

NEURAL NETWORK-BASED SPECIES IDENTIFICATION IN VENOM- INTERACTED CASES IN INDIA

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ABSTRACT: India is home to a number of venomous species. Every year in harvesting season, a large number of productive citizens are envenomed by such species. For efficient medical management of the victims, identification of the aggressor species as well as assessment of the envenomation degree is necessary. Species identification is generally based on the visual description by the victim or a witness and is therefore quite likely to be erroneous. Symptomatic identification remains the only available method. In a previous published work, the authors proposed a classification table for snake species based on manifested symptoms applicable in Indian subcontinent. The classification table serves the purpose to a great deal but as a manual method it demands human expertise. The current paper presents a neural network-based symptomatic species identification system. A symptom vector is fed as input to the neural network and the system yields the most probable species as well as the envenomation severity as the output. The severity status can be very helpful in calculating the antivenom dosage and in deciding the species-specific prognostic measures for efficient medical management.

KEY WORDS: bites and stings, symptoms, species identification, neural network.

CONFLICTS OF INTEREST: There is no conflict.

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INTRODUCTION

India, as a tropical country, has warm and humid climate suitable for a number of arthropod and reptile species which can interact venom. In Indian terra firma, scorpions and snakes are considered the major lethal venomous species of medical importance.

The majority of Indian population resides in villages, where agriculture is the prime occupation. Rainy season is the most productive time for farmers and is the peak season of reptile and arthropod activities. The search for food and shelter brings these species closer to human dwellings. The close proximity and survival instincts often result in deadly encounters, resulting in the animal death or injury to the human being. The situation is so gloomy that every year more than 15,000 people reportedly die due to snakebites (1). However, unreported estimates range from 30,000 to 50,000 (2, 23) and scorpion sting deaths of infants and younger victims have not been included in this figure.

Establishment of the species identity is very important in cases of venom interaction for effective medical management. Many times, snake-bitten victims bring along the dead snake for identification, but this method involves risk of a subsequent bite as well as ecological issues, so this practice is discouraged. On the other hand, description by a witness or the patient may not be authentic and thus the species identification has to be done remotely based on a reliable technique. At the same time, if the severity grade of the venom interaction is assessed, prognostic measures can be taken together with a broad estimation of the dose and schedule. In the absence of any other scientific method available at the grassroots level, symptomatic identification remains the only alternative. However, with the symptoms standardization, the system becomes precise and accurate.

Venom and Venomous Species

Venom is a mixture of proteins and peptides (6, 16). It is found in nature as one of the earliest survival means. A number of species evolved venom and, in the continuous quest for survival, improved their venom constituents and delivery apparatus (5, 9). Venomous species use venom to control, kill and digest their prey. Alternatively, it is used as a defense means against an aggressive enemy. Once the venom enters the victim's body at subcutaneous level, its different constituents start working synergistically, which includes decomposition of cell membranes, cleavage in

tissues, proteolysis, synaptic blockades, cardiac complications, etc. (4, 20). Some components in the venom target some specific organs or systems for faster degeneration of the victim (18, 28).

With the course of time, the victim general condition deteriorates in all venom interacted cases. The *in vivo* venom attacks specific target systems and a number of complications may be triggered. The symptoms, the development rate of symptoms, the clinical support and the required medicinal attention vary with the species. So, identification of the aggressor venomous species and the envenomation degree play an important role in medical management.

Snakes are the most familiar venomous reptiles all over the world. Being poikilothermic, they prefer warm climates for inhabitation (11). Unlike most other animals, they do not have any limbs. They have only teeth to attack and grab the prey or defend themselves against an aggressor. A snake bites a human being in order to defend itself when approached too close.

Snakes can be divided into three categories: aglyphs, opisthognaths and proterognaths (12). Aglyphs do not have venomous teeth and opisthognaths have posterior venom-delivery teeth. Proterognaths have their fangs located in the maxilla and connected to the modified salivary gland, which produces highly toxic venom. Venomous snakes belong to four families Viperidae, Elapidae, Colubridae and Hydrophidae (10). The current discussion is related to the former two families only. Viperidae venom is largely hemotoxic and primarily causes local symptoms (26), whereas Elapidae venom is often neurotoxic and may cause neuropathy as well as cardiomyopathy (13).

Scorpions, another medically important venomous species, belong to the phylum Arthropoda, order Scorpionida, class Arachnida. Their venom delivery apparatus is a pincer located in the caudal tip. Their venom is primarily neurotoxic, meant to immobilize small insects.

Venom Interactions and Physiological Manifestations in India

Only four venomous snake species from the families Elapidae (cobra and krait) and Viperidae (saw-scaled viper and Russell's viper) have medical importance in India (8). The topology of limited species has made identification simpler, but despite the limited number, recognition of biting species is still a challenge. Research has indicated that specific monovalent anti-snake venom (ASV) serum is the method of

choice (22), but due to the non-availability of standard techniques for species identification, administration of quadrivalent ASV serum catering to all venomous snakes is the only method currently practiced.

India harbors many scorpion varieties as well and the most deadly scorpions are those of *Buthus* or *Mesobuthus* genus. It is believed that the shorter the pedipalp, the more lethal the scorpion. The Indian red scorpion (*Mesobuthus tamulus*) is considered the most frightening scorpion in India.

Viperidae Envenomation

Saw-scaled viper (*Echis carinatus*) and Russell's viper (*Daboia russelli* or *Vipera russelli*) are common vipers in India. A victim of a viper bite manifests local symptoms with minimum neurological signs. A few systemic symptoms like coagulopathy, renal failure, etc, may be observed depending on the *in-vivo* amount of venom and the delay in medical aid.

Saw-scaled viper is a smaller snake, compared with Russell's viper, and so are its anatomical features. The difference in anatomy may be observed in the fang marks left at the bitten area.

The average gap between the fang marks of a saw-scaled viper is less than 1.75cm (1.27 ± 0.39 cm), whereas the fang marks of a Russell's viper have a wider spread (2.07 ± 0.43 cm). The fang spread statistics allows the deduction that, in a Viperidae bite, a fang gap of less than 1.75cm may be due to saw-scaled viper and a larger one may be attributed to Russell's viper. Also, Russell's vipers have been observed to have another pair of fangs protruding from the fangs' base. In such a case, one or two additional adjacent fang marks may also confirm a Russell's viper bite. The sizes of the puncture marks are obviously large in case of Russell's viper bite.

Viper bites are often followed by edema development. In case of saw-scaled viper, the edema is often centered at the fang marks and the back side of the limb has lesser edema compared with the area around the fang marks. However, in Russell's viper bites, the edema engulfs the whole limb; it is more or less uniform in the transverse plane with excessive fluid accumulation, termed as hyperedema. In delayed cases, the pressure inside the limb is often so large that there may be small fissures on the skin and there may be blood oozing from the bite marks and the fissures. In a few hours, blisters/blebs may also be formed on the extremities.

Viper bites cause minimal neurological complications, compared with developed local symptoms. Systemic features have a slow onset targeting the platelets, the clotting mechanism and the renal system. In delayed cases of viper bites, hematuria, oliguria or renal failure is commonly seen. Viperidae envenomation can be confirmed with the increase in bleeding time and clotting time.

Elapidae Envenomation

Elapidae envenomation in India is often more complex. Cobras have three variations, binocled cobra (*Naja naja naja*), monocled cobra (*Naja naja kaouthia*) and black cobra (*Naja naja oxiana*) whereas the kraits have two varieties, banded krait (*Bungarus fasciatus*) and common krait (*Bungarus caeruleus*) (24). All these cobras are biting species with similar venom constituents, and no separate ASV is prescribed for each variety. Bites by banded krait have not been reported in literature and this snake is believed to be a non-biting species for human beings. On the other hand, common krait is a very aggressive snake in the night, but a very docile creature during the day (14).

Cobra and krait-bitten patients manifest a few neurological features after bite. These include dilatation of pupils, heaviness in the eyes, difficulty in respiration, irregular speech, and a little later respiratory arrest. Cobra envenomation causes local symptoms like edema, pain and necrosis near the fang marks. In krait bite, local symptoms are often absent. As a result, the victim, often asleep, does not learn about the bite immediately. A little later, when the neuromuscular symptoms start developing, the victim awakes. This particular feature of krait bite is responsible for a large number of snakebite mortalities in India.

Scorpion Envenomation

Scorpion sting victims feel a shooting pain locally and often only one sting mark is seen. The neurological features start taking place soon and the pupils of the victim get constricted. Other features include peripheral hypothermia, tachycardia, respiration difficulty, renal failure, convulsions, hyperglycemia and coma. If the victim is a child, these features develop rapidly. The only prescribed treatment is administration of Anti-Scorpion Venom (AScV) serum (17, 27).

Remote Species Identification

Enzyme-linked immunosorbent assay (ELISA) is a successful technique used in a number of medical applications (22). ELISA performed on a sample from the bite site is considered the most reliable and effective method for species identification because there are vast variations in venom constituents among different species. There have been attempts of making a field ELISA kit for snakebites in India too but with limited success (21). In such a situation, the symptomatic identification remains the only choice currently, which is often practiced by the medical staff, but due to a large number of features, the method requires human expertise.

Thus, remote identification of the aggressor species by the manifested symptoms is the only available method. The quest for species-specific symptoms has led to analysis of the venom constituents of all venomous species. However, there might be large variations in controlled environment laboratory experimentation and the manifestations observed at the grassroots level. Hence, the authors have collected clinical profiles of forty patients and enlisted the physiological manifestations as well as supporting data of medical importance.

An attempt was made by the authors to categorize the snakebite symptoms in a tabular form to be used at the healthcare centers, as given in Table 1 (15). But this table did not include the scorpion sting cases, which also manifest neurological complications. To avoid any possible misclassification and to make the classification exhaustive, a modified table with scorpion sting symptoms is being proposed below. It is pertinent to mention here that every envenomation grade includes symptoms of its lower grade as well.

Table 1: Symptomatic identification of venomous snakes in India.

	Envenomation Grade Species	Grade I (Mild)	Grade II (Moderate)	Grade III (Severe)	Grade IV (Very Severe)	Distinct Feature
Viperidae	Saw-Scaled Viper	One or two punctures, ecchymosis, swelling, local pain	Rise in BT/CT, edema, local cyanosis, bleeding from the bite site	Hemorrhage, hematuria, melena, anemia, coagulopathy	Renal failure, hypotension, severe anemia and low SpO ₂	<i>Rapid discoloration near the puncture, bites often on the apex</i>
	Russell's Viper	One or two punctures, ecchymosis, swelling, local pain	Along with the above, blisters on the limbs	Along with the above, hyper-edema, blisters and necrosis on the limbs	Along with the above, hyper-edema and blisters on the limbs	<i>Blisters, wider puncture marks than those of Saw-scaled viper</i>
Elapidae	Cobra	One or two distinct fang marks, local pain, ecchymosis and swelling	Sluggish optical response, edema, diplopia and confusion	Ptosis, dilated pupils, local necrosis, low SpO ₂ , arrhythmia, difficulty in respiration, CNS & cardiac features	hypotension, unconscious state, cardiac arrest, respiratory arrest	<i>Rapid cardiac and systemic features with prominent local features</i>
	Krait	Miniscule fang marks, difficulty in swallowing after 5-12 hours	Sluggish optical response, diplopia, ptosis, glossopharyngeal dysfunction	Dilated pupils, ptosis, low SpO ₂ , poor respiration, arrhythmia, glossopharyngeal palsy, colic pain	hypotension, unconscious state, coma, respiratory arrest, sudden cardiac arrest	<i>Minimal local symptoms, colic pain and hypokalemia</i>
Scorpionida	<i>Mesobuthus tamulus</i>	One sting mark and shooting pain	ecchymosis, miosis, tachycardia, hyperglycemia	Peripheral hypothermia, hyperkalemia, renal failure, hypotension, low SpO ₂	Neuromuscular convulsions, respiratory arrest, coma	<i>Miosis or contracted pupils and hyperglycemia</i>

BT=bleeding time, CT= coagulation time, SpO₂= oxygen saturation level, CNS= central nervous system

MATERIALS AND METHODS

Parameter Selection for Remote Species Identification

Every year, more than a hundred patients report to healthcare centers in Kota division of Rajasthan (India). They are victims of different species and have envenomation of different degrees. These patients manifest various symptoms which include local, neurological, systemic and circulatory abnormalities. In the current medical practice in India, species-specific symptoms have not been given due importance, but a systematic observation of manifested symptoms can reveal the species.

Clinical profiles of forty patients have been studied which included all the possible symptoms of snakebites and scorpion stings. All these patients had reported to the

healthcare center without any medicine administered. The patients belong to all four grades and five species (one patient bitten by a non-venomous snake has also been included in the study and his psychosomatic symptoms were also observed). A written and informed consent was obtained from the patients or the accompanying relatives in all the cases. All the observations were taken without disturbing the medical management. No experiment on animals was conducted.

The Manifested Symptoms

The manifested symptoms have been selected in such a way that either they are manifested or are absent in cases of at least one species. It has also been kept in mind that all the symptoms are obtainable with minimal instrumentation in minimum time. There are twenty-nine symptoms which suit the constraints. All these symptoms are considered in binary form in the feature vector with a numerical value of one or zero.

- i. **Single fang marks:** if there is only one fang/sting mark at the bite site.
- ii. **Paired fang marks:** If there is a pair of fangs or more than two fang marks at the bite site, representing multiple bites.
- iii. **Gap in fang marks:** If the gap between the fang marks from a bite is more than 1.75cm.
- iv. **Local edema:** If there is edema developed, and if so, it is centering the fang marks alone.
- v. **Local pain:** If there is pain at the bite/sting site.
- vi. **Hyper-edema:** If there is excessive fluid pressure inside the affected limb and the whole limb is edematous.
- vii. **Ecchymosis:** If the bite site and adjacent areas are getting discolored.
- viii. **BT/CT:** If there is a marked rise in the bleeding time/coagulation time.
- ix. **Bleeding from the site:** If the bite site is bleeding, non-incised and non-manipulated.
- x. **Blisters on limbs/trunk:** If the body extremities or trunk present blisters/blebs.
- xi. **Hemorrhage:** If there is bleeding from the gums or other openings of the body.
- xii. **Hematuria:** If the urine is reddish.
- xiii. **Renal failure:** If the subject is unable to urinate (even when the bladder is not empty).
- xiv. **Ptosis:** If the eyelids are swollen and not opening fully.
- xv. **Pupil dilatation:** If the pupils are dilated (mydriasis).
- xvi. **Choking:** If the subject is unable to swallow and has difficulty in breathing.

- xvii. **Colic pain/vomiting:** If the subject reports pain in the abdomen and tendency to vomit.
- xviii. **Hemoptysis:** If there is blood in the sputum.
- xix. **Glossopharyngeal paralysis:** If the voice is obstructed or there is difficulty in speech.
- xx. **Neuromuscular paralysis:** If the neuromuscular tone is abnormal.
- xxi. **Respiratory paralysis:** If the ventilation is abnormal and oxygen level falls in the blood.
- xxii. **No local symptom:** If there are no marked symptoms on the affected limb.
- xxiii. **Tachycardia:** If the heart rate is higher than the normal limits.
- xxiv. **Bradycardia:** If the heart rate is low than the normal limits.
- xxv. **Pupil constriction:** If the pupils are constricted (miosis).
- xxvi. **Hyperglycemia:** If the blood glucose level is above the normal limits.
- xxvii. **Peripheral hypothermia:** If the extremities are getting cold (with excessive perspiration).
- xxviii. **Convulsions:** If the subject is convulsive and hypertonic.
- xxix. **Coma:** If the subject is in comatose condition.

Normalization of Age, Delay and Oxygen Saturation Level

To identify the severity of envenomation, the patient's age, delay in transportation and blood oxygen level were also accounted. These features were normalized between zero and one.

The relationship between the age and the severity grade was exercised after a study of different cases with a group of medical practitioners on different non-linear models. The prescribed doses of ASV were considered as quantification of severity. The age factor has been observed to be inversely proportional to the severity grade, and the rate of development of symptoms is higher in juveniles, who are at higher risk when all other conditions are the same. The age factor is less significant once the patient crosses childhood. This method yielded a sigmoid relationship and the age can be normalized as below:

$$\text{Normalized age factor} = 1 - \frac{\text{age}}{\text{age} + 5} \quad \dots(1)$$

where age is expressed as years. The number 5 is obtained repeatedly.

The delay in transportation plays a vital role in the development of features prior to the onset of treatment (3). Features develop very rapidly in the initial two hours in Elapidae and scorpion envenomation (7). So, the delay was normalized as follows:

$$\text{Normalized delay} = \frac{\text{delay}}{\text{delay} + 2} \quad \dots(2)$$

where delay is expressed as hours.

Blood oxygen saturation (SpO_2) is very significant for medical management. Reduction in blood oxygen saturation causes tachycardia, seizure, confusion, coma and eventually death in a few cases. So, it was considered inversely proportional to the severity grade and normalized as follows:

$$\text{Normalized } SpO_2 = \frac{100 - SpO_2}{100} \quad \dots(3)$$

where SpO_2 figure is expressed as percentage.

The Feature Vector

The combination between twenty-nine binary and three normalized parameters resulted in a feature vector comprising of thirty-two distinct features. The values of the features ranged between zero and one.

It would be pertinent to mention here that some features were interrelated as well as opposite to each other, e.g. bradycardia and tachycardia. In early hours of Elapidae as well as of Viperidae snakebites, the victim is in a state of shock and anxiety. Soon after the bite, heart beats faster and later the heart may beat slower due to the venom effect or depression.

The Neural Network

It was experienced that the species identification and the severity grading depend on the presence and absence of certain symptoms. The perceptron-type neural network model offers simplicity and proportional significance of the inputs with respect to the output (19). So, a perceptron model was considered with no hidden layer and no sigmoidal non-linearity at the output node. The perceptron type neural network would demonstrate quantitative significance of manifested symptoms for particular species by means of the connecting weights.

The proposed neural network consists of two layers only, one input layer and one output layer. There are thirty-three input nodes, one input for each feature and one bias node, which would have an inbuilt consistent input having value one. The output layer is consisted of six output nodes; one output for each venomous species and the sixth output node for non-venomous category. All the inputs are connected to the outputs by means of weights. It is expected that the node corresponding to the most probable species would yield the highest magnitude and this magnitude would be proportional to the severity grade by the given relationship

$$O_j = \sum W_{ij} * I_i \quad \dots(4)$$

where O_j is the j^{th} output, corresponding to j^{th} species

I_i is the i^{th} input, corresponding to i^{th} symptom

W_{ij} is the weight connecting i^{th} symptom and j^{th} species.

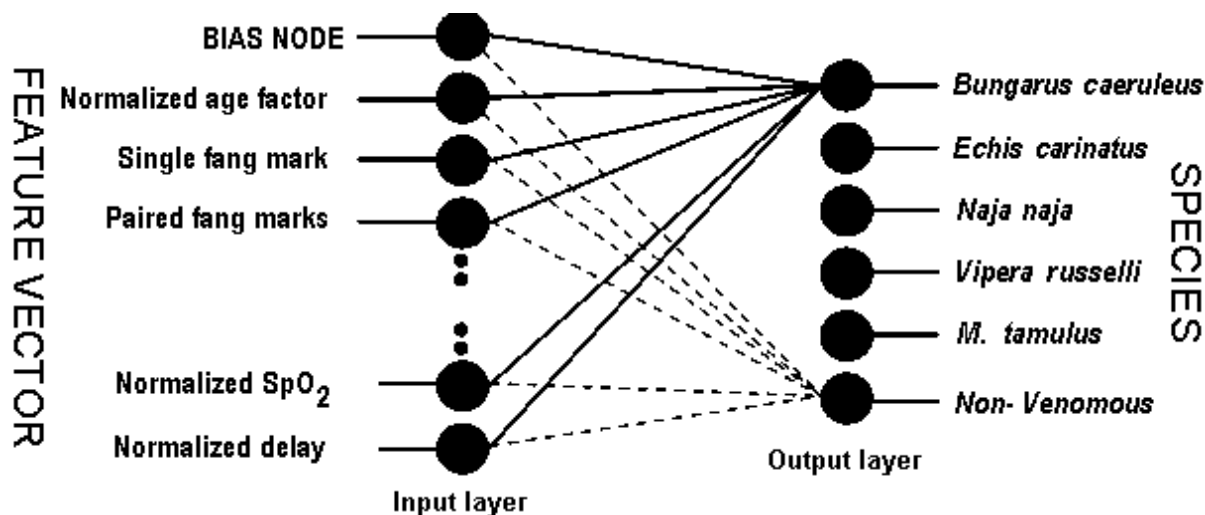


Figure 1: Neural network topology, feature vector as input and species as output.

Forty cases of venom interaction were selected, in which the aggressor species were well identified. Out of these cases, twenty-one were chosen for the training. This group was comprised of all four severity grades of all five venomous species. One case of bite by a non-venomous rat snake (*Ptyas mucosus*) was chosen; the patient was under shock and exhibited some psychosomatic symptoms. The grades were converted into numeral values with mild envenomation as one, moderate envenomation as two, severe envenomation as three, and very severe envenomation as four. Each case with symptoms, species and severity was taken as one training set.

The initial weight matrix was randomized and the symptoms were assigned at the input nodes. The outputs were evaluated at the output layer. The resultant outputs were compared with the desired output and error was fed back to readjust the weights. This process was repeated exhaustively until the error was below a predefined tolerance level, which is known as training of the neural network. Training was repeated for all twenty-one training sets in random order exhaustively until the error in each training cycle confined within a predefined tolerance band.

RESULTS

After a rigorous training and adjustment of weights, the model was tested on nineteen cases in which the species identification and severity grading was available. The neural network results are reproduced in Table 2.

No error was observed in species identification. However, the envenomation grades had minor variations compared with the physician's assessment. Training with more number of cases is expected to improve the accuracy of envenomation grading.

Table 2: Classification results of the perceptron model and the medical opinion.

No.	Classification results of the perceptron model						Medical opinion	
	BC	EC	NN	RV	Scorpion	Non-Venomous	Species	Severity
1.	1.1	0.2	-0.2	-0.1	0.0	0.0	BC	1 (Mild)
2.	2.0	-0.1	0.0	0.1	0.1	0.0	BC	2 (Moderate)
3.	2.9	-0.4	0.7	0.1	-0.3	-0.3	BC	3 (Severe)
4.	4.0	-0.1	0.2	0.0	-0.1	0.0	BC	4 (Very severe)
5.	0.0	1.7	-0.4	0.3	0.4	0.2	EC	2 (Moderate)
6.	0.0	2.7	-0.5	0.3	0.5	0.0	EC	3 (Severe)
7.	-0.2	3.5	0.6	0.4	0.0	0.1	EC	4 (Very severe)
8.	-0.1	-1.3	1.1	0.1	0.2	0.0	NN	1 (Mild)
9.	-0.1	-1.2	2.7	0.3	-0.3	0.3	NN	2 (Moderate)
10.	0.0	-1.1	2.9	0.3	0.1	0.0	NN	3 (Severe)
11.	0.0	-0.8	3.6	0.2	0.5	0.1	NN	4 (Very severe)
12.	-0.1	-2.2	-0.1	1.5	0.5	0.2	RV	1 (Mild)
13.	0.0	-0.7	-0.4	2.1	0.4	0.1	RV	2 (Moderate)
14.	0.0	-1.0	-0.5	3.3	0.8	-0.2	RV	3 (Severe)
15.	0.0	-0.9	-0.3	4.1	0.3	0.1	RV	4 (Very severe)
16.	0.0	-0.6	0.0	0.0	1.1	0.1	Scorpion	1 (Mild)
17.	0.0	-0.6	-0.1	0.0	2.1	0.1	Scorpion	2 (Moderate)
18.	-0.2	-0.5	-0.4	0.0	3.4	0.3	Scorpion	3 (Severe)
19.	0.0	-0.2	0.1	0.0	3.8	0.3	Scorpion	4 (Very severe)

BC: *Bungarus caeruleus*

EC: *Echis carinatus*

NN: *Naja naja*

RV: *Vipera russelli*

Non-Venomous: No venomous species detected

Scorpion: *Mesobuthus tamulus*

DISCUSSION

The species symptomatic identification is usually performed by experts. A large number of symptoms have been found and reported by different research groups. The authors have concentrated on the most usual symptoms.

The proposed method identifies the aggressor species based on the manifested symptoms, which can be very useful in the medical management. There were minor variations in the severity grading provided by the physicians and calculated by the neural network. Generally, the attending medical staff takes into account a number of other physical parameters which have not been considered in the domain of this network, like the general health state and the psychological state of the victim, the first aid method used, etc, which may be responsible for the difference.

The results of the neural network are consistent in the classification. However, there are grading differences regarding "mild", "moderate", "severe" and "very severe". Practically, it is difficult to draw crisp boundaries among different grades of envenomation. Still, with more training on different cases, the error in severity grading may be reduced.

CONCLUSION

The remote identification of venomous species is not a part of medical curricula in India. Therefore, the medical community resorts to a quadrivalent ASV serum as the standard medical practice in case of snakebites. However, this approach poses an economical burden to the family of a poor victim and, at the same time, the attending medical staff is not prepared to cope with rapid developments in symptoms in cases of a few species. If this method is adopted by the medical community, cheaper and specific monovalent ASV will be used as per the WHO guidelines, helping to reduce the treatment costs (25).

The method proposed above is realizable in software, hardware or in a hybrid system. Now, with the popularity of OS-based handheld gadgets, a handy solution using the proposed method can be provided to the medical staff at the grassroots level for species and severity grade identification.

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