnaire after availing necessary ethical approval from the institution and cases were meticulously looked for various aspects such as age, address, urban or rural area, presenting complaints, bite site, species of snake (if identified), pain or bleeding from the site of bite, ptosis, breathing difficulty, excessive salivation, bleeding from gums or other mucosal membranewere identified.

All cases underwent clinical follow up from the period of their admission to their discharge to collect information about requirement of ASV, duration of hospital stay, duration of ventilator support (if required), any complications like Acute kidney injury, Cellulitis and about patient status whether



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patient got discharged or in case of death of patient. Lab investigations like complete blood count, total leucocyte count, platelet count, 20 mins whole blood clotting *test* (*WBCT*), prothrombin time international normalized ratio (PT INR), renal and liver function tests, Serum potassium level were assessed.

The collected data were tabulated and statistically analyzed using SPSS© for windows™ Vs 17, IBM™ Corp NY and Microsoft excel™ 2007. Kolmogorove-Smirnove analysis was performed for checking linearity of the data. Chi square test/ Fischer's exact test was used to analyze the significance of difference between frequency distribution of the data. Comparison of mean and SD between two groups was done by using students t test and Analysis of variance (ANOVA). P-value <0.05 was considered as statistically significant.

## Results

Patients demographic data showed that the most common age group which presented belonged to age interval of 21-30 years (26.7%). This was followed by age groups 31-40 years (22.7%) and </=20 years (20.0%). While few subjects were present in age group 41- 50 years(17.3%), age group 51 -60 years (9.3%), and least cases pertained to the category >60 years of age (4.0%).

Gender wise appraisal showed that out of total patients there were 52% Males and 48% Females. In the present study, maximum number of patients belonged to rural areas (78.7%) while rest cases were from urban areas (21.3%).

During appraisal for comparison of treatments given, average dose of ASV for Hematotoxic snake bite was 50.06 vial while for neurotoxic snake bite it was 61.79 vials and no significant difference was observed between two types of snake bites regarding ASV requirement. (P-value =0.101). Significant difference was observed between two types of snake bites regarding neostigmine and atropine requirement. (P-value <0.001 and P-value =0.001). The duration of ventilator support was found to be significantly longer in case of neurotoxic snake bite (P-value =0.004). On the other hand, we could not establish significant difference between both the snake species in regards with duration of hospital stay (P-value =0.63)

Also in present study, while comparing outcomes with treatment regimen, we could not establish significant differences for ASV dose required (P-value =0.35), atropine (P-value =0.083), neostigmine (P-value =0.067), and duration of ventilator support (P-value =0.083) with respect to the outcomes in the study subjects.

## Discussion

### Baseline characteristics

Out of 75 patients of pancreatitis, in the present study, majority of study subjects were found to be 21-30 years (26.7%). This was followed by 17 (22.7%) and 15 (20.0%) in the subjects respectively in age groups 31-40 years and </=20 years. While 13 (17.3%) subjects were present in age group 41- 50 years, 7 (9.3%) subjects were found under the age group 51 -60 years, and only 3 (4.0%) subjects fell under the category >60 years of age. These observations were in consensus with studies done by Biradar et al, Bhalla et al, and pandey et al [12-14].

During genderwise appraisal, out of 75 subjects in total we found that male preponderance with 39 (52.07%) males and 36 (48.0%) females. Male preponderance was observed in some other studies as well such as Hansdak SG et al., who found that snake bite was 2.5 times more common in males [15]. In the study by Paul V et al., male preponderance was 75% [16]. Mahajan et al., in 2015 also conducted similar study and found 66% of the patients to be males [17]. The high incidence of snake bite in the male is due to the following reasons India is basically agricultural nation with rich tropical climate with lush vegetation. Males are more exposed to snake bite because they are the main breadwinners in the Indian family set up and women are housewife mainly in the rural setup. So this preponderance is mainly an occupational risk. In the case of urban population, the male children and adolescents are more commonly affected as they spend more time outdoors than female counterparts. In the rural setup, the female children and adolescents are mainly burdened with taking care of the family chores and males are expected to earn.

In present study, out of 75 subjects in total, 59 (78.7%) subjects lived in the rural area while, 16 (21.3%) subjects lived in the urban area. In our study snakebite was mainly seen in rural area. Similar



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observations were made by Biradar et al., with 66.6% cases from rural area, and also by Mahajan et al., with 85% incidences from rural area [12,17] The higher rate of incidence in rural areas is due to the fact that snake seek preys such as rodents in the cultivated field.

**Distribution of study subjects according to snake bites**

In present study, out of 75 subjects in total, the snake bite in 57 (76.0%) subjects was found to be neurotoxic and 18 (24.0%) subjects it was hematotoxic. Our study findings were in consensus with Lingayat et al., as they found higher neurotoxic cases similar to our study [18]. Also, in our study the most common site of bite was found to be lower limb in 39 (52%) subjects. This was followed by upper limb in 28 (37.33%) subject and other sites like trunk in 4 (5.3%) subjects, face in 3 (4.0%) subjects and head in 1 (1.3%) subject. Reid et al., also further supported our findings as they mentioned that most of the bites in tropical countries were on lower extremities because the victims are bitten by treading on or near the snake, while in non-tropical countries most bites are on fingers and hands because the victim deliberately handles the snake [19]. Pandey et al., also observed that most frequently bitten site was the lower extremity (83%) and in few over upper extremity (17%) [14].

**Comparison of treatment in types of snake bite**

In present study, average dose of ASV required in the study subjects was assessed and was found out to be 58.97 vials. In Hematotoxic snake bite, requirement was 50.06 vials whereas in Neurotoxic it was 61.79 vials. The management of neurotoxic snake bite victim was primarily ASV administration along with mechanical ventilation as supportive therapy. For hematotoxic either low dose infusion therapy or high dose intermittent bolus therapy is followed. In a study conducted by Sharma et al., the average dose of antivenom was 51.2 vials for elapid bites (Neurotoxic) and 31 vials for viper bites similar to our study [20]. In another study conducted by Agrawal et al., the mean total amount of ASV used was 412 ml(41.2 vial) in neurotoxic snake bite [21]. Biradar et al., in their study treated 66.7% patients with ASV**.** Only 28 % of patients received more than 20 vials of ASV **[12].** The mean dose of ASV given in a study conducted by Pandey et al was 16.99 vials (169.90 ml) [14]. The mean dose of ASV which was given for the neuroparalytic snake bites was 16.2 vials (range 10-32 vials) and 21 vials (range 10-40) were given for the viper bites [22]. The main indication for ASV was vasculotoxic snake bite (75%) followed by neurotoxic snake bite (16%). Mean dose of ASV was 18.63 ± 14.52 vials by Pore et al [23]. The difference in recommended dose in our study as compared to others could be because the treatment is based on the severity of bite, clinical features and features of systemic envenomation. Also there is geographical variation in species and venom composition.

Requirement of Atropine and Neostigmine was more in neurotoxic snake bites as compared to hematotoxic snake bite in our study. In a study conducted by Pandey et al., Neostigmine in a dose range of 0.01-0.04 mg/kg every 1-3 hour up to a maximum of 10 mg/24 hour was administered by intramuscular or intravenous route. Patients were observed over 30-60 min for improvement of ptosis. In their study 84% subjects responded to neostigmine and showed improvement in ptosis and in rest of the 16% patient neostigmine was discontinued in view of lack of response [14]. Anticholinesterase drugs have a variable, but potentially useful effect in patients with neurotoxic envenoming. Anticholinesterases acts against the postsynaptic toxins (such as those of cobra) that induce a myasthenia-like block. They are not active against toxins acting presynaptically (common Krait). They are also not useful if administered late, as binding of toxin to acetylcholine receptors becomes relatively irreversible with time. Atropine must be given to counteract the unwanted muscarinic side effects of neostigmine. Comparison of outcomes with treatment regimen in the study subjects was performed. No significant differences was found for ASV dose (P-value =0.35), atropine (P-value =0.083), neostigmine (P-value =0.067), and duration of ventilator support (P-value =0.083) with respect to the outcomes in the study subjects.

**Conclusion**

Snake bite in the tropics is a rural and an occupational hazard of farmers, plantation workers, herders and hunters. The available data on the treatment protocol for snake bite in the Indian subcontinent is sparse. Most of the traditional methods for the first aid treatment of snake bite have



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been found to result in more harm than good. The immobilization and the prompt transport of the snake bite victims to the hospital, along with the prompt administration of ASV, remains the mainstay to reduce the morbidity and the mortality which are associated with snake bites. Important findings of our study are high ASV dose requirement in neurotoxic snake bites as compared to hematotoxic snake bites with use of prophylactic premedication like neostigmine and atropine. In future, development of region specific, highly potent antivenom, and prospective evaluation of its safety and efficacy is needed. Development of appropriate local guidelines and training of physicians involved in the treatment of snake bite is equally important.

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## Tables And Figures

**"Table 1 : Baseline characteristics of patients included in the study (n=75)"**

| **Categorical variables** | **Percentage** |
|---|---|
| **Sex** | |
| Males | 52 |
| Females | 48 |
| **Residential area** | |
| Rural | 78.7 |
| Urban | 21.3 |
| **Age (Years)** | |
| </=20 | 20.0 |
| 21-30 | 26.7 |
| 31-40 | 22.7 |
| 41-50 | 17.3 |
| 51-60 | 9.3 |
| >60 | 4.0 |

**"Table 2 : Distribution of study subjects according to snake bite (n=75)"**

| **Type of snake bite** | **Percentage** |
|---|---|
| Neurotoxic | 76 |
| Hematotoxic | 24 |
| **Site of snake bite** | |
| Lower limb | 52.0 |
| Upper limb | 37.33 |



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| | |
|---|---|
| Trunk | 5.3 |
| Face | 4 |
| Head | 1.3 |
| Trunk | |

**"Table 3 : Comparison of treatment in types of snake bite (n=75)"**

| **Severity indices** | **Parameter** | **Mean ± SD** | **P-value** |
|---|---|---|---|
| **ASV** | Hematotoxic | 50.06 ± 24.28 | 0.101 |
| | Neurotoxic | 61.79 ± 29.97 | |
| **Neostigmine** | Hematotoxic | 0.56± 1.11 | <0.001 |
| | Neurotoxic | 2.98± 2.66 | |
| **Atropine** | Hematotoxic | 0.67± 1.33 | 0.001 |
| | Neurotoxic | 3.65± 3.42 | |
| **Ventilatory support** | Hematotoxic | 0.00 ± 0.00 | 0.004 |
| | Neurotoxic | 1.53± 2.15 | |
| **Duration of hospital stay** | Hematotoxic | 5.1667 ± 2.00734 | 0.63 |
| | Neurotoxic | 4.8246 ± 2.79108 | |

**ASV- Anti-snake venom, SD- Standard Deviation**



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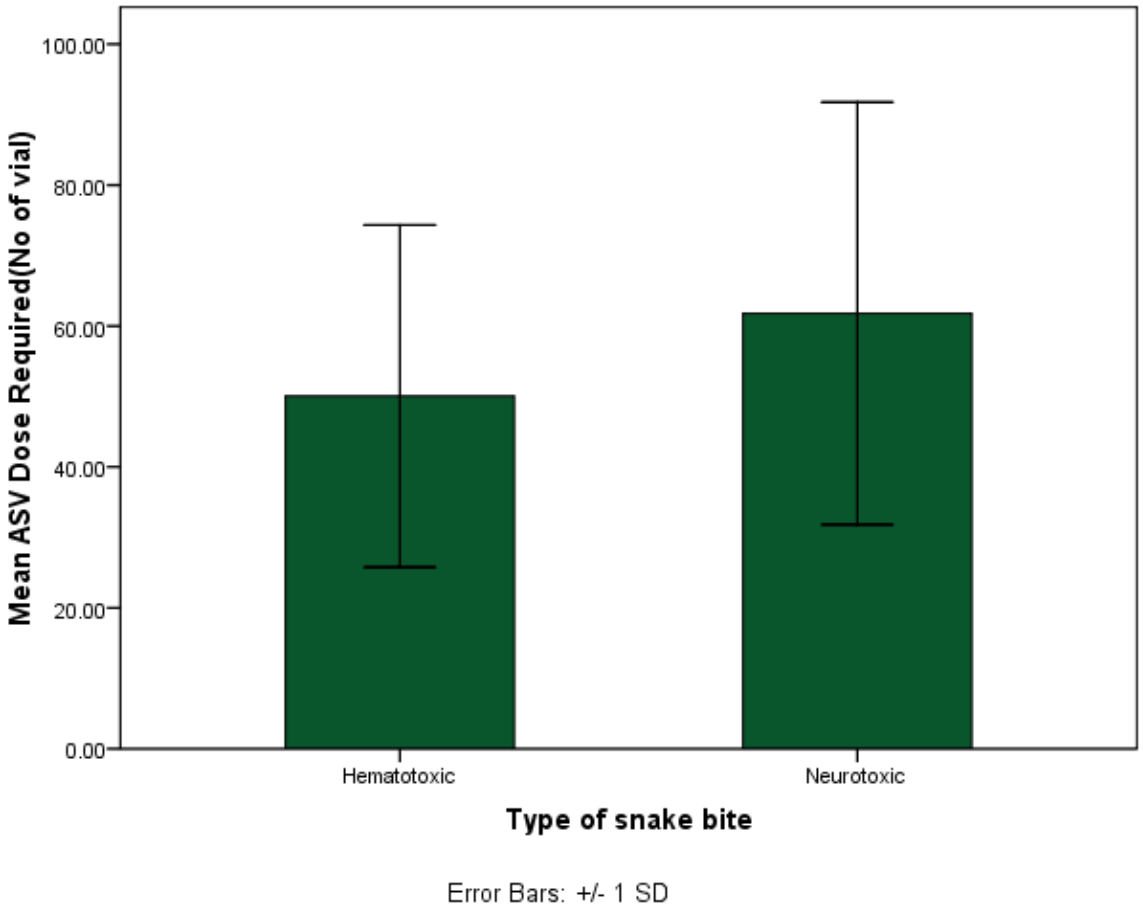
**Figure 1: Comparison of average dose of ASV required in types of snake bite**




**"Table 4 : Comparison of outcomes with treatment regimen in the study subjects (n =75)"**

| | | Mean | S.D. | 95% Confidence Interval for Mean | | P -alue |
|---|---|---|---|---|---|---|
| | | | | Low | High | |
| ASV Dose Required(No of vial) | Death | 41.00 | 21.62 | 14.15 | 67.85 | 0.35 |
| | Discharge with disability | 58.25 | 30.33 | 38.98 | 77.52 | |
| | Discharge | 60.67 | 29.15 | 53.01 | 68.34 | |
| | Total | 58.97 | 28.99 | 52.30 | 65.64 | |
| Atropine (mg) | Death | 3.56 | 1.57 | 1.61 | 5.51 | 0.083 |
| | Discharge with disability | 1.00 | 1.54 | 0.02 | 1.98 | |



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| | | | | | | |
|---|---|---|---|---|---|---|
| | Discharge | 3.28 | 3.55 | 2.35 | 4.22 | |
| | Total | 2.94 | 3.31 | 2.18 | 3.70 | |
| Neostigmine (mg) | Death | 3.12 | 1.09 | 1.76 | 4.48 | 0.067 |
| | Discharge with disability | 0.83 | 1.29 | 0.02 | 1.65 | |
| | Discharge | 2.66 | 2.78 | 1.93 | 3.39 | |
| | Total | 2.40 | 2.59 | 1.80 | 3.00 | |
| Duration of Ventilator Support (Days) | Death | 1.20 | 1.10 | -0.16 | 2.56 | 0.083 |
| | Discharge with disability | 0.00 | 0.00 | 0.00 | 0.00 | |
| | Discharge | 1.40 | 2.16 | 0.83 | 1.96 | |
| | Total | 1.16 | 1.98 | 0.70 | 1.62 | |

**ASV- Anti-snake venom, SD- Standard Deviation**



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