

Innovations

Treatment, First-Aid and Prevention of Snake Bites in India: A Brief Review

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Abstract: *In 2005 alone, an estimated 45,900 people succumbed to snakebite across India. It highlights the importance of effective snakebite management. This review synthesizes existing knowledge on snakebite management in India. We summarized available treatments, first aid procedures and preventive measures. We also identified research gaps and issues with the current antivenom used in India, as well as harmful first aid practices prevalent in the country. This suggests urgent need to develop a better antivenom for India and spread public awareness about snakebite first aid, treatment and prevention.*

Keywords: *Venom, Antivenom, Envenomation, Polyvalent, Monovalent*

Introduction

Snakebite is a global health issue. Managing snakebites properly and addressing the issue of snakebite calls for widespread public awareness on prevention, complex medical treatments, as well as knowledge to proper first aid procedures. It is of extreme importance in India since India accounts for a huge number of snakebite envenomations. Envenomation, in the context of snakebite refers to the pathological condition that occurs when someone is injected with venom due to a venomous snakebite. Venom is a type of toxic substance produced by certain animals like snakes, scorpions etc. Snakebite management is also a relatively neglected area in scientific research. Therefore, it comes with huge opportunity for researchers to discover new things and make improvements on existing models. Snakes are creatures with vital ecological value and addressing snakebite management can help in their conservation by reducing the widespread fear of snake and reducing human-snake conflicts. Antivenom, the medicine used to treat snakebites is produced by a complex scientific process and requires proper understanding of science and the scientific way to manage snakebites. In India, the type of antivenom used to treat snakebites is polyvalent, meaning it is designed to be effective against multiple snake species. Monovalent on the other hand, would mean it is designed to be effective only

against one species. The topic of how to manage snakebites can also help with public health planning by providing data on patient demographics, geographical distribution etc. It is also an important topic to be considered while developing infrastructure for healthcare. All combined, management of snakebite is a topic of extreme importance.

Review of Literature

Snakes Found In India

India is home to a rich biodiversity. It houses an estimated 300 species of snakes^[1]. Most of them are non-venomous. Only around 60+ species are significantly venomous, 40+ species are mildly venomous (their bites do not pose dangers to humans in most cases) and around 180 species are non-venomous^[1]. These species are distributed in various families. Among these, the most common families are —

- Colubridae
- Elapidae
- Viperidae
- Pythonidae

A brief introduction about these families are given below: -

Colubridae

Housing around 2000 species (approx.), Colubridae is the largest family of snakes in the world^[2]. Colubrids are found in all continents except Antarctica (no snakes are found in Antarctica)^[2]. Some snakes of this family have toxic salivary secretions. These secretions may enter the bite wound when a person is bitten^[3]. Colubrids that are medically significant have opisthoglyphous dentition (rear fanged)^[2]. It means their fangs are located at the posterior end of the maxilla and are only capable of restricted movement^[4]. Around 30-40% of colubrids have a gland called Duvernoy's gland in their temporal region^[5]. This is a specialized oral gland^[5]. The secretions of this gland can have toxins which are used by a few colubrids to kill prey^[5]. However, the method of venom delivery of colubrids is far less efficient than snakes having a true venom gland, such as elapids and vipers. Due to all these factors, in order to envenomate, the snake has to 'chew' a bit on its victim making it unlikely for a human to be envenomated.^[2]

Indian colubrids consists of mostly non-venomous and some mildly venomous snakes^[6]. Therefore, in India, typically, colubrids are not considered to be medically significant. Examples include – Oriental rat snake (*Ptyas mucosa*), Checkered keelback (*Fowlea piscator*), Common wolf snake (*Lycodon aulicus*), Buff striped keelback (*Amphiesma stolatum*), Indian vine snake (*Ahaetulla oxyrhyncha*), Indian gamma snake (*Boiga trigonata*).

It is to be noted, that venoms of colubrids have been relatively less well studied compared to other families like elapids and vipers. This leaves a lot to still be explored about their venoms^[7].

Elapidae

Elapidae are a family of snakes that are relatively new in evolution. Venomous elapids have short front fangs^[1,8]. Elapids are usually venomous^[9]. Snakes belonging to the genus *Emydocephalus* are the only non-venomous snakes that belong in the Elapidae family^[10]. Certain species of the Elapidae family like the spectacled cobra (*Naja naja*) are recognizable by their hood which acts as a threat display^[11]. Examples of commonly found elapids in India includes – Spectacled cobra (*Naja naja*), Monocled cobra (*Naja kaouthia*), Common krait (*Bungarus caeruleus*), Banded krait (*Bungarus fasciatus*), King cobra (*Ophiophagus hannah*).

Viperidae: With more than 200 species distributed across the world and with all of them being venomous, they include quite a few medically significant species^[2]. Vipers are usually considered to be ambush predators because of their relatively heavy body. The Gaboon viper (*Bitis gabonica*) is a member of the Viperidae family. It has the highest venom yield among all venomous snakes across the world^[12]. They also possess the longest fang out of any snake in the world (>50mm)^[3]. Snakes belonging to Crotalinae (known as pit vipers), a subfamily of the family Viperidae, possesses a pit organ capable of sensing infrared radiation. This organ is known as loreal pit and is located bilaterally between the eye and nostril^[13].

Examples of vipers in India includes, Russell's viper (*Daboia russelii*), Indian green pit viper (*Craspedocephalus gramineus*). 2 out of the 4 species that are responsible for the most deaths in India (collectively known as the big four) are vipers. The big four is described in more detail in a later part of this article.

Pythonidae

The Pythonidae family comprises of some of the largest snakes in the world. They are non-venomous and rely on their ability to constrict their prey for food^[14].

In India, although not medically significant, they still sometimes come in contact with humans^[15]. Their large size can be a scary sight due to the fear of being eaten. The truth is however, although there have been instances of pythons swallowing humans, (such cases are extremely rare) most fully grown adult pythons would not be able to swallow a human^[16]. Despite this, if they bite a person, it could cause injury due to their strong nature and considerable size. However, such instances are rare because by nature of behaviour, pythons are not keen to bite humans unless they are provoked^[16]. There is sometimes a superstitious myth/belief among people that pythons can hypnotize their prey. However, scientific evidence doesn't support such claims^[17]. The Indian Rock python (*Python Molurus*) is a well-known python species found in India.

Statistics

According to the estimates of WHO (World Health Organisation), every year there are about 5.4 million snakebites, 2.7 million envenomings, leading to 81,000 –

138,000 deaths. In addition to it, around 400,000 amputations along with other permanent disabilities occur as a result of snakebites every year^[18-20]. However, quite often snakebites and deaths occurring due to snakebites go unreported. According to a large, community level study, an estimated 45,900 (99% CI: 40,900 – 50,900) snakebite deaths occurred in India in the year 2005, which is more than 30 times higher than the official number provided by the Government of India^[21]. Another study, which analysed 2833 snakebite deaths from 611,483 verbal autopsies in the nationally representative Indian Million Death Study from 2001 to 2014 and used other data, estimated around 1.2 million snakebite deaths (average 58,000/year) in India during the time period of 2000 to 2019. In a cruder estimate, 1.11-1.77 million snakebites are attributed to the year 2015^[22]. Since, India contributes to a considerable portion in the number of snakebite deaths globally, it is reasonable to assume that global estimates for total deaths from snakebite are also underestimated^[21].

Snake Venom

Snake venoms are complex cocktails of enzymes, proteins, lipids, amines, nucleosides and carbohydrates^[23]. They help the snake in immobilizing their preys, aids in digestion and acts as a method of defence against predators. Despite its lethal nature, snake venom consists of 90% water (approx.)^[24]. Most snake venom contains hyaluronidase, which catalyses the cleavage of internal glycoside bonds and mucopolysaccharides and therefore, potentiates action of other toxic agents^[24]. Phospholipase A is also present in several snake venoms and it results in hydrolytic breakdown of membrane phospholipids^[24]. Phospholipase A shows cytotoxic (cell damaging), anticoagulant (inhibiting blood coagulation) and neurotoxic properties^[24]. Composition of snake venom often varies based on various factors. Between different species of snakes, or different members of the same species of snake, or even in the same snake during different times of the year and varying age, composition of snake venom may vary considerably^[2]. Susceptibility of potential preys to different snake venom also shows considerable variation^[25].

Based on composition and effects, snake venom is classified into three main categories: -

- ❖ Neurotoxic (meaning it negatively affects the nervous system)
- ❖ Haemotoxic (meaning it negatively affects the cardiovascular system)
- ❖ Cytotoxic (meaning it negatively affects and damages cells and tissues)

There is another major category of venom called proteolytic venom. However, it is left off the list as it is present in all venomous snakes. This category of venom aids the snake in digesting/breaking down tissues of its prey, with the help of enzymes present in it^[26].

Problems with Traditional Healers

India has often been stereotyped as the 'land of snake charmers. Unfortunately, even in the light of modern medicine and medical research, this notion is held true by some people^[27,28]. Even today, people in rural areas of India often goes to snake charmers and traditional healers for snakebite treatment instead of hospitals. This is aggregated due to various factors like lack of knowledge, lack of access to medical facilities and superstitious believes^[29,30]. However, traditional healers and snake charmers often does more harm to the victim than to cure him/her. One such incident occurred when a snake charmer put potassium nitrite in the eyes of a rural farmer (age - 24 years). It resulted in severe chemical injury in both of the farmer's eyes^[27]. Another tool in the snake charmer's arsenal is the healing stone. Healing stones or snake stones are often used by traditional healers in treatment of snakebite^[31,32]. It is claimed that these stones have the ability to extract the snake venom, attaching itself at the bite site. Once all of the venom has been extracted, it falls off by itself. However, this claim is baseless and unscientific. Studies prove that this method of treatment using a healing stone does not alter the effects of snake venom^[33].

Yet, traditional healers continue to thrive in various areas of rural India. The reason behind people putting their trust on these healers is simple statistics. The majority of snakebites occur from non-venomous species. Out of the remaining cases where the snakebite is actually from a venomous species, a significant portion are 'dry bites' (no envenomation). Therefore, majority of people coming to a traditional healer with a snakebite would have no envenomation. This is the secret behind the traditional healer's miraculous 'cure'^[32,34,35].

These snake charmers/traditional healers do not have any actual remedy for envenomation resulting from a venomous snakebite. The healer would often show disinterest in treating such victims as their death would cause people to lose their trust on the healer. These victims end up a medical facility, eventually^[32].

Outdated and/or Unsupported Practices

The highly potent venom in certain snakes have the potential to kill humans^[18]. This leads to fear and the fear clouds judgement^[36]. In the event of a snakebite, a variety of factors such as- fear, panic, lack of knowledge, lack of access to medical facilities, cultural beliefs, misinformation etc. might cause people to resort to treatment methods that are outdated and/or not supported/recommended by modern science. A few of them are discussed below: -

- **Tourniquet/ligatures** – Application of tourniquet/ligature is a common practice in snakebite, even today. However, it is ineffective in stopping the effects of envenomation^[37]. They may even cause more harm than good by resulting in ischemia, gangrene, increased fibrinolysis, rapid development of severe systemic envenomation (may happen at the time of releasing a

tight tourniquet)^[38,39]. Tourniquets and ligatures may also give an unhealthy confidence to the victim, who might falsely believe that venom flow has been stopped. This could cause the victim to delay seeking medical attention and potentially lose their life^[32].

- **Sucking the bite wound** – Attempting to suck out the snake venom from the wound of a bitten person is an ineffective method^[40]. Not only does it not work, it also increases risk of secondary infections. Also, if the person who's attempting to suck out the venom has any oral wound, then that could act as a potential pathway for the venom to enter that person's system and result in another case of envenomation^[41].
- **Incision/cutting open the bite site** – A common practice (especially in rural areas), in the event of a snakebite is to cut/incise the location of the bite (wound scarification)^[32]. This is done with the hope of draining out blood and thereby, the venom with it. This practice, however, is not supported by scientific studies and it often causes more harm than good due to the following reasons –
 - Venom is seldom injected directly into the circulatory system. Most of the time, injection of the venom takes place into fat/muscle tissues and then the lymphatic system spreads it. Cutting open the site of the bite wound and then draining blood from it would do little to stop the venom from spreading in such cases^[42].
 - It can cause damage to adjoining muscle tissue, tendons, ligaments, result in blood loss and increase the risk of secondary infections^[42].
- **Venom extractors** – Some commercially available devices that applies negative pressure over the bite wound, claims to be effective in extracting snake venom and work as a temporary first aid measure that can be deployed on the field. Sean Bush researched this claim using such a device made by Sawyer Products. They injected a standardized amount of venom (25mg) in pig models. The extractor did not cause any difference in local tissue swelling. Furthermore, Necrosis was noted in 2 instances where the device was used and it suggests that the device may even cause harm^[43]. Another study, used human volunteers and aimed to find out what the extractor actually sucks out. Using the extractor after injecting radioactively labelled mock venom, they found that it extracted virtually no amount of venom^[40].
- **Cryotherapy** – Do not apply ice to the bite wound. The World Health Organisation in its guidelines for management of snakebites and other academic sources advises against the application of ice for snakebites^[39,44].
- **Electrotherapy** – Do not give electric shocks^[39,45].
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Big-Four (Indian Snakes)

Majority of medically significant snakebites on the Indian subcontinent are caused by 4 species. These four species are collectively referred to as the big four. They are the following four species: -

- ❖ Spectacled cobra (*Naja naja*)
- ❖ Russell's viper (*Daboia russelii*)
- ❖ Common krait (*Bungarus caeruleus*)
- ❖ Saw-scaled viper (*Echis carinatus*)

It is to be noted that these aren't the only medically significant snake species in India. Although, the big-four is responsible for the largest number of medically significant bites and deaths, there are other species who are also known to cause medically significant bites. These includes the monocled cobra (*N. kaouthia*), banded krait (*B. fasciatus*), Sind krait (*B. sindanus*), Sochurek's saw-scaled viper (*E. c. sochureki*) and several others^[46,47].



Figure 1 (top left): Spectacled cobra (*Naja naja*), Figure 2 (top right): Russell's viper (*Daboia russelii*), Figure 3 (bottom left): Common krait (*Bungarus caeruleus*). Figure 4 (bottom right): Saw-scaled viper (*Echis carinatus*)

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Antivenom/Antivenin

Antivenom are antibodies extracted from the blood of another animal. These antibodies are produced by the animal as a response to venom. Snake antivenom are usually made using the serum from animals such as sheep and horses. These animals are usually hyperimmunized with snake venom, before their blood is drawn and purified to prepare antivenom. When a person is bitten by a snake, antivenoms are injected in his/her body to stimulate his/her immune system against the venom^[48-50]. Snake antivenoms are available in two types: -

- **Monovalent** – Monovalent antivenoms are designed to only be effective against the venom of a single, specific snake species. For their use, the snake species that bit the victim needs to be objectively identified. They may sometimes also be used against venom of other closely related species^[51]. Monovalent antivenoms are not available in India^[47].
- **Polyvalent** – Polyvalent antivenoms are designed to be effective against the venom of multiple snake species^[51].

In clinical practice, it is often impossible to objectively identify the snake species for a snakebite victim. Using monovalent antivenom is difficult in such cases. It is more practical to treat the patient with a polyvalent antivenom that is designed to work against all the common species known to cause snakebites in the region. This makes polyvalent antivenom to be the favourable choice for hospitals^[51].

Antivenoms can be lifesaving when administered promptly. However, they are not able to reverse certain effects of venom such as necrosis or kidney failure that may occur if treatment is delayed^[51].

Clinical Features

It is important to know the clinical features of ophitoxaemia to ensure prompt medical attention with reduced complications and ensure a good outcome overall. The local and systematic indicators are listed below: -

- **Local signs/symptoms**
 - Presence of fang marks
 - Pain/tenderness
 - Rapidly increasing swelling (oedema)
 - Blistering (bullae, vesicles, blebs)
 - Necrosis

- Bleeding
- **Systemic signs/symptoms**
 - Abdominal pain
 - Vomiting
 - Nausea
 - Drowsiness
 - Drooping of upper eyelids (bilateral ptosis)
 - Paralysis
 - Double vision (diplopia)
 - Shortness of breath (dyspnoea)
 - Low pitch voice (dysphonia)
 - Difficulty swallowing (dysphagia)

 - Difficulty speaking (dysarthria)
 - Spontaneous systemic bleeding including bleeding from the gums (gingival haemorrhage) and nosebleed (epistaxis)
 - Bruising (ecchymosis)
 - Subconjunctival haemorrhage
 - Presence of blood in urine (haematuria)
 - Impaired consciousness

Remember, the fear and anxiety associated with a snake bite can result in striking signs/symptoms in a victim. The common clinical manifestations arising from post-snakebite fear are listed below: -

- ❖ Nausea
- ❖ Vomiting
- ❖ Diarrhoea
- ❖ Sweating
- ❖ Trembling
- ❖ Dizziness
- ❖ Pins and needles sensation in extremities (paraesthesia)
- ❖ Increased Blood Pressure (stress-induced hypertension)
- ❖ Increased Pulse rate (sinus tachycardia)
- ❖ Fainting with drastic drop in heart rate (vasovagal shock)

These signs and symptoms may be present even without the injection of any actual venom, such as in cases of dry bites or if the species is non-venomous. This has the potential to confuse and mislead first-aid providers like neighbours and family members and even medical staff or doctors. Therefore, it is important to be able to distinguish them from signs/symptoms resulting from an actual envenomation due to a snakebite^[32,39].

Management of a Snakebite

Anti Snake Venom (ASV)

The gold standard for snakebite envenomation in India is Anti Snake Venom (ASV)^[52-54]. It is a polyvalent antivenom that neutralises venom from the big-four species (*Naja naja*, *Daboia russelii*, *Bungarus caeruleus*, *Echis carinatus*)^[55]. 1 ml of ASV is supposed to neutralize: -

- ❖ 0.6 mg venom of spectacled cobra (*N. naja*)^[55]
- ❖ 0.45 mg venom of common krait (*B. caeruleus*)^[55]
- ❖ 0.6 mg venom of russell's viper (*D. russelii*)^[55]
- ❖ 0.45mg venom of saw-scaled viper (*E. carinatus*)^[55]

The venom used in making ASV is primarily supplied by the Irula Snake Catchers' Industrial Cooperative Society, Chennai. The irulas extract snake venom from the big-four which is then freeze-dried. The freeze-dried venom is then sold to various antivenom manufacturers like Haffkine Institute, Mumbai, who then produces ASV^[56]. ASV is available in two types: -

- ❖ Powdered (lyophilised)
- ❖ Liquid

Clinical superiority of one specific type isn't evidence supported. Both types have their pros and cons. Lyophilised ASV needs 30-60 mins time to be reconstituted before use. Liquid ASV can be used instantly but has a shorter shelf life of 2 years, as compared to the 5-year shelf life of lyophilised ASV. Unlike lyophilised ASV, liquid ASV needs a cold chain for storage and therefore, it might not be the best choice for hospitals in areas where power outages are frequent^[53,54].

Field level management (on site) and first aid (family/bystanders)

Proper first aid is essential in a snakebite and has the potential to significantly influence patient outcome. The protocol – “Do it R.I.G.H.T.” can be followed and is explained below: -

- ❖ **R (Reassure the victim)** – Reassure the victim that most snakebites are non-venomous and that there is also the possibility of a dry bite. This is to calm down the victim and prevent complications arising from fear and anxiety^[52].
- ❖ **I (Immobilize the bitten limb)** – Immobilize the bitten limb as if it's a fractured limb. However, blood supply should not be occluded. Pressure Immobilization (PI) can be used to occlude the superficial lymphatics and inhibit the spread of the venom in case of a neurotoxic envenomation. PI is not recommended for haemotoxic bites^[52,54,57].
- ❖ **GH (Go to Hospital)** – Transport the victim to a medical facility with availability of antivenom as soon as possible. The victim should not attempt to walk or run to the hospital by themselves. A car or an ambulance is ideal. Motorcycles can be used as a transport mean in rural areas in the absence of availability of ambulance/cars. The victim should be supported

by one person at the front and one at the back when transported by a motorcycle^[52,54].

- ❖ **T (Tell the doctors about the symptoms)** – Inform the doctor about the history of the bite and about any local/systemic signs/symptoms that have manifested. This helps in making a proper diagnosis and early detection of the clinical features associated with envenomation^[52].

There is no need to try to kill or capture the snake. This leads to wastage of precious time. There is also the risk of another person getting bit in the process. However, if the snake is already killed, take it to the hospital with you so that it can be identified. Otherwise, if possible, take a picture of the snake. However, it is not justified to waste time behind this as treatment of snakebite in India is done based on clinical features and not on the basis of the identification of snake^[54].

Hospital level management (medical staff/doctors)

Diagnosis phase: upon arrival

Follow the ABC protocol and make sure that the patient's airway, breathing and circulation is okay. All patients coming in with a bite should receive an injection of Tetanus Toxoid (TT). However, administration of TT injection should be held back when it is contraindicated due to presence of coagulopathy. In such cases, it should be given to the patient after the restoration of coagulopathy^[53,54]. There is no reason to administer antibiotics routinely except for certain specific species like Chinese cobra (*Naja atra*) and Malayan pit viper (*Calloselasma rhodostoma*)^[54,58]. However, antibiotic should be given in cases with necrosis, cellulitis, wound scarification or if infection is anticipated^[39,53,54,58]. Try to objectively identify the species of snake if the circumstances allow it. Perform a physical examination of the bite location and check for swelling, tenderness, bleeding, blistering, necrosis, local lymphadenopathy and other local signs^[39]. Ask questions and try to determine the exact time when the patient was bitten and if any alternate medicine was used. This will help in estimating how the symptoms may progress over time as well as in understanding the various confusing, misleading symptoms and harmful effects alternate medicine may cause^[27,53].

Diagnosis phase: Symptoms

Depending on the circumstances, observing the signs and symptoms in a snakebite patient can sometimes help with objective identification of the snake. Species identification is not a mandate in India for snakebite treatment. This is because monovalent antivenom is unavailable in India and victims are usually treated with polyvalent antivenom. However, if the species can be identified, the knowledge will help in indicating what kind of complications may occur. As a rule of thumb, viper bites cause haemostatic irregularities and cobras/kraits causes neurotoxic symptoms^[53]. The following table shows evidence based common

symptoms of a viper and elapid bite: -

VIPERS	ELAPIDS
<ul style="list-style-type: none"> • Local pain • Local swelling • Tender lymphadenopathy • Blistering • Necrosis • Compartment syndrome • Ecchymosis • Subconjunctival haemorrhage • Gingival bleeding • Epistaxis • Haematuria • Bleeding from freshly healed wounds • Venom Induced Consumption Coagulopathy (VICC) • Acute Kidney Injury (AKI) • Lateralizing neurological symptoms like asymmetrical pupils (indicating possibility of intracranial bleeding) 	<ul style="list-style-type: none"> • Local pain and swelling • Ptosis • Paralysis (descending) • Diplopia • Dysarthria • Dysphonia • Dysphagia • Dyspnoea

- **Acute abdominal tenderness**
(indicating possibility of gastro-intestinal/retro peritoneal bleeding)

Figure: Clinical features of snakebite^[53,54]

However, this is only a general guide and exceptions take place. For example, the venom of Russell’s viper (*Daboia russelii*) has been found to show neurotoxic properties along with its haemotoxicity^[59,60]. Another thing to remember is that krait bites often happen without local symptoms and a visible bite mark. This is because krait fangs are extremely short (~3mm length) and as a result, the venom is often injected superficially^[54,61]. Krait bites often occur at night. In such cases, the victim often presents with severe abdominal pain, vomiting in the morning and it progresses with neurological symptoms^[54,62]. It is important for doctors to keep this in mind to avoid misdiagnosing such cases.

Clinical features	Spectacled cobra	Common krait	Russell’s viper	Saw-scaled viper
Necrosis	Yes	No	Yes	Yes
Ptosis	Yes	Yes	Yes	No
Haemostatic irregularities	No	No	Yes	Yes
Renal failure	No	No	Yes	No
Response to Anti Snake Venom	Yes	Yes	Yes	Yes

Figure: Clinical features of bites from the big-four^[54]

Diagnosis phase: Investigations

- **Single Breath Count (SBC)** – SBC is an easy to perform, bedside test that can help detect early signs of impending respiratory failure. It can be performed without the absence of sophisticated lab equipment. Ask the patient to take a maximum inhalation and then count digits using a normal speaking voice. If the patient is able to count till or more than 30, it’s

normal. Otherwise, he/she might be going for an impending respiratory failure^[53,54,63,64].

- **20-minute whole blood clotting test (20 WBCT)** – 20 WBCT is a reliable bedside test to check for coagulopathy in snakebite patients in absence of sophisticated equipment. To perform the test, collect a few millilitres of fresh, venous blood and put it in a clean, dry glass tube. Leave the tube undisturbed for 20 minutes without shaking. After 20 minutes, tilt the tube and see if the blood is clotted. The test is positive if the blood doesn't clot and it indicates possible coagulopathy. However, this test may give false positives sometimes. PT/INR therefore, is a better choice, whenever it is available^[53,54,65,66].

Other useful investigations

- **PT/INR** – Prothrombin Time test with INR (PT/INR) can be a reliable test to detect coagulopathy. However, a study found point-of-care INR to be unreliable in detecting coagulopathy for snakebites in Australia. Therefore, it might be best to stick to using lab PT/INR and avoid using point-of-care INR^[66,67].
- **Complete Blood Count (CBC)** – To check for decrease in platelet count^[53].
- **Peripheral Smear** – To check for any evidence of haemolysis and coagulopathy^[53,54].
- **Blood gas analysis** – To check for acidosis^[39].
- **Renal Function test** – To assess renal damage^[54].
- **ECG** – To check for Cardiovascular toxicity (arrhythmia, blocks)^[39,53,54].
- **CPK** – To check for skeletal muscle breakdown as a result of myotoxicity^[54].
- **Sr. Electrolytes/ABG/LFT** – To check for various systemic manifestations^[39,54].
- **Urine routine** – To check for proteinuria, haematuria, myoglobinuria^[53,54].
- **PT/aPPT/Serum Fibrinogen/FDPs** – Coagulation screening is a must for snakebite patients^[39,53,54].
- **Chest X-Ray** – To check for pulmonary edema or pleural effusion^[39].
- **Oxygen Saturation/Blood Pressure**^[39,54]

Diagnosis phase: Dealing with tourniquets or ligatures

It is not recommended to use any tourniquet/ligatures for snakebite^[53,54]. This is an outdated practice and is already discussed in a previous section of this article. However, due to being misinformed, people with snakebite often go to the hospital with a tourniquet. As per a study conducted in Himachal Pradesh, as high as 80.6% patients came to the emergency room with a tourniquet^[68]. It is

important to know how to deal with them as sudden release of a tourniquet/ligature can release a lot of venom and lead to complications like neurological paralysis, hypotension caused by vasodilation etc^[39,53,54]. If distal pulse is absent in a patient with a ligature, always make sure that a doctor is present when removing it. BP cuff can be utilized to gradually diminish pressure, if distal pulse is found to be occluded^[53,54]. As per expert consensus, all ligatures but the most proximal one can be removed inside the emergency room for patients with more than one ligature. The most proximal ligature should be removed after the patient is admitted and necessary treatment preparations are complete^[54].

Treatment phase: pain management

Snakebite often comes with tremendous local pain and therefore, pain management is an important topic in snakebite management. Aspirin or NSAIDs (Non Steroidal Anti Inflammatory Drugs) should never be used to manage snakebite pain. This is because, they may cause bleeding and is hence, contraindicated for patients with coagulopathy. Paracetamol is a good choice. Dosage for adults should be 500 – 1000mg, not exceeding 4000mg/24hrs. For children, the dosage is 10-15mg/kg of bodyweight, not exceeding 100mg/kg/24hrs. Extreme pain may be managed with mild opiates like Tramadol^[39,53,54].

Anti Snake Venom (ASV)

The gold standard for snakebite envenomation in India is Anti Snake Venom (ASV)^[52-54]. It is a polyvalent antivenom that neutralises venom from the big-four species (*Naja naja*, *Daboia russelii*, *Bungarus caeruleus*, *Echis carinatus*)^[55]. 1 ml of ASV is supposed to neutralize: -

- ❖ 0.6 mg venom of spectacled cobra (*N. naja*)^[55]
- ❖ 0.45 mg venom of common krait (*B. caeruleus*)^[55]
- ❖ 0.6 mg venom of russell's viper (*D. russelii*)^[55]
- ❖ 0.45mg venom of saw-scaled viper (*E. carinatus*)^[55]

The venom used in making ASV is primarily supplied by the Irula Snake Catchers' Industrial Cooperative Society, Chennai. The irulas extract snake venom from the big-four which is then freeze-dried. The freeze-dried venom is then sold to various antivenom manufacturers like Haffkine Institute, Mumbai, who then produces ASV^[56]. ASV is available in two types: -

- ❖ Powdered (lyophilised)

❖ Liquid

Clinical superiority of one specific type isn't evidence supported. Both types have their pros and cons. Lyophilised ASV needs 30-60 mins time to be reconstituted before use. Liquid ASV can be used instantly but has a shorter shelf life of 2 years, as compared to the 5-year shelf life of lyophilised ASV. Unlike lyophilised ASV, liquid ASV needs a cold chain for storage and therefore, it might not be the best choice for hospitals in areas where power outages are frequent^[53,54].

Treatment phase: ASV administration Administration criteria

Only administer ASV if there is: -

- ❖ Justified reason to believe the presence of systemic envenomation^[53].
- ❖ Severe local envenomation is present currently^[53].

This is because ASV is an expensive, life saving drug which suffers from shortages^[20,53]. ASV is also difficult to produce. Therefore, unnecessarily administering it to someone is a huge wastage. It also comes with a risk of anaphylaxis to the patient^[20,53].

Test dose

Late serum reaction or anaphylactoid cannot be anticipated using test dose of ASV (since these reactions don't involve IgE). Test doses are of no use and can even harm the patient by resulting in pre-sensitisation. Therefore, do not use them^[53,54].

Administration method

In terms of methods of administering the ASV, there are two options: -

- ❖ Slow IV injection (2ml/min)
- ❖ IV infusion after diluting ASV in either isotonic saline or glucose (5 – 10ml/kg of body weight)

ASV should be administered at a steady rate over a 60 min period. The patient is to kept under careful observation for 2 hours. Adrenaline injection might become necessary and should be ready^[52,53].

Dosage

Initial and repeat dosage for ASV therapy is given below: -

Initial dosage

Initially, a dosage of 10 vials of ASV is recommended and is based on the average venom yield from the big-four snakes. If the bite is already known to be from a saw-scaled viper, a comparatively lower dose of 5 vials can be used^[52-54]. In certain rare occurrences (Eg- intracranial bleed), surgery would be needed to save the patient's life. In such a scenario, the initial dose can be increased till 30 vials. This is because if the patient has coagulopathy during surgery, it can potentially result in fatal bleeding^[53,54]. Dosage of ASV for children does not differ from adult dosage since snakes do not inject any less amount of venom in a child than it would in an adult. There hasn't been a lot of research about pregnant women being bitten by snakes and the same 10 vial of dosage is used^[53,54].

Repeat doses

- **Haemotoxic envenomation** – Coagulopathy should be checked every 6 hours. The reasoning behind this is that a time period of 6 hours (approx.) is needed by the liver to replace clotting factors. Therefore, coagulopathy should be checked once every 6 hours. If coagulopathy persists, an additional dosage of 5-10 vials should be administered. Continue this till clotting factor restores or if the biting species is discovered to be one, against which polyvalent ASV is ineffective. However, If, even after administering a total of 30 vials of ASV, additional usage of ASV might not be helpful. In such cases, if situation permits, usage of Fresh Frozen Plasma (FFP) should be brought into consideration^[53,54].
- **Neurotoxic envenomation** – If symptoms deteriorate or do not improve within 1-2 hours after administering the initial dosage, administer the same number of vials of ASV as the initial dosage. After administering a total of 20 vials in this way, if symptoms still do not improve or respiratory failure occurs, patient should be put on ventilator and no additional ASV should be given^[53,54]. Neostigmine test should be performed in all neurotoxic cases. However, neostigmine does not work for krait bites (even with increased dosing than usual)^[69].

Prophylaxis

Usually, two options are available as prophylactic regimens to prevent ASV reactions: -

- Hydrocortisone + antihistamine^[53]
- Adrenaline subcutaneous (0.25 – 0.3 mg)^[53]

However, there is a lack of proper clinical trials and statistical evidence proving the usefulness of these regimens in preventing ASV reactions in Indian polyvalent ASV and there is a research. A Sri Lankan study found adrenaline to be effective in treating antivenom reaction. However, it did not find hydrocortisone to be similarly effective^[70].

ASV reaction (Anaphylaxis): In case of anaphylaxis, ASV should be paused and the patient should be treated with adrenaline. When the patient is alright, ASV therapy should start at a slower pace. After 15 – 20 minutes, ASV therapy can continue at its regular pace^[53,71].

Follow up

A snakebite patient should stay in the hospital for at least 24 hours even if the patient thinks the snake was non-venomous. This is in case the patient misidentified the snake. This rule should be followed even if the patient is asymptomatic. In cases of bites from certain species (Eg – *B. carruleus*) the symptoms may show up quite late as compared to other snakes like the spectacled cobra. At the time of discharge, the patient should be advised to return to the hospital if any snakebite symptoms manifest and informed about late serum sickness^[53,72].

Problems with Indian polyvalent ASV

India accounts for a lot of deaths and permanent disabilities caused by snakebites^[19]. The gold standard treatment available to snakebite patients in India is the polyvalent ASV. This makes it extremely important to understand the problems and research gaps associated with Indian ASV. These problems are listed below: -

- **Intraspecific venom variation** – The composition, effectiveness and other factors of snake venom can differ significantly with change of geographical location. This can be true even in the same snake species^[73,74]. To prepare a good antivenom, venom should be collected across varying geographical locations to account for such intraspecific variation. However, in India, all of the venom used to prepare antivenom is collected from a single place (Irula Snake Catchers' Industrial Cooperative Society, Chennai)^[56]. The biogeographical influence on snake venom is also not well studied in India. As a result, Indian ASV is not well designed keeping the problem of intraspecific venom variation in mind.

- **Medically significant species other than the Big-Four** – The Indian ASV is a polyvalent antivenom. It is designed only against the big-four species (*N. naja*, *B. caeruleus*, *E. carinatus*, *D. russelii*). However, there are a lot of other species of snakes in India that are medically important (Eg: - *H. hypnale*). Indian ASV is not designed for them and is largely ineffective. However, Indian ASV has also been found to be ineffective against venomous species that are closely related to the big-four^[47]. This highlights the need of monovalent antivenom for certain species in India.



Figure: Hump nosed pit viper (*Hypnale hypnale*)

Source: Photo by Daniel Liepack, obtained from iNaturalist (CC-BY-NC) (www.inaturalist.org)

- **Lack of research** – There is a significant lack of research about the polyvalent ASV used in India. Proper preclinical research and clinical data is not available. Biogeographical impact on venom is not well understood in India. Such research gaps and lack of basic research data makes it difficult for new research in this field.

Preventive measures for snakebite

Development in treatment is important but prevention is the true key in management of snakebite in India. Some preventive measures are discussed below: -

- **Maintain a clean household** – Unclean environment can serve as a breeding ground for rodents^[75]. These rodents attract certain species of snakes like the rat snake. In turn, the rat snake attracts more venomous counterparts such as the spectacled cobra^[76]. So, a good strategy to prevent snakebites, is to maintain proper cleanliness at the household.
- **Use torch when it's dark** – Some of the snakes are nocturnal in nature and as a result snakebites often occur at night^[77]. Using a torch will help in preventing such accidents.
- **Watch where you place your hands and feet** – According to statistical evidence, most snakebites occur in the lower extremities, followed by the upper extremities^[22]. In order to prevent snakebites, be aware of your hand and feet placement.
- **Sleep above ground and/or use mosquito nets** – Most krait bites occur at night. A study that looked at 23 krait bites, found that out of those 23 bites, 22 happened when the victim was sleeping on the floor^[78]. For this reason, sleeping on the floor in rural areas is not ideal. Sleep above the floor and use a mosquito net as a preventive measure.
- **Wear shoes when walking** – The same study discussed above also found instances of spectacled cobra bites occurring while walking barefeet^[78]. This is correlated by another study. It found snakebites mostly occur in the lower limb^[22]. So, wear shoes covering the entire feet in areas where snakes are in abundance as a prevention strategy
- **Awareness** – Spreading awareness about snakebite and how to prevent them is essential. A study aimed at the prevention of krait bites found drastic reduction in krait bites after providing awareness^[79].

Conclusion

India accounts for a huge number of snakebite envenomations. Treatment is available in form of polyvalent ASV. However, current ASV suffers from significant flaws. Single point of venom collection does not account for intraspecific venom variations and is designed to only treat bites from the big four. In addition, lack of public awareness has resulted in prevalancy of harmful first-aid practices. We also identified significant research gaps. Proper preclinical and clinical research data on current ASV is not available and the efficacy of prophylactic regimens

which are currently in use, in preventing ASV reactions and late serum sickness are not well studied. All of this calls for the development of a better antivenom and spreading public awareness about snakebite prevention and treatment. Snakebite is an accident. With proper preventive measures in place, we can prevent it.

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