

## Case study

### ROLE OF ANTI SNAKE VENOM IN SNAKE BITE IN THIRD TRIMESTER OF PREGNANCY

**Abstract** A Case of Pregnancy associated with Neurotoxic Snake Bite presenting with Neuropathic symptoms and systemic envenomation complicated by disseminated intravascular bleeding is uncommon. We present a case of 22-year-old Primigravida at 32 weeks gestation with snake bite on left-hand, with left-hand swelling, Nasal bleeding and neuropathic signs. At presentation, there was Pallor, Tachycardia, Hypotension, a gravid uterus with a single live fetus, & regular fetal heart rate. Primi Gravida with Venomous snake bite with Neuropathy with Disseminated Intravascular Coagulation was diagnosed. Conservative management with Anti Snake Venom instituted led to survival of both mother and continuation of Pregnancy.

**Comment [P1]:** Kindly use lowercase.

#### KEYWORDS

Anti snake venom, snake bite, pregnancy

#### INTRODUCTION:

Millions of people are bitten or stung by venomous animals yearly throughout the world. the relationship of the total number of snakebites to envenoming is highly variable and may be influenced by a number of factors like. It is estimated that the number of envenoming ranges from 421,000 to as high as 1,841,000 annually & 1,200,000 to 5,500,000 snake bites may occur globally per year [1].

**Comment [P2]:** Add some factors over here.

Snake-bites remains a public health problem in most countries, even if it is difficult to be precise about the actual numbers involved. The true incidence of and mortality from snake envenomation could exceed 5 million per year, with an associated mortality level of 125000 persons per year. About 2.5 million people are envenomed each year, half of whom request medical care, and probably more than 100000 individuals suffer from severe sequelae [2].

Although rare, venomous bites and stings during pregnancy may have a significant adverse effect on the fetus as well as the mother. The overall case-fatality rate in the pregnant females is approximately 4%, and the fetal loss rate approximately 20% [3].

**Comment [P3]:** Introduction would be more organized, if this para is in second last.

The challenge in this scenario is the serious consequence to the mother in terms of coagulopathy and shock. The fetus is at grave risk of hypoxia and demise. There is also a mention of fetal anomalies and the anaphylactic reaction of the anti-snake venom serum. (4)

**Comment [P4]:** This can be the last paragraph of Introduction. Kindly use past tense, as you have already performed the research.

Much remains unknown about snakebites in India. Knowledge about the snakes responsible is still developing: the major snakes of medical importance in India have historically been considered to be: the Russell's viper (*Daboia russelii*), the saw-scaled viper (*Echis carinatus*), the Indian cobra (*Naja naja*) and the common krait (*Bungarus caeruleus*), which together are known as the 'Big Four'. (5)

**Comment [P5]:** Please use same referencing style throughout the article.

**Comment [P6]:** Kindly merge it with the fourth para.

The highest burden of snakebites is in Asia and Sub-Saharan Africa, but the precise incidence is underestimated due to lack of data. However, it was recently estimated that over 314,000 bites, 7300 deaths, and nearly 6000 amputations occur from snake bites annually in Sub-Saharan Africa and Nigeria, the most common poisonous snakes are the elapids and viperids. (6)

**Comment [P7]:** Kindly add this para after the second paragraph. Make it the third paragraph as we follow the flow first globally, other countries and at the end your own country.

India is the largest single contributor to the global tally of snake bite deaths, with the numbers ranging between 15,000 and 50,000 a year. Accurate statistics are not available and there is no standardized reporting of bites and identification of snakes. (7)

**Comment [P8]:** It should be the fourth paragraph.

Snakebites tend to be high in areas which have agriculture as the major occupation of the people. Coupled with the fact that there are several challenges militating against the easy access to timely and appropriate healthcare services, snakebites pose serious threat to the victim and mostly result in lasting morbidity or mortality. (8)

**Comment [P9]:** It should be the fifth paragraph and merge it with the next paragraph.

The majority of bites occur among people with low socioeconomic status and have been linked to the occupations such as farming, fishing, animal rearing, and hunting. The factors associated with snakebite depends on people's occupation, thus, some cases derived from victims doing farm worker busy with other works either in the community or nearby bush, hence, exposes many to high risk of snakebite. (9)

**Comment [P10]:** Kindly add full stop after the reference and use same reference style.

### Case Description:

A 26-year-old Primi Gravida Period of Gestation 32 weeks presented with Alleged history of Snakebite 12 hours back on the left-hand, while sleeping on floor at home. The snake escaped and the species was unidentified. Patient Developed Nasal Bleeding and Drooping right eyelid followed by left eyelid Patient was unable to keep her eyes open and developed redness and Paresthesia at the site of bite. A few hours after bite she noticed Nasal bleeding, she had Drooping of Right upper eye lid, abdominal pain, change in taste, mouth numbness, dizziness. there was no difficulty in breathing, cough, & muscle pain.

**Comment [P11]:** Please use same formatting style either Uppercase in all of the headings or lowercase with capital first letter.

**Comment [P12]:** The snake with unidentified species escaped and later on patient developed.....

On Examination patient was conscious oriented having Glasgow Coma scale score of 15/15. Pallor was present, afebrile and anicteric. there was unilateral left-hand oedema with discoloration and excoriation, there was fang mark on left hand. there was bleeding from nose, no bleeding from oral cavity or intravenous cannula site. pulse rate was 110 beats per minute, blood pressure was 94/62mm Hg on Auscultation first and second heart sounds were heard and were normal, the respiratory rate was 24 cycles per minute and the chest was clear clinically.

**Comment [P13]:** Kindly rephrase it. Along with fang mark on left hand and also there was bleeding from nose but no such bleeding from oral cavity or intravenous cannula site was being reported.

**Comment [P14]:** Merge these lines with "and".

Per abdominal Examination Symphysis fundal height was compatible with 32 weeks pregnancy the fetus was in longitudinal lie and cephalic presentation, fetal heart rate was 156 beats per minute and regular. her vulva was stained with blood and digital examination was deferred. a clinical assessment of preterm contraction with antepartum hemorrhage due to venomous snake bite was made to rule out placenta previa. Multidisciplinary management was instituted in conjunction with gynecologist and neurologist

**Comment [P15]:** Please merge these lines.

**Comment [P16]:** Add "Moreover"

**Comment [P17]:** Bring this line to the start of the paragraph after rephrasing it.

laboratory investigation revealed packed cell volume of 22 % white blood cell count 10500 cells /mm cubes and platelet count 70000 cells / mm cube. Beside clotting time was prolonged on admission which later reduced to 4 minutes after treatment was instituted. Prothrombin time was also prolonged.

**Comment [P18]:** Please merge it with the above paragraph.

PT was 21 seconds with International Normalized Ratio of 1.3, while the Activated Partial Thromboplastin Time APTT for patient was 60 seconds and control was 45 seconds. Patient had a total of three units of Fresh Frozen Plasma transfused.

Liver Function Test, Kidney Function Test were in normal limit, while urine analysis shows proteinuria<sup>1</sup> +. Indian Polyvalent Anti Snake Venom 100 ml in 1000 ml of normal saline was infused intravenously over 12 hours.

**Comment [P19]:** Add Moreover before this and merge it with above para.

The patient recovered gradually and her symptoms of loss of taste, numbness in mouth, ptosis were recovered. Hypotension was recovered after fluid therapy, while tachycardia resolved spontaneously after 3 days.

**Comment [P20]:** Please check formatting.

## Discussions

**Comment [P21]:** Kindly remove "s"

India has always been known as country of Snakes and Snake Charmers, Snakes are part of the rich heritage of the Country and have always been worshiped by the natives. Venomous snakes are not uncommon and any physician working in this large country will face challenges regarding the management. Identifying the correct species or giving the correct dose of ASV is always a challenge due to paucity in the availability of proper guidelines and literature people often reach health care facilities in the later part of the disease and often only complicated cases reach hospital. Physician need to be very vigilant and a high suspicion is required for the correct diagnosis and treatment.

**Comment [P22]:** Kindly check again. Remove "and" & add Moreover,

**Comment [P23]:** Rephrase it " hospital register complicated cases more often. Add reference at the end of the para.

Snake venoms are secretions of venomous snake which are synthesized and which are stored in venomous gland. The glands which secrete the zootoxin is a modification of the parotid salivary gland and are situated on each side of head below and behind the eye encapsulated in muscular sheath. The glands have large alveoli in which venom is stored before being conveyed by the duct to the tubular fangs, through which it is injected. Snake venom is a combination of many different proteins, peptides and enzymes and they are generally not dangerous when ingested. Snake venoms are complex mixture of enzymatic and toxic proteins, which include phospholipase A2 (PLA2s), mycotoxins, hemorrhagic metalloproteinases and other proteolytic enzymes, coagulant components, cardiotoxins, cytotoxins and neurotoxins (

**Comment [P24]:** Kindly remove this line as it is repetitive one. Adjust the next line at the end and add reference.

Different species have different types venom which depends upon its species, geographical location, its habitat, climate, age etc.

**Comment [P25]:** Kindly rewrite it in paragraph form. Use same reference style.

There are three types of venom according to its effect viz. Hemotoxic, Cytotoxic & Neurotoxic.

- Haemo-toxic venoms are one which affects cardiovascular system
- Cytotoxic venoms target specific cellular sites
- Neuro-toxic venoms harm nervous system of human body.

Enzymes present in snake venom hydrolyze protein and membrane components which lead to tissue necrosis and blood clotting (11)

The only available treatment against snake bite is the usage of anti-venom. The first anti-venom was developed by Alberte Calmette against the Indian cobra (NajaNaja). Anti-venom is made by immunizing mammals such as horse, goat, rabbit with particular snake venom and the specific immunoglobins are isolated from the blood. The subject animal will undergo an immune response to the venom, producing antibodies against the venom's active molecule which can then be harvested

**Comment [P26]:** Kindly rephrase this line and merge it with next line. Anti-venom is the only available treatment against snake bite, with first anti venom developed.....

from the animal's blood and used to treat envenomation. Antivenom is classified into two types. Monovalent antivenom when they are effective against a given species venom. Polyvalent when they are effective against a range of species

**Comment [P27]:** Kindly recheck again and add reference at the end.

The cost effectiveness of the treatment is also a factor to be considered as the approx. cost of 1 vial anti snake venom which is nearing 300-500 and sometimes in thousands, hence the decision to choose between low dose regimen or high dose regimen can be impacted not on the clinical condition but also the financial restraints of the patient

**Comment [P28]:** Kindly mention the currency

**Comment [P29]:** It would be more better if used" depends upon patient's financial condition rather than clinical condition.

All patients with clinical manifestations or laboratory abnormalities, or both, because of snakebites ought to receive the antivenom as soon as possible, but many of them receive the antivenom too late. (10)

**Comment [P30]:** Kindly merge it with the above para.

Ricky Lee Langley in study Snakebite During Pregnancy: A Literature Review concluded that although rare, venomous bites and stings during pregnancy may have a significant adverse effect on the fetus as well as the mother.

**Comment [P31]:** Kindly remove the highlighted line & add reference also.

Anuradhani Kasturiratne ET AL in study The Global Burden of Snakebite: A Literature Analysis and Modelling Based on Regional Estimates of Envenoming and Deaths concluded Snakebites cause considerable morbidity and mortality worldwide. The highest burden exists in South Asia, Southeast Asia, and sub-Saharan Africa.

**Comment [P32]:** Use lowercase for et al and remove the highlighted line.

**Comment [P33]:** Kindly merge it with previous line and add "with" and "existing".

Chippaux ET AL showed that snake-bites remained a public health problem in most countries, even if it is difficult to be precise about the actual numbers involved. The global figures given by Swaroop & Grab (102) over 40 years ago were greatly underestimated. The true incidence of and mortality from snake envenomation could exceed 5 million per year, with an associated mortality level of 125000 persons per year. About 2.5 million people are envenomed each year, half of whom requested medical care, and probably more than 100000 individuals suffer from severe sequelae. The global disparity in the epidemiological data for snake-bites reflects the variation of health reporting accuracy and the great diversity of ecological and economic conditions throughout the world. Agricultural activities are associated with most of the bites. The snake species involved can be very dangerous because of the toxicity of their venom or abundance in areas close to human settlements.

**Comment [P34]:** Rephrase the highlighted line" & actual numbers are difficult to be measured" and add reference

**Comment [P35]:** Kindly remove irrelevant numbers.

Finally, health facilities and availability of antivenin have to be considered in implementing the treatment of envenomation. Clearly in developing countries, where snake-bites are the most prevalent, none of the required conditions for their correct management is fulfilled. In most developing countries, lack of medical attention, specially antivenom therapy, leads to high mortality levels. Considerable effort will be needed to develop studies on snake-bite epidemiology and improve the distribution and use of antivenom.

**Comment [P36]:** Please use past tense in the whole paragraph.

**Comment [P37]:** Please rephrase this line.

**Comment [P38]:** Kindly check spellings.

**Comment [P39]:** Kindly remove this repetitive line, as you have mentioned same things in the next line and add reference also.

AUSTIN GIDEON ADOBASOM-ANANE 2018 study shows that most of the snakebite victims were discharged as cured, but may have suffered some form of complication from the envenomation. It is also possible that the number of cases that were discharged against medical advice may have also died due to the poor prognosis of the cases hence indicating an increased number of deaths from snake bites. Delayed initiation of treatment for snakebite tends to lead to less favorable outcomes for the victims involved.

**Comment [P40]:** Please use lowercase and remove "2018 study" and use showed instead of show

**Comment [P41]:** Remove "hence indicating" and use "leading to" in this line

**Comment [P42]:** Kindly rephrase this line & add reference. Leads to less favorable outcomes for the victims.

## CONCLUSION

Neurotoxic Snake Bite presented with Neuropathic symptoms and systemic envenomation can be a treating dilemma for any treating Physician. Role of Anti Snake Venom in pregnancy and whether to use Anti Snake Venom in Pregnancy can be an ethical question. Absence of proper clinical guidelines and scarcity of relevant research sources leaves chunk of treatment on clinical knowledge and expertise of treating physician. Outcome may depend on the degree of envenomation, gestational age at presentation, timing, duration and quality of treatment along with the clinical sense and justification of empirical treatment given.

**Comment [P43]:** Merge these two lines with "as".

It has been seen in this study that there is a significant decrease in morbidity and mortality of pregnant female having snake bites in terminal pregnancy i.e., third trimester, who are getting treatment from anti snake venom whether low or high dose on early presentation to the health facilities. Moreover, no significant changes were seen in outcome of fetal health, although some cases show increase in fetal mortality and morbidity which can be more due to other maternal and fetal health issues.

**Comment [P44]:** Kindly add reference.

**Comment [P45]:** Kindly rephrase this line "The current study highlighted that there was a".

**Comment [P46]:** Use either instead of whether.

**Comment [P47]:** Use reported instead of show and add reference.

## Reference

1. Kasturiratne A, Wickremasinghe AR, de Silva N, et al. **The global burden of snakebite: a literature analysis and modelling based on regional estimates of envenoming and deaths.** *PLOS Med.* 2008;5: 1591-1604.

**Comment [P48]:** Don't use bold in references.

**Comment [P49]:** Kindly add full stop at the end of each reference.

2. Chippaux JP. Snake-bites: appraisal of the global situation. *Bull World Health Org.* 1998; 176:515-524

3. R.L. Langley, Snakebite during pregnancy: a literature review, *Wilderness Environ. Med.* 21(2010)54-60, <http://dx.doi.org/10.1016/j.wem.2009.12.025>.

4. 2017 David et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and build upon your work non-commercially

**Comment [P50]:** Kindly write complete reference.

5. 2013 Vaiyapuri et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

**Comment [P51]:** Kindly write complete reference.

6. Department of Emergency Medicine, Smt. NHL M Medical College, VS General Hospital, Ahmedabad, Gujarat, India Received 2013 Jan 10; Accepted 2013 Jun 18. Copyright: © Journal of Emergencies, Trauma, and Shock

**Comment [P52]:** Incomplete reference.

**Comment [P53]:** No need to write received date and remove irrelevant words and add issue and page number.

7. RETROSPECTIVE STUDY OF SNAKEBITE CASES AT THE TAMALE TEACHING HOSPITAL. AUSTIN GIDEON ADOBASOM-ANANE 2018

**Comment [P54]:** Kindly use same referencing style.

8. Ndu IK, Edelu BO, Ekwochi U. Snakebites in a Nigerian children Population: A 5-year review. *SahelMedJ* 2018; 21:204-7

**Comment [P55]:** Please check formatting again and use fullstop at the end of each line.

9. Descriptive analysis of Snake bite surveillance data in North Bank West Region, The Gambia, 2017 - 2021

**Comment [P56]:** Kindly write date of citation.

10. A Ministry of Health, Information Systems for Notifiable Diseases - SINAN. Accidents by venomous animals. Brasília (DF): Ministry of Health; 2004 [cited 2015 Feb 12].

**Comment [P57]:** Please add your date of citation over here.

11. Jin H, Varner J. Integrins: roles in cancer development and as treatment targets. *Br J Cancer* 2004;90(3):561-65.

**Comment [P58]:** Please write full name of journal.

12. Kini RM. Excitement ahead: structure, function and mechanism of snake venom phospholipase A2 enzymes. *Toxicon* 2003;42(8):827-40.

13. Soares AM, Fontes MRM et al. Phospholipase A2 myotoxins from Bothrops snake venoms: structure-function relationship. *Curr Org Chem* 2004;8(17):1677-90.

14. Jin H, Varner J. Integrins: roles in cancer development and as treatment targets. *Br J Cancer* 2004;90(3):561-65

**Comment [P59]:** Please write full name of journal.

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