

## Management of snakebite victims using low dose antsnake venom in a tertiary hospital in Southern Nigeria: A 5-year Retrospective study

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### Abstract

**Objective:** Antsnake venom (ASV) is a specific antidote for the management of snake bite envenomations. This study profiled the treatment and outcome of adult snake bite victims managed using low dose antsnake venom.

**Methods:** This was a 5-year retrospective study that involved all adult patients who presented in University of Benin Teaching Hospital, Benin City, Nigeria, with a history of snake bite. Information obtained were demographic characteristics, clinical features, and administered treatment per established. All patients with a diagnosis of snake bite envenomation were administered ASV.

**Results:** Sixty patients were seen during the study period, 35(58.3%) males, 25(41.7%) females with a mean age was  $34.7 \pm 13.3$ . The mean time from bite to presentation was  $14.67 \pm 14.05$  hours with range of 1-48 hours. Twenty patients (33.3%) had snake bite envenomations, of these eleven (57.9%) were managed and discharged after administration of 30 to 40 mls of polyvalent ASV. The mean dose of PASV used was  $3.9 \pm 2.0$  vials. The most encountered clinical indication for ASV administration was progressive painful swelling. No death was recorded throughout this period studied.

**Conclusion:** Adoption of the low dose regimen in the management of snake bite envenomations may be as effective as the traditional high dose regimen.

**Key words:** Snake bite, envenomation, polyvalent antsnake venom, Nigeria.

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Received: April 25, 2018

Accepted: June 06, 2018

Published: June 30, 2018

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<http://dx.doi.org/10.4314/rejhs.v6i2.5>

## **Le traitement des morsures de serpents chez les adultes, par l'administration d'une faible dose d'anti-venin de serpent. Une étude rétrospective étalée sur 5 ans, dans un centre hospitalier universitaire à Benin City au Nigéria.**

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### **Résumé**

**Objectif:** L'anti-venin du serpent (AVS) est un antidote destiné à traiter les envenimations causées par les morsures de serpents. Cette étude s'intéresse au traitement donné aux adultes victimes de morsure de serpent et à leur état de santé, après avoir reçu une faible dose d'anti-venin de serpent.

**Méthodes:** tous les patients adultes qui avaient été reçus aux services des urgences du CHU de Benin City au Nigéria, suite à une morsure de serpent, ont pris part à cette étude. Les informations récoltées l'ont été sur les données démographiques, les manifestations cliniques et les traitements donnés selon un protocole établi. Cette étude rétrospective et descriptive fut menée entre janvier 2013 et octobre 2017. L'ensemble des patients à qui on a diagnostiqué une envenimation par morsure de reptile a reçu un anti-venin de serpent (AVS).

**Résultats :** soixante patients ont été examinés pendant l'étude, 35 hommes (58,3%) et 25 femmes (41,7%). La moyenne d'âge se situait à 34,7 ans (+ ou – 13,3), avec des âges compris entre 18 et 83 ans. Le délai moyen observé entre la morsure et la présentation au CHU s'élevait à 14,67 heures (+ ou – 14,05 heures), avec des variables de 1 heure à 48 heures. Vingt patients (33%) furent infectés par une morsure de serpent, onze d'entre eux (57,9%) ont été traités et libérés après l'administration de 30 à 40 millilitres d'anti-venin de serpent polyvalent (AVSP). La dose moyenne administrée d'anti-venin de serpent polyvalent (par ampoule) s'est élevée à 3,9 (+ ou – 2.0). La justification médicale la plus avancée pour répondre de l'injection de l'anti-venin de serpent polyvalent résidait dans l'apparition d'un gonflement progressif douloureux. Aucun décès n'a été enregistré au cours de l'étude.

**Conclusion :** cette étude a montré qu'opter pour un traitement à faible dose après une morsure infectée de serpent pouvait être aussi efficace qu'une administration usuelle à forte dose. A terme, elle peut encourager une utilisation judicieuse de l'anti-venin de serpent.

**Mots clés :** morsure de serpent, envenimation, anti-venin de serpent polyvalent, Nigéria

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*Received: April 25, 2018*

*Accepted: June 06, 2018*

*Published: June 30, 2018*

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<http://dx.doi.org/10.4314/rejhs.v6i2.5>

## INTRODUCTION

Envenomation following Snake bite is a neglected clinical problem especially in the tropics (1). Accurate disease burden data is lacking, and documented estimates underscore the scale of the problem. However, a study in West Africa reported an annual incidence of 54/100,000 persons per year (PPY) and a mortality of 1.35/100,000 persons per year (PPY) annually (2).

There are many species of snakes worldwide but only 10-15% are poisonous. Venomous snakes are widely distributed in almost every country between 50° N and 50° S in the western hemisphere and 65° N and 50° S in the Eastern hemisphere (3). This includes Africa, Asia, Latin America, and the Oceanic countries. In Africa, they belong to four main families - *viperidae*, *elapidae*, *hydrophidae*, and *colubridae*. However in Nigeria, the most common poisonous snakes are the *elapids* and the *viperids* (4). Antisnake venom (ASV) is the only specific antidote for the management of snake bite envenomations. The conventional administration of ASV is based on the Blaylock algorithm (5) which follows a syndromic approach and puts into cognizance the clinical presentation of the patient, the severity of the bite, and the dose of the antivenom administered. This approach to snake bite management requires that victims receive polyvalent ASV at initial doses of 50mls for mild envenomations, 100mls for moderate envenomations, and 150mls for severe envenomations, despite the challenges of availability, accessibility and cost. This has led to a number of studies utilizing low dose ASV regimen (6-8), as against the conventional high doses with comparable efficacy in patient outcome.

The burden of snake bite in Nigeria is highest in the northern regions especially the Benue valley where incidence as high as 467 per 100,000 PPY has been reported (9). It is therefore not surprising that most of the research studies on snake bite in Nigeria have come from this region. This retrospective study has therefore been undertaken to profile the treatment and the outcome of adult snake bite victims managed in our centre using a low dose treatment regimen.

## MATERIALS AND METHODS

This study was carried out in the University of Benin Teaching Hospital (UBTH), Benin City, Edo State, South South, Nigeria. It is a federal government tertiary hospital with a 850 bed space capacity, and a referral centre for Edo

State and the adjoining states. This study was conducted between January 2013 and October 2017. It is a retrospective study. All adult patients with a history of snake bites who presented to the adult Medical Emergency Department were included in this study. Data were extracted from case notes and entered into a predesigned proforma data sheet. Information extracted included patients demographics, place of bite, time of bite, site of bite, clinical presentation, treatment given before and during hospitalization, doses of antisnake venom administered, occurrence of adverse drug reaction, length of hospital stay and outcome of treatment.

## Treatment Protocol

All patients with a diagnosis of snake bite were categorized into 2 groups- those with envenomation and those who had unconvincing features of envenomation. The latter group were observed for at least 24 hours thereafter are either discharged home or admitted if signs of envenomation become evident. Patients with features of envenomation were administered antisnake venom (ASV) a liquid, polyvalent, Enzyme refined Equine immunoglobulins (PASV), manufactured by Premium Serums and Vaccines PVT LTD, Maharashtra, India. The polyvalent ASV consists of hyperimmune horse serum against four common snakes- cobra, common krait, Russell's viper and saw- scale viper. Patients were administered low doses of the PASV in line with the treatment regimen adopted (10). Each patient with envenomation had an initial dose of 20mls of PASV diluted in 100mls of 5% glucose solution given intravenously over one hour, after an intradermal test dose. Thereafter the patient is reassessed for progression of clinical features. If no changes a further 10mls of PASV in 100mls glucose 5% solution is administered over four hours. This is repeated until there is improvement of clinical condition, then 10mls of PASV in 500mls of glucose 5% solution is administered for the next 24 hours. Patients were closely monitored for allergic reactions and managed accordingly with epinephrine, promethazine and hydrocortisone. All patients had crude clotting time done and had tetanus toxoid administered. Other medications administered included tramadol and prophylactic antibiotics.

Ethical approval was obtained from the University Teaching Hospital Ethics and Research Committee.

### Statistical Analysis

All data from the proforma data spread sheet were coded accordingly and entered for statistical analysis using SPSS software version 21. Results were expressed as means ( $\pm$  SD) and percentages where necessary. Descriptive statistics was used to summarize baseline values and demography. Chi square test was used to compare proportions. A P-value of  $< 0.05$  was considered as statistically significant.

### RESULTS

A total of 60 patients were seen during the study period, of these 35 (58.3%) were males while 25 (41.7%) were females. The overall mean age was  $34.72 \pm 13.3$ , with an age range of 18-83 years. Although more males were recorded in this study however differences in gender were not significant. The age group 18-40 years constituted 73.3% of the victims, Table 1.

Most of the patients (95%) had bites to the lower limbs, although there was also a report of upper limb and ocular envenomation. The mean time from bite to presentation was  $14.67 \pm 14.05$  hours (median time 11.5 hours, range (1-48) hours). The most encountered clinical presentation was localized pain (45%) at the site of bite, followed by progressive pain and swelling (13.3%). Other manifestations were prolonged clotting time (5%), local bleeding (3.3%), hypotension (3.3%) and constitutional symptoms (1.7%). Compartment syndrome was diagnosed clinically in only one patient who was bitten by a puff adder and subsequently had fasciotomy and removal of two gangrenous digital fingers. There were no neurological manifestations. (Table 2). Most bites were recorded in April and September. (Figure 1).

The management and outcome of snake bite is presented in Table 3. A total of twenty patients (33.3%) received Polyvalent antsnake venom (PASV). Of these, eleven (57.9%) were managed and discharged after administration of 30 to 40 mls of PASV (a vial equivalent to 10 mls). The mean dose (vials) of PASV used was  $3.9 \pm 2.0$  STD. Those who had only a single dose of antsnake venom could not purchase additional vials due to financial constraints. The only patient that had 8 vials of PASV presented with compartment syndrome. All patients with snake bite envenomation also received prophylactic antibiotics mostly ceftriaxone and metronidazole combination (32.6%). Tramadol was the most prescribed analgesic (43.3%). Very few (8.3%) of the snake bite victims developed allergic reactions to the PASV and were managed with a

combination of hydrocortisone and promethazine Tetanus toxoid was administered to all patients with snake bite. No death was recorded throughout this period of study.

### DISCUSSION

This study highlighted and brought to fore some perspective of clinical presentation and care of patients presenting with snake bites. Studies of snake bite that are hospital based are 3 to 5 times lower in prevalence compared to household or community based studies (11). A previous study showed that only 8.5% of snake bite victims present to hospital facilities in Nigeria (12), as most victims patronize traditional healers. This may be a reflection of the number of cases that reported in our facility during this period of study. More males and younger adults were most affected. This group is known to be more adventurous and more likely to engage in activities that puts them at a higher risk of snake bite such as farming, bush clearing and burning, and keeping late nights. Most victims reported in the month of April. This is the beginning of the raining season which coincides with the snake breeding periods and an increase in agricultural activities, thus contacts between snakes and humans are relatively common (13). Another peak period of snake bite is the dry season when farm produce are usually harvested and there is increased bush burning. Snakes being ectothermic, come out of hiding during this period to find heat so as to regulate their body temperature. They are also said to be more active when warmer.

Sixty seven percent of victims were not administered the antsnake venom since there were no clinical features suggesting snake bite envenomations after 24 hours. Definite snake bites that result in negligible or no symptoms may have been 'dry bites' inflicted by venomous snakes or bites by non-venomous snakes. It is important to note that a proportion of bites do not result in the injection of sufficient venom to cause clinical effects. The amount and potency of the venom usually depends on the specie type, size of the snake, mechanical efficiency of the bite, and the aggravating factor.<sup>[14]</sup> Victims of snake bite usually know they have been bitten except those who experience painless nocturnal bits by Kraits while asleep. In this study the average dose of PASV administered in vials was  $3.9 \pm 2.0$ . This was less when compared with other low dose studies (6, 15). The most common indication for use of polyvalent antsnake venom (PASV) in this study was progressive painful swelling.

Vasculotoxic snake envenomations are usually associated with local tissue swelling within 2-4 hours and could extend rapidly to reach its peak in 2nd to 3rd day. Blistering and tissue necrosis becomes obvious within the first day of bite, while coagulopathy and bleeding may develop within a few hours (14,16). The only patient who presented with compartment syndrome was reported to be bitten by the puff adder. Depending on the size of the fangs, venom is injected either subcutaneously or intramuscularly. The incidence of clinical compartment syndrome in snake bite is low because most snake fangs penetrate the subcutaneous tissue rather than the muscle compartment (17).

The relative delay in the presentation of these patients were due mostly to self medications and patronage of traditional healers. Traditional medical practitioners make use of concoctions which are administered either orally or applied topically. In Nigeria, certain herbs such as *Aristollichia albida*, *Guiera senegalensis*, were found to act on snake venoms in experimental animals but findings were not conclusive (12). Prior visits for traditional treatment should be highly discouraged because it delays presentation, may distort the clinical picture, with the increased risk of other complications such as bleeding, infection and gangrene.

We also discovered that 16% of the patients could only afford one vial of the PASV and were unable to purchase more due to their high cost (a vial cost 45 to 46 US dollars). . Again, at other occasions, the unavailability of the PASV in the hospital puts the burden on the care givers to scout for these medicines in pharmacy outlets, at the risk of purchasing substandard products. Hence the victims are only given supportive treatment until the antivenoms are made available. Antisnake venom is the only effective specific antidote for snake bite envenomation (14). Polyvalent antisnake venom are raised against the venoms of the most medically important snakes species in a particular geographical area. If given early it reverses both the local and systemic presentations. However their cost, availability and accessibility, still remains a challenge especially in areas of high demand (18). Available studies have shown that low doses of PASV are as good or even better (lesser complications) when compared with conventional high doses (19,20). However the recent situation of unavailability of PASV as was recently the case in Gombe and Plateau states, of Nigeria, which led to the death of 91 victims

within a period of three weeks reaffirms the need for judicious use of these essential medicines (21).

The incidence of allergic reactions was low among these patients administered the antisnake venom. This may not be associated with the doses of the antivenom since the reactions are often immunological. This is because the antivenom is hyperimmune globulin extracted from the plasma of the animal that has been immunised with the appropriate venom. The oral flora of snakes is heavily colonized by bacteria which predisposes these victims to early bacterial infection with the possibility of developing tetanus infection. As such, in our centre, all snake bite victims are given tetanus toxoid and those with envenomations administered prophylactic antibiotics. However some centers encourage the use of antibiotics only in the presence of necrosis or iatrogenic interference of bite site. Although no mortality was recorded throughout this study period, the outcome of patients who discontinued treatment and discharged themselves due to financial constraints was not ascertained.

## CONCLUSION

In conclusion, the use of low dose antisnake venom in the snake bite victims in this study was found to be effective in ameliorating the features of envenomation. Cost consideration of the PASV is an important factor in the treatment of snake bite envenomation. There is need for government and funding agencies to give more attention to snake bite envenoming in order to ensure that antisnake venom are highly subsidized or are given to these victims at no cost.

**Conflict of interest:** The authors declare no conflict of interest.

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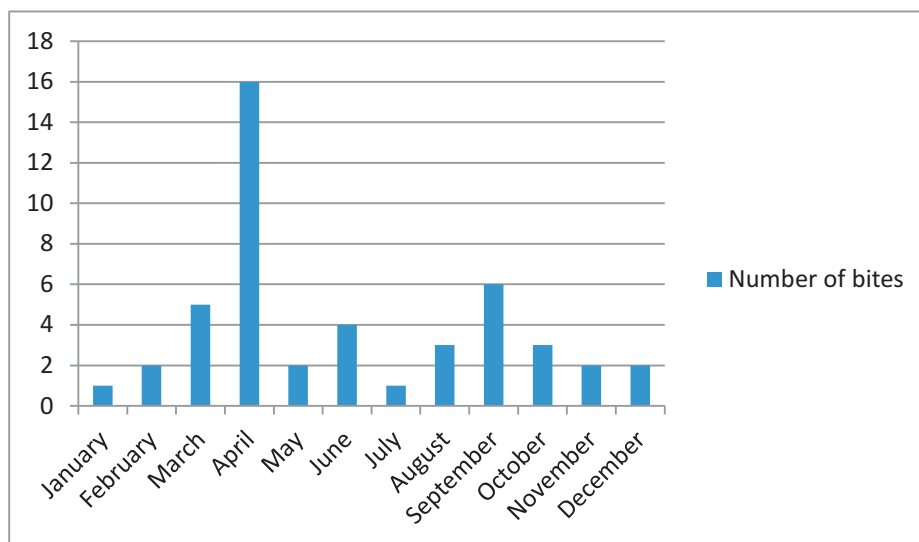
**Table 1: Age and Sex characteristics of patients seen with snake bite at the adult medical emergency of UBTH.**

Age group (Years)	Gender	
	Male (%)	Female (%)
18-40	23(52.3)	21(47.7)
41-65	11(73.3)	4(26.7)
65-99	1(100)	0

$\chi^2=2.768, p = 0.251.$

**Table 2: Site of bite and clinical presentations of snake bite victims in the adult medical emergency department.**

Site of bite	Number of victims (n)	Percentage (%)
Foot	57	95.0
Hand	1	1.7
Thigh	1	1.7
Ocular Envenomation	1	1.7
<b>Clinical presentations</b>		
Local Pain	27	45
Local pain and swelling	8	13.3
Local bleeding	2	3.3
Hypotension	2	3.3
Prolonged clotting time	3	5
Constitutional symptoms	1	1.7
Compartment syndrome	1	1.7



**Figure 1: Monthly distribution of presentation of snake bite victims to the adult medical emergency in UBTH.**

**Table 3: The management and outcome of patients with snake bite**

<b>Admission status</b>	<b>Number of victims(n)</b>	<b>Percentage (%)</b>
Admitted	20	33.3
Not admitted	40	66.7
<b>Administration of PASV</b>		
Yes	19	95
No	1	5
<b>Antibiotic use</b>		
Yes	19	32.8
No	41	67.2
<b>Tetanus toxoid use</b>		
Yes	60	100
No	0	
<b>Analgesics</b>		
Paracetamol	2	3.3
Tramadol	26	43.3
Pentazocine	2	3.3
Diclofenac	1	1.7
<b>Steroids</b>		
Hydrocortisone	5	8.3
<b>Antihistamine</b>		
Promethazine	5	8.3
<b>Blood transfusion</b>		
Yes	1(6 units of blood)	1.7
<b>Other medicines</b>		
Amitriptyline	1	1.7
Omeprazole	1	1.7
<b>Outcome</b>		
Discharged	50	83.3
Discharged against medical advice (DAMA)	10	16.7
Death	0	0
<b>Doses of PASV administered</b>		
<b>(mls)</b>	<b>Number of Patients (n)</b>	
10	3	15.8
20	1	5.3
30	3	15.8
40	8	42.1
60	2	10.5
80	2	10.5
<b>Antibiotics administered</b>		
Ceftriazone	14	32.6
Metronidazole	16	37.2
Levofloxacin	6	14.0
Ciprofloxacin	3	7.0
Cefuroxime	2	5.0
Ofloxacin	1	2.3
Coamoxiclav	1	2.3