Austin Journal of Vaccines and Immunotherapeutics

Open Access

Austin Publishing Group

Review Article

Current Status of Snake Antivenom in India: KNOW-It-ALL

Kalaivani M*
Indian Pharmacopoeia Commission, Ministry of Health and Family Welfare (Govt. of India), Ghaziabad, India

***Corresponding author:** Kalaivani M, Senior Scientific Officer, Indian Pharmacopoeia Commission, Ministry of Health and Family Welfare, Govt. of India, Sector-23, Raj Nagar, Ghaziabad-201 002, UP, India
Email: kalaivani.ipc@gov.in

Received: April 15, 2025
Accepted: April 25, 2025
Published: April 30, 2025

Abstract

Snake envenoming is a life-threatening condition caused by poison in the bite of venomous snake. It is a serious public health issue in developing countries like Asia, Africa, the Middle East, and South America. World Health organization (WHO) has finally included snake bite in WHO's list of neglected tropical diseases in year 2009. Immunoglobulins are the only specific antidotes used against snake-envenoming but the lack of good quality antisera emerged as a serious health concern at global level. The poor quality manufactured antivenom causes high rate of adverse reactions like anaphylaxis, including hypotension, cyanosis and delayed antivenom reaction. In India there has always been a shortage of good quality anti-snake venom. In view of the present situation, this review briefs about the current status and the challenges faced by the nation with respect to the availability of snake good quality venom antiserum in India and worldwide as well.

Keywords: Snake envenoming; Snake antisera; Snake-bite; Antivenom

Introduction

Snake envenoming is a serious public health issue in developing countries including Asia, Africa, Middle East and South America. Recently, World Health organization (WHO) included snakebites in the list of neglected tropical disease [1]. According to the recent data published from WHO revealed that about 5.4 million snakebites with 94000 deaths occur each year at global level where most snake bites envenoming occur in Asia, Southeast, sub-Saharan Africa, with India reporting highest mortality rate due to snake bites with a number of 81410 and 137880 deaths and around three times as many amputations and other permanent disabilities each year [2]. Accurate statistical data is not available due to variability in the reporting like most of the rural victims initially approach traditional healers for treatment.

From more than an era the primary treatment for snakebites has been the administration of antivenom herbs and antisera. Antisera are the specific immunoglobulins used for the treatment of envenoming caused by snakebites. Antisera play important role in minimizing mortality and morbidity by preventing or reversing the envenoming effects like severe paralysis, fatal haemorrhage, irreversible kidney failure and local tissue damage [3]. Antisera are prepared by injecting venoms in large animals such as horses and sheep followed by extraction and purification of the antibodies from their plasma. Anti sera can be monovalent which is specific for particular species or polyvalent specific for various different species. In India, antisera are prepared by immunizing the horses against venoms of four commonly found poisonous snakes– "Big four" (Cobra, Krait, Russell's viper and saw-scaled viper) [4]. This review briefs about the current status and challenges faced by the nation with respect to the availability of anti-snake venom in India and worldwide as well.

Geographical Distribution of Poisonous Snakes in India

In India, there are around 216 species of snakes out of which 60 species of snakes are venomous in nature and cause severe envenoming. The venomous species include Cobra (*Naja naja*), Common krait (*Bungarus caeruleus*), Russell's viper (*Daboia russelii*) and Saw-scaled viper (*Echis carinatus*) [5]. Different species of cobra like *Naja naja* are mainly found throughout the India whereas *Naja kaouthia* and *Naja Oxiana* are mainly found in Northeast and northwest India respectively and *Naja sagittifera* mainly found in Andaman Islands. World's longest and venomous snake King cobra (*Ophiophagus Hannah*) generally found to be located in South, Northeast and Andaman Islands [6]. In northern India, it located in the Garhwal in Uttarakhand, in Uttar Pradesh and Sikkim. In the Eastern Ghats, it found from coastal Odisha to Andhra Pradesh [7]. Kraits species include *Bungarus caerulens, Bungarus fasciatus, Bungarus niger* and *Bungarus indanus* found in Indian subcontinent, northeast region and peninsular India. Different Viper species like Russell's Viper (*Daboia russelii*), is abundant in Punjab and in southern India especially in the state of Karnataka. It is uncommon to rare in the Ganges valley, northern Bengal, and Assam. Other viper species like Saw-scaled viper (*Echis carinatus*), Sochureki's saw scaled viper (*Echis carinatus sochureki*) are predominantly found in Southwest and northwest regions of India [8]. Additionally, other snake species like sea snakes, and two other pit viper species also classed as venomous species as evidenced with the clinical records of fatalities from their bites. Recently the hump-nosed pit viper (*Hypnale hypnale*) documented nearly 10% of venomous bites in the state of Kerala and generally found in peninsular India to the Western Ghats as far north as 16° N [5]. Apart from this, there are variations in poisonous snake species state wise according to the geographical distribution of India [9-24].

Citation: Kalaivani M. Current Status of Snake Antivenom in India: KNOW-It-ALL. Austin J Vaccines & Immunother. 2025; 6(1): 1013.

Table 1: List for manufacturers of antisera against snake venom.

S.No.	Manufacturers Name	Composition of snake venom manufactured
1.	Bharat Serums & Vaccines Ltd.	Each ml of which neutralises: Cobra (*Najanaja*).....0.6 mg Common Krait (*Bungaruscaeruleus*).....0.45 mg Russell's Viper (*Viperarusselli*).....0.6mg Saw-scaled Viper (*Echiscarinatus*).....0.45 mg Preservative: Cresol I.P/Phenol I.P./ Glycine I.P./Sodium Chloride I.P. NMT 0.25% v/v
2.	Biological E. Ltd	
3.	Haffkine Biopharma Ltd.	
4.	Mediclone Biotech Ltd.	
5.	Premium Serums Ltd.	
6.	VINS Bioproducts Ltd	
7.	Virchow Biotech Private Limited	
8.	Central Research Institute, Kasauli	

Availability of Anti-snake Venom (ASV)

The antidote prepared against snake venom is called anti-snake venom (ASV). Snake anti-venomimmunoglobulins (antivenoms, antivenins, anti-snake venom, ASV) are the only specific treatment for envenoming caused by snakebites. They are produced by fragments $F(ab)^2$of IgG purified from the serum or plasma of a horse or sheep that has been hyper immunized against relevant venoms. Recently, plasmapheresis is used to produce antibodies where erythrocytes are re-injected into the donor animal within 24 hours of blood collection and plasma is used for the extraction of immunoglobulins [25]. ASV neutralizes the venom of a particular species or in some instance can also neutralize the venom of closely related species. In India, anti-snake venom is produced only against four common poisonous snakes "big four" (Cobra, Krait, Russell's viper and Saw-scaled viper), the horses are generally hyper immunized against the venom of these "big four" to produce poly specific anti-snake venom [25]. These ASVs are relatively cheap in India as compared to Western countries, one vial of ASV costs around Rs. 350-2500 (5-30 US$). Currently, eight ASV manufacturers producing antivenom in India and its composition in India are described in Table 1 which clearly shows that anti-venoms are available only for big four snake bite. The snake venomous species were catch from wild for milking which often done in intervals generally 3-4 times in a month. After milking the snakes were tagged and release back in to the wild preferably from the same location that they were caught from. The collected venom is then freeze-dried to make them in powered form or sold to the antisera manufacturers. Each ml of the ASV preparation contains sufficient antivenom globulins to neutralize the venom i.e.0.60 mg of dried Indian Cobra (*Najanaja*) venom, 0.45 mg of dried Common Krait (*Bangarus Caeruleus*) venom, 0.60 mg of dried Russell's Viper (*Vipera Russelli*) venom, 0.45 mg of dried Saw scaled Viper (*Echis Carinatus*) venom.

Is Currently Available Anti-Snake Venom Adequate and Specific?

Currently available ASV in the country is only against big four snake but there are various other venomous snake species also found in the different geographical regions. The variability in the antigenic reactivity of the venom restricts the use to particular ASV against all species as there is no concept of 'One size fit to all'. Several studies have been reported for ineffectiveness of ASV due to regional variation like *D. russelii* venom from northern and western parts of India was more toxic from venom samples taken from southern parts of India [26]. Not only venom content, venom composition of two snakes also vary like for example *D.russelii* venom composition is totally different form *N. Naja* venom [27]. India has polyvalent antisera against big four but when snake bite occurs through species other than the big four, and then the ASV was found to be ineffective for treatment of patient even though used in high quantity.

Apart from unavailability of ASV against all species of venomous snake in the country, the quality and potency of currently available ASV also creates a critical issue in treatment of snake envenoming in the country. The amount of antivenom required to neutralise the venom is variable and depend on the snakebite severity. A scientific study states that potency of the currently available ASV may sometimes require more than 30 ampoules of polyvalent antisera to neutralize the venom on snake bite [28]. These quality and potency related issue are due to repeated milking of snake, age of snake used for milking and lack of traceability with respect to milking of snake [29,30]. Such inadequate quality may also lead to loss of confidence on some of the available ASV by clinicians, health managers, and patients.

Snake Anti-venom and its Adverse Effects

ASV available in the country was also found to be associated with various adverse effects/allergic reactions due to activation of the immune system that can be immediate or delayed [4, 31]. According to the published WHO/SEARO (South-East Asia Regional Office) guidelines on the management of snake bites, more than 10% of patients develop a reaction either early (within a few hours) or late (five days or more) after being given antivenom [32]. The antivenom reactions were documented and classified as early anaphylactic reactions, Pyrogenic (endotoxin) reactions and late (serum sickness type) reactions [33]. The immediate or early reactions consist of urticarial cough, fever, nausea, vomiting, abdominal colic, diarrhoea and tachycardia and minority of patients even develops life-threatening anaphylaxis characterized by bronchospasm, hypotension and angio-oedema. The pyrogenic reactions comprise of chills (rigors), fever, vasodilatation and hypotension while the delayed version involves serum sickness characterized by fever, rash, lymphadenopathy, proteinuria with immune complex nephritis and, rarely, encephalopathy [34]. Adverse reactions to available snake antivenoms are common in many parts of the world where snakebite is prevalent [35, 36]. There are various scientific reports discussing the issue like the recently seen events of acute severe anaphylaxis in Nepali patients where the neurotoxic snakebite envenoming was treated with the Vins polyvalent anti-venom [26]. A study of prospective, consecutive case series of 158 snakebite patients revealed high incidence of anaphylactic shock to horse derived F(ab')2 antivenom [37]. In India, an observational study was conducted in Maharashtra on 296 snake bite cases retrieved from the indoor records section to observe the antivenom reaction. As an outcome of the study, it was found that 56.10% (92 patients) received ASV and suffered from antivenom reactions. Chills and rigor mortis (69.56%) were the most common reactions followed by nausea and vomiting (34.8%). The severe reactions like hypotension

Table 2: Quality Control Parameters considered for Snake Antiserum (39-42).

Parameters				
	IP 2022	**BP 2025**	**Ph. Eur.11.0**	**WHO-TRS**
Name of the monograph	Snake Venom Antiserum	European Viper Venom Antiserum	Viper Venom Antiserum, European	*Annex 5*Guidelines for the production, control and regulation of snake antivenom immunoglobulins
Species covered	Indian cobra (*Naja naja*) and Russell's viper (*viper russelli*) suitable venoms and not less than 0.45 mg of common krait (*Bangarus caeruleus*) and Saw scaled viper (*Echis carinatus*)	*Vipera ammodytes,* or *Vipera aspis*, or *Viper aberus*, or *Vipera ursinii*	*Viper ammodytes,* or *Vipera aspis*, or *Vipera berus*, or *Vipera ursinii*	-
Defination	A clear to slightly opalescent, colourless or pale yellow liquid, free from suspended particles or cream-coloured powder or pellet which when reconstituted with the diluent supplied by the manufacturer with the freeze-dried product yields a clear, colourless or pale yellow liquid.	European viper venom antiserum is a preparation containing antitoxic globulins that have the power of neutralising the venom of one or more species of viper. The globulins are obtained by fractionation of the serum of animals that have been immunised against the venom or venoms.	European viper venom antiserum is a preparation containing antitoxic globulins that have the power of neutralising the venom of one or more species of viper. The globulins are obtained by fractionation of the serum of animals that have been immunised against the venom or venoms.	The appearance of the product (for example, colour and clarity of the liquid, appearance of the powder) should comply with the description in the marketing dossier.
Identification	Specifically renders the corresponding venom or venoms harmless to susceptible animals. It may also be identified by any other alternate suitable *in vitro* method.	It neutralises the venom of *Vipera ammodytes,* or *Vipera aspis*, or *Viper aberus*, or *Vipera ursinii* or the mixture of these venoms stated on the label, rendering them harmless to susceptible animals	It neutralises the venom of *Viper aammodytes,* or *Vipera aspis*, or *Viper aberus*, or *Vipera ursinii* or the mixture of these venoms stated on the label, rendering them harmless to susceptible animals	When several types of antivenoms are produced by a single production facility, asystem to identify each batch of antivenom should be established for monitoring and auditing purposes. Identity tests may include biological assays as well as physicochemical and immunological tests. Double immunodiffusion assays, confronting the antivenom with the venoms against which the antivenom is designed to act, are often used. In the case of laboratories that use various animal species to raise antivenoms, that is, horses and sheep, an immunological identity test should be used to identify the mammalian species in which the antivenoms are produced.
Tests				
Potency.	The potency of the snake venom antiserum is determined by estimating the ability of the antiserum to protect mice or other suitable animals against the lethal effect of a fixed dose of a reference preparation of snake venom of the relevant species or by comparing its ability to do so with that of a reference preparation of antiserum of established potency at two or more dose levels of the venom.	The potency of European viper venom antiserum is determined by estimating the dose necessary to protect mice against the lethal effects of a fixed dose of venom of the relevant species of viper.	The potency of European viper venom antiserum is determined by estimating the dose necessary to protect mice against the lethal effects of a fixed dose of venom of the relevant species of viper.	Potency assessment should be done by in vivo assay
Other tests.	Complies with the tests stated under Antisera.	-	-	-
Storage.	Store the freeze-dried preparation in a cool, dark place and avoid exposure to excessive heat. Store the liquid preparation at a temperature between 2° and 8° C. It should not be allowed to freeze.	Protected from light, at the temperature stated on the label. Do not allow liquid preparations to freeze.	Protected from light, at the temperature stated on the label. Do not allow liquid preparations to freeze.	For long-term storage, venom should be appropriately aliquoted to minimize wastage and must then be stored in sealed vials until use. Liquid venoms should be stored frozen at −80 °C, while lyophilized or dried venoms may be stored at −20 °C. After opening the vial, the venom required should be used and any surplus product discarded. Unused venom should not be re-lyophilized, re-dried or refrozen (in the case of liquid venom).
Labelling.	The label states (1) the volume of the contents and in case of freeze-dried preparation, the directions for reconstitution; (2) the species of snake against whose venom the antiserum is effective; (3) the animal species from which the antiserum has been obtained; (4) the name and proportion of any preservative added; (5) that in case of a liquid preparation, it should not be allowed to freeze.	The label states the venom or venoms against which the antiserum is effective.	The label states the venom or venoms against which the antiserum is effective.	The label should be waterproof and heat resistant, and contain the following information: specificity of antivenom, plasma unit number and date of collection.

and sudden respiratory arrest were also observed in 10-15% patients [4]. To prevent these acute or chronic adverse reactions and medical emergencies, the use of best prophylactic agent, to manage the acute as well as delayed reactions, is very much needed. Adrenaline, antihistamines and steroids are the main drugs which can be given, along with the antivenoms or before the antivenoms, to treat the adverse effects [38].

National and International Regulation for Anti-snake Venom

In India, Central Drugs Standard Control Organization (CDSCO) is the National Regulatory Authority (NRA) for regulation and approval of ASV manufacturing and marketing in the country. Respective State Drug Regulatory Authorities also plays an important role in the regulating the manufacturing of ASV. Central Drug Laboratory (CDL) acts as National Control laboratory for testing and release of ASV in India.

Indian Pharmacopoeia Commission (IPC) is an autonomous body which set quality standards for pharmaceutical substances, excipients and dosage forms and are published in the form of monographs in Indian pharmacopoeia (IP). The standards set out in IP for time being a reenforced by the Central and State drug regulatory authorities of India and are followed not only by industry stakeholders but also central and state drug testing laboratories to assess the quality of the drug product before and after the product in the market. As per inclusion criteria of IP Standards for a drug will be established only after it gets marketing authorisation from NRA. The current edition of Indian Pharmacopoeia, IP 2022 prescribes standards for ASV through specific monograph and general information [39]. A monograph of ASV prescribes standards i.e analytical methods and their acceptable limits for identity, purity and potency for ASV against big four- Russell's viper, common Krait, Indian cobra and Saw scaled viper (Table 2) [39-42].

To support NRA and to improve quality, safety and regulation of ASV in various countries WHO published Guidelines on production, control and regulation of ASV in 2008 [49]. These Guidelines covered all the steps involved in the production, control and regulation of venoms and anti-venoms. The purpose of these guidelines is that all countries should follow good manufacturing practices for the production of ASV. In order to provide manufacturers strong guidance on high-quality antivenom design, production, quality control, preclinical and clinical testing so that product abides with high quality standards, the WHO has taken a positive step by publishing guidelines for "Production Control and Regulation of Snake Anti-venomImmunoglobulins" [42]. Even the national regulatory authorities follow the WHO guidelines for issuance of the licenses to the manufacturers. These guidelines mainly cover the information about each venom batch stating the scientific names of the snake species (and subspecies if any), their geographical origin and the number of animals used in collecting the batch, the date of collection of the venom, and any other relevant information to the antivenom manufacturer and also to the regulatory authority, if required [42]. Each and every batch should have consistency within established limits of composition and quality of venom batches produced over time for the same venomous species of the same origin should be guaranteed. An important consideration has also been made in WHO Guidelines regarding the establishment of international reference preparations for venoms and anti-venoms. But unfortunately, only few countries are on the path of creating national reference preparations, whereas the majority let producers use in-house reference standards. However, due to immunological differences and regional variations in venom composition, it will not be easy to create international reference standards for anti-venoms. On the other hand, if countries manage to create National reference pools for each medically important snake species, that could eventually lead to an international stock of global reference standards, which can be used for further tests and assessments. Very few National Regulatory Agencies have the technical knowledge about the WHO Guidelines despite the presence of specific recommendations for national regulatory authorities such as those regarding distribution, management and control. WHO has also included ASV in the WHO List for Essential Medicines, encouraging countries to do the same and thereby ensuring national ASV stocks.

Quality Control of Antisera

Inadequate attention has been paid towards this subject. As the quality control of the anti-snake venom is a key element of assurance of patient safety. Quality control tests should be performed by the manufacturer or under their responsibility before the product is released in the market for its medicinal use. In addition, relevant analyses should be performed on any intermediate steps of the manufacturing protocol as part of the in-process quality control system. In order to provide manufacturers strong guidance on high-quality anti-venom design, production, quality control, preclinical and clinical testing, and national regulatory agencies with framework guidance to ensure that products which they license meet the highest quality standards a positive step has been taken by WHO by publishing guidelines for Production Control and Regulation of Snake Anti-venom Immunoglobulins [42]. These guidelines mainly covers the information about each venom batch stating the scientific names of the snake species (and subspecies if any), their geographical origin and the number of animals used in collecting the batch, the date of collection of the venom, and any other relevant information, must be provided by the venom supplier to the anti-venom manufacturer and also to the regulatory authority, if required. Each and every batch should have consistency within established limits of composition and quality of venom batches produced over time for the same venomous species of the same origin should be guaranteed. An important consideration has also been made in WHO Guidelines regarding the establishment of international reference preparations for venoms and anti-venoms. But unfortunately, only few countries are on the path to creating national reference preparations, whereas the majority let producers use in-house reference standards. But due to immunological differences in venom composition it will not be easy to create international reference standards for anti-venoms. However, if countries manage to create national reference pools for each medically important snake species, that could eventually lead to an international stock of global reference standards, which can be used for further tests and assessments. Very few National Regulatory Agencies have the technical knowledge about the WHO Guidelines despite the presence of specific recommendations for national regulatory authorities such as those regarding distribution, management and control.

Further, manufacturers generally follow the information published in the form of national or international guidelines and pharmacopoeias for good laboratory practices and good manufacturing practices. Finally, all the final anti-venom products produced by the facilities surveyed undergo rigorous testing (including Pyrogen test, potency test, abnormal toxicity, sterility, pH, appearance). These guidelines ensure that polyvalent snake anti-venom will have adequate potency to neutralise envenomation to reduce anti-venom reactions and reduce batch to batch variability in potency and purity. Still the situation highlights the fact that poor manufacturing standards persist, and products have minimal efficacy and unacceptably high adverse reaction rates. In addition, lack of proper regulatory capacity for the control of anti-venoms in countries with significant snake bite problems results in an inability to assess the quality and appropriateness of the anti-venoms.

Current Challenges and Need

Not only in India but also other developing countries face various challenges leading to lack of quality and efficacy of ASV. To produce quality anti-snake venom involves significant challenges related to assessment, design, potency and production to meet the current need. One of the main challenges within the global antivenom market is the production and trade of sub-optimal antivenom preparations. Currently, there are only few institutes with necessary permission to extract venom on a commercial scale. Irula snake catcher industrial co-operative society (ISCICS), Madras crocodile bank and centre for Herpetology, and Haffkine Institute are the major supplier of venom for the whole country both for research purposes and to produce antisera against the venom. There are no proper National guidelines for snake antisera production and quality control for stakeholders to follow. However, WHO guidelines and Technical Report Series (TRS) for detailed methodologies for Production, Control and Regulation of snake antivenom Immunoglobulins. The antisera now available are only specific for snake venom which are either monovalent or polyvalent which can be used against big four snakes bite only. Scientists are yet to map the variations of toxicity in venom from snakes belonging to various species and geographical locations, and variations within the same species in similar regions. To match the current requirement production of recombinant antivenom is necessary that selectively targets all of the clinically important toxins would be a step forward for the snakebite therapy at global level. These high-quality standards antisera can be produce only with multidisciplinary international collaboration efforts. Snake antisera are currently not pre-qualified by WHO, due to inter and intra-species specificities in venom composition, a key aspect in antivenom quality control lies in the evaluation for the venom of capacity of antivenom for the venom of snakes in a specific country or region. Ability to trace each individual snake from which venom is collected used for antivenom immunoglobulins production with each batch of the final product is one another lacuna in antivenom production.

To minimize this, it is recommended to collect venom from capitative snakes maintained in well-designed serpentariums only rather than collecting from wild snakes. Identification of all snakes used like species or sub-species, their bio-geographical origin each snake is specified since differences in venom composition may occur. Full traceability of each venom batch should be ensured. Batch-to-Batch consistency of venom of the same origin should be confirmed. Unavailability of reference standards for venom encourages stakeholders to use in-house reference preparations of venoms and antivenoms to ensure consistency of their products. WHO recommends that national reference venom collections should be established which cover each medicinally important snakes used to produce Anti-snake immunoglobulins. Large variations in venom composition even within a single species it is recommended National Reference Standards should be established which covers the intra-species variability. The characterized and maintenance of reference venom collections should be performed with oversight from National Regulatory Authority and other competent authorities. There should be remarkable regulatory control frameworks for manufacture, import and sale of ASV, which can save many lives from snake envenoming. Lack of National and International regulations of antivenoms results in sub-optimal products being made which are available in market. Those that end up being affected by this global negligence are the patients.

Conclusion

Apart from WHO's recommendation and guidelines for antivenom production and quality standards, there should be National guidelines for production, control and regulation of snake antivenom immunoglobulins. It is to be concluded that for patient's safety, the antivenoms should be of best quality and polyvalent in nature in compliance with quality standards.

References

1. Williams DJ, Faiz MA, Abela-Ridder B, Ainsworth S, Bulfone TC, Nickerson AD, et al. Strategy for a globally coordinated response to a priority neglected tropical disease: Snakebite envenoming. PLoS Negl Trop Dis. 2019; 13: e0007059.
2. World Health Organization. Snake bite envenoming. Global situation.
3. Gutiérrez JM, Calvete JJ, Habib AG, Harrison RA, Williams DJ, Warrell DA. Snakebite envenoming. Nat Rev Dis Primers. 2017; 14: 17063.
4. Deshpande RP, Motghare VM, Padwal SL, Pore RR, Bhamare CG, Deshmukh VS, et al. Adverse drug reaction profile of anti-snake venom in a rural tertiary care teaching hospital. J Young Pharm. 2013; 5: 41–45.
5. Gupta YK, Peshin SS. Do Herbal Medicines Have Potential for Managing Snake Bite Envenomation? Toxicol Int. 2012; 19: 89–99.
6. Whitaker R and Martin G. Diversity and Distribution of Medically Important Snakes of India 2015 Clinical Toxinology in Asia Pacific and Africa. 2015; 115-136.
7. Dey A and De JN. Traditional use of plants against snakebite in Indian subcontinent: are view of the recent literature. Afr J Tradit Complement Altern Med. 2012; 9: 153-174.
8. Holla SK, Rao HA, Shenoy D, Boloor A, Boyanagari M. The role of fresh frozen plasma in reducing the volume of anti-snake venom in snakebite envenomation. Trop Doct. 2018; 48: 89-93.
9. Brunda G, Sashidhar RB. Epidemiological profile of snake-bite cases from Andhra Pradesh using immunoanalytical approach. Indian J Med Res. 2007; 125: 661–668.
10. Longkumer T, Armstrong LJ, Finny P. Outcome determinants of snakebites in North Bihar, India: a prospective hospital based study. J Venom Res. 2017; 8: 14-18.
11. Jarwani B, Jadav P, Madaiya M. Demographic, epidemiologic and clinical profile of snake bite cases, presented to Emergency Medicine department, Ahmedabad, Gujarat. J Emerg Trauma Shock. 2013; 6: 199-202.

12. Singh A, Goel S, Singh AA, Goel AK, Chhoker VK, Goel S, *et al*. An epidemiological study of snakebites from rural Haryana. Int J Adv Med Health Res. 2015; 2: 39-43.

13. Raina S, Raina S, Kaul R, Chander V, Jaryal A. Snakebite profile from a medical college in rural setting in the hills of Himachal Pradesh, India. Indian J Crit Care Med. 2014; 18: 134-138.

14. Mitra S, Agarwal A, Shubhankar BU, Masih S, Krothapalli V, Lee BM, et al. Clinico-epidemiological Profile of Snake Bites over 6-year Period from a Rural Secondary Care Centre of Northern India: A Descriptive Study. Toxicol Int. 2015; 22: 77-82.

15. Suchithra N, Pappachan JM, Sujathan P. Snakebite envenoming in Kerala, South India: clinical profile and factors involved in adverse outcomes. Emerg Med J. 2008; 25: 200-204.

16. Chaaithanya IK, Abnave D, Bawaskar H, Pachalkar U, Tarukar S, Salvi N, et al. Perceptions, awareness on snakebite envenoming among the tribal community and health care providers of Dahanu block, Palghar District in Maharashtra, India. PLoS One. 2021; 16: e0255657.

17. Vijayaraghavan B, Ganesh SR. Venomous Snakes and Snakebites in India. In: Gopalakrishnakone P, Faiz A, Fernando R, Gnanathasan C, Habib A, Yang CC. (eds) Clinical Toxinology in Asia Pacific and Africa. Toxinology, 2015: 2. Springer, Dordrecht.

18. Kundu S, Lalremsanga HT, Tyagi K, Biakzuala L, Kumar V, Chandra K. Mitochondrial DNA discriminates distinct population of two deadly snakes (Reptilia: Elapidae) in Northeast India, Mitochondrial DNA Part B. 2020: 2: 1530-1534.

19. Chauhan V, Thakur S. The North-South divide in snake bite envenomation in India. J Emerg Trauma Shock. 2016; 9: 151-154.

20. Samuel SP, Chinnaraju S, Williams HF, Pichamuthu E, Subharao M, Vaiyapuri M, *et al*. Venomous snakebites: Rapid action saves lives-A multifaceted community education programme increases awareness about snakes and snakebites among the rural population of Tamil Nadu, India. PLoSNegl Trop Dis. 2020; 14: e0008911.

21. Mapping snakes in Uttarakhand for safer coexistence with humans. 2023.

22. Mana K, Ghosh R, Gantait K, Saha K, Parua P, Chatterjee U, *et al*. Incidence and treatment of snakebites in West Bengal, India. Toxicol Rep. 2019; 6: 239-243.

23. Chandramouli SR. Snake fauna of the Andaman Islands, Bay of Bengal—A review of species richness, taxonomy, distribution, natural history and conservation status. 2022; 5209: 3.

24. Yaqoob A, Ali Mufti S. A study on the clinical, epidemiological profile and the outcome of the snake bite victims in Kashmir valley. J Family Med Prim Care. 2022; 11: 680-684.

25. SenjiLaxme RR, Khochare S, de Souza HF, Ahuja B, Suranse V, Martin G, *et al*. Beyond the 'big four': Venom profiling of the medically important yet neglected Indian snakes reveals disturbing antivenom deficiencies. PLoS Negl Trop Dis. 2019; 13: e0007899.

26. Sharma SK, Alirol E, Ghimire A, Shrestha S, Jha R, Parajuli SB, *et al*. Acute Severe Anaphylaxis in Patients with Neurotoxic Snakebite Envenoming Treated with the VINS Polyvalent Antivenom. J Trop Med. 2019; 2019: 2689171.

27. Shashidharamurthy R, Jagadeesha D, Girish K. Variation in biochemical and pharmacological properties of Indian cobra (*Najanaja*) venom due to geographical distribution. Mol Cell Biochem. 2002: 229; 93–101.

28. Whitaker R and Whitaker S. Venom, antivenom production and the medically important snakes of India. Current Sci. 2012; 103: 635-643.

29. WHO. Guidelines for the Production, Control and Regulation of Snake Antivenom Immunoglobulins. 2016.

30. Warrell DA, Gutiérrez JM, Calvete JJ, Williams D. New approaches & technologies of venomics to meet the challenge of human envenoming by snakebites in India. Indian J Med Res. 2013; 138: 38–59.

31. de Silva HA, Ryan NM, de Silva HJ. Adverse reactions to snake antivenom, and their prevention and treatment. Br J Clin Pharmacol. 2016; 81: 446–452.

32. WHO/SEARO Guidelines for the clinical management of snake bites in the Southeast Asian region. 2nd edition. 2016.

33. Duru M, Sahan M, Ozcan O, Karakus A, Ozkan M, Kuvandik G. Snake Antivenom, Anaphylaxis and Afterwards: Case Report. Austin J Surg. 2017; 4: 1112.

34. Amin MR, Mamun SMH, Rashid R, Rahman M, Ghose A, Sharmin S, *et al*. Anti-snake venom: use and adverse reaction in a snake bite study clinic in Bangladesh. J. Venom. Anim. Toxins incl. Trop. Dis. 2008; 14: 665.

35. Isbister GK, Brown SG, MacDonald E, White J, Currie BJ. Current use of Australian snake antivenoms and frequency of immediate-type hypersensitivity reactions and anaphylaxis. Med J Aust. 2008; 188: 473-476.

36. Acikalin A, Gökel Y, Kuvandik G, Duru M, Köseoğlu Z, Satar S. The efficacy of low-dose antivenom therapy on morbidity and mortality in snakebite cases. Am J Emerg Med. 2008; 26: 402-407.

37. Vongphoumy I, Chanthilat P, Vilayvong P, Blessmann J. Prospective, consecutive case series of 158 snakebite patients treated at Savannakhet provincial hospital, Lao People's Democratic Republic with high incidence of anaphylactic shock to horse derived F(ab')2 antivenom. Toxicon. 2016; 117: 13–21.

38. Premawardena AP, de Silva CE, Fonseka MMD, Gunatilake SB, de Silva HJ. Low dose subcutaneous adrenaline to prevent acute adverse reactions to antivenom serum in snake bite: a randomized placebo-controlled trial. BMJ. 1999; 318: 730–733.

39. Indian Pharmacopoeia 2022. Snake Venom Antiserum. IP Commission. 2022; 3: 4470.

40. British Pharmacopoeia 2022. European Viper Venom Antiserum. BP Commission. 2022.

41. European Pharmacopoeia 11.0. Viper Venom Antiserum, European monograph. European Directorate for the Quality of Medicines & HealthCare.

42. World Health Organization. WHO Technical Report Series, No. 1004, 2017. Annex 5 Guidelines for the production, control and regulation of snake antivenom immunoglobulins Replacement of Annex 2 of WHO Technical Report Series, No. 96. 2017; 197-388.