

CLINICAL PROFILE AND OUTCOME OF NEUROTOXIC SNAKE ENVENOMATION IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Introduction: There are approximately 3000 species of snakes existing in Earth, of which only 600 species are poisonous. Snake population, venom composition and related human health hazards are variable in geographic areas and seasons.

Aims: To work out predictive factors of requirement of Invasive and Non-Invasive Ventilation in Neurotoxic snake envenomation.

Materials and Methods: The present study was a Prospective, observational and analytical study. This Study was conducted for one year at N.R.S. Medical College and Hospital, Kolkata

Result: In our study, Krait bite was responsible for maximum no. of envenomation in the study population (69%) followed by unknown snake bite (21.5%), whereas cobra bite was least among study population (9.5%) and Maximum no. of patients presented to Health Centre within 6 hours, where they were given initial 10 vials of ASV (69%).

Conclusion: Presence of dysphagia, pain abdomen, ophthalmoplegia, hypotension and others (neck weakness, limb weakness and unconsciousness) were found to be statistically associated with development of respiratory paralysis.

Keywords: Envenomation, hypotension, ophthalmoplegia, dysphagia and snakebite.

INTRODUCTION

There are approximately 3000 species of snakes existing in Earth, of which only 600 species are poisonous¹. Snake population, venom composition and related human health hazards are variable in geographic areas and seasons¹. Ophitoxaemia (snake envenomation) is commonly encountered among human population engaged in farming, fishing, plantation workers and herders. Snake venom can cause local necrosis, anaphylaxis, hemolysis, DIC (disseminated intravascular coagulation), coagulopathy, AKI (acute kidney injury), acute neuromuscular paralysis, rhabdomyolysis, muscle necrosis and consequent deaths. However, mortality and morbidity can be prevented through use of anti- snake venom and supportive care.

There are 300 species of snakes in India, most of which are non-poisonous. Around 52 species are poisonous. The venomous snakes found in India belong to three families Elapidae, Viperidae,

Hydrophidae (sea snakes). In India, approximately 80,000-1,00,000 snake envenomation occurs annually and death varies from 3,000-10,000 annually. Most common snake species in India causing significant envenomation are BIG FOUR (COBRA, COMMON KRAIT, RUSSELL'S VIPER, SAW SCALED VIPER) ². Viper envenomation is associated with hemotoxicity, AKI and local necrosis. Myotoxicity is associated with Sea snakes. Cobra and Krait are associated with acute neuromuscular paralysis. Local features are minimal or absent in Krait bite whereas, Cobra bite is associated with local swelling with severe local pain which in extreme cases can lead to necrosis³. Cobra venom produces neurotoxicity through blockade of post-synaptic acetylcholine (ACh) receptors whereas Krait venom causes damage of pre-synaptic ACh vesicles. Neurotoxic envenomation presents with ptosis, external ophthalmoplegia, bulbar palsy, facial palsy, diaphragm palsy and respiratory paralysis ⁴. Since there are possibilities of changing species, intra species variation and venom compositions in snakes, there may be a theoretical possibility of changing spectrum of manifestation and outcome. Predictive factors for requirement of ventilation would be worthwhile in making decision of transfer of cases to Tertiary care center from rural health centers. Hence the study is undertaken to document clinical profile and outcome of neurotoxic snake envenomation and work out predictive factors of requirement of ventilator support in patients with respiratory paralysis.

MATERIALS AND METHODS

Study site: N.R.S. Medical College and Hospital, Kolkata.

Study population: All patients getting admitted in IPD with neurotoxic snake bite.

Study design: A Prospective, observational and analytical study.

Period of study: One year (1st April 2021-31st March 2022).

Selection Criteria

Inclusion Criteria –

- Age >12 but <70.
- Neurotoxic Features- Ptosis, Dysphagia, Ophthalmoplegia, Pain Abdomen, Respiratory paralysis, Head drop (neck weakness), Limbweakness.

Exclusion Criteria –

- Similar presentation without definite history of snake bite.
- Age <12 and >70.
- Pre-existing neurological and respiratory disorder.
- Co-morbidity -Hypertension, Diabetes mellitus, chronic liver disease, chronic kidney disease, Tuberculosis, Asthma, chronic obstructive lung disease, HIV, Cardiac disease.

RESULT AND DISCUSSION

The present study was a Prospective, observational and analytical study. This Study was conducted for one year at N.R.S. Medical College and Hospital, Kolkata.

Demographic profile:

This study revealed that most common age group admitted with neurotoxic snake envenomation was middle aged population (26-50 years) [56%] with Males preponderance [56%]. Studies done by Ahmed SM et al. (2012)⁵, showed similar results, with most common age group being (20-40 years) [52.5%] and male preponderance [69.4%].

The usual explanation for such fact as revealed in this study is that the working population in India including West Bengal is middle aged population with male preponderance who are exposed to snake bites, during their outdoor activities. Sex ratio in West Bengal is 950, hence it might be the reason for male preponderance. Middle aged population is also predominant in West Bengal. Krait bites which were maximum in the study occurred within the household premises, therefore female involvement was more in the study (44%). The difference in results worked out in studies⁶ was probably due to the involvement of different age group including younger and older population in different parts of India outside the West Bengal as per changing social and socioeconomic infrastructure.

Neurotoxic snake envenomation was common among farmers and labourers (39.7%). Similar scenario was seen in study conducted by Jarwani B et al. (2013)⁷. People involved in agricultural activities. House wives and students comprised a large chunk of victims (55.1%).

The involvement of Housewives and students were more in the study because of nocturnal biting pattern of Krait within the household premises. In study conducted by Anjum et al. (2012)⁸ students (10.7%) and housewives (26.6%) were involved.

Snake bite-event profile:

Krait was involved in maximum no. of envenomation (69%), followed by Cobra (9.5%). Similar results were found in studies by Jarwani B et al. (1998)⁷.

Most snake bites occurred during rainy season from June-September. similar observation was seen in studies by Harsoor SS et al. (2006)⁹. Rain floods the habitat of snakes causing them to come to ground surface and take refuge in dry houses. Krait and Cobras become less active during other seasons. They are more active during rainy season and breeds during this season.

Most bites occurred in the upper limbs (46.6%). Previous studies stated most bites occurred in the lower limbs. The logical explanation to this finding is most Krait bites occurred within household premises, during sleeping in floor, where entire body surface is contact with the floor, hence upper limb involvement increases.

Higher incidence of Krait bite in May and June corresponds to the growing population of Krait in West Bengal during this time. Although Cobras grow in similar pace during this period, they remain in their natural habitat- fields and jungles. Hence the chance of human contact is less. Incidence of Cobra bite rises to maximum in July, the time of heavy rainfall in West Bengal. Rain water fills the holes and crevices and drives them out from their natural habitats. Thus, chances of contact with Cobras increase during mid-monsoon. There is substantial delay in

reaching hospital and getting treated with 1st dose of ASV in the study. Only 25% of patients of the patients received ASV before 3 hours. Mean bite to ASV time in the study is 4.6 hours. Several factors can be implicated for this delay:¹⁰

1. Long distance between spot to nearest hospital.
2. Lack of facility of transport in rural areas.
3. Dependence of rural people on practitioners of occult science and witchcraft.
4. Lack of public awareness regarding snake bites and its treatment.
5. Social, economic and cultural barrier.
6. Status of road ways and transport system is still poor in this state.

These factors support unusual delay of initiating delay in our study as well as in the studies from other states with similar health care infrastructure.

Clinical profile on admission:

Clinical manifestations of neurotoxic envenomation are outcome of complex interplay between snake venom and the detoxification system of host.

In this study profile of clinical presentation of Neurotoxic snake envenomation according to incidence were Ptosis (100%), Dysphagia (95.7%), Ophthalmoplegia (84.5%), Pain abdomen (67.2%), Respiratory paralysis (44%), others including neck, limb weakness and unconsciousness (44%), hypotension (28.4%), local features (11.2%) and hemotoxic features (0.9%).

Ptosis is the most common symptom reported followed by dysphagia and ophthalmoplegia. Other studies showing more or less similar results are-Local features were minimal in this study because maximum no. of patients presented with Krait bites. Krait doesn't cause local inflammation and hence local features are minimal or nil. Many patients do not realize that they have been bitten by snakes unless neurological symptoms appear. Local features are characteristics of Cobra bites, which cause local swelling and severe local pain which can lead to necrosis. Similar observation was seen in the studies done by Bhalla A et al. (2014)¹¹.

Hypotension was seen in 28.4% of patients, which is higher as compared to other studies, because of increased frequency of respiratory paralysis in the study.

The variation from other studies may be due to - delay to administer ASV, variation in snake species and venom composition, pre-dominant Krait or Cobra bites in other studies, and possibility of ASV reaction (hypotension and ARDS). Another cause may be, because no comparable studies in this regional population are available.

Laboratory parameters on admission:

Mean WBC count in the study population is 11117cells/mm³. Hence, leukocytosis is present. This is seen in other studies conducted by Suchithra N et al. (2008)¹²Leukocytosis is due to inflammation (local as well as systemic) associated with snake bite.

Mean Spo₂ is 89% in the study population, which is low as compared to normal value (94-100). This is due to presence of respiratory paralysis in 52.6% of patients.

Parameters observed during treatment:

In some patients who presented with serious condition such as impending/developed respiratory failure, unconsciousness was administered more than 20 vials, because of fear and apprehension. Hence mean is more than 20 vials. ASV reactions were noted in 3.4%(4 patients) of study population. No ASV skin test was done.

Complications developed during treatment were:

1. Cellulitis in 4.3% patients. 2. Respiratory paralysis in 5.2% patients
2. Respiratory paralysis in 5.2% patients.

1. Cellulitis was seen in Cobra bite patients, who presented with local swelling, pain as symptoms. Other reason for developing cellulitis is tying tourniquet above the bite site. Local features occur in Cobra and Russell's viper bite and can be late by 24-72 hours.

2. Respiratory paralysis developed in 5.2% patients who didn't presented with respiratory paralysis and were received full dose of ASV. Delayed neuro-paralysis in neurotoxic envenomation is very unusual. Neurotoxic venom is rapidly absorbed through blood circulation and attaches to the pre-synaptic or post-synaptic receptors.

Outcome:

Group A-Those patients who didn't developed respiratory paralysis. Group B-Those patients who developed respiratory paralysis.

In this study bite to ASV time, Site of bite, Total ASV dose, Dysphagia, Pain abdomen, Ophthalmoplegia, others including neck weakness, limb weakness, unconsciousness, hypotension, WBC, Spo2, Con. Bil. On presentation were found to be statistically significant and were associated with poor outcome (respiratory paralysis).

1. Group B patients (mean=21.475 vials) received higher dose of ASV than Group A (20 vials), which is statistically significant. This suggests that use of higher than recommended dose of ASV in patients with neurotoxic envenomation does not improve outcome. This result confirms the recommendation of WHO/SEARO (2016) guidelines and National standard treatment guideline of Snake bite treatment (2016) that maximum dose required for treatment of neurotoxic snake envenomation is 20 vials.

2. Upper limb bite (51.9%) has poor outcome (respiratory paralysis) than lower limb bite (42.9%). This may be due to increased vascularity of upper limbs as compared to lower limbs and also due to increased mobility of upper limbs. This finding is opposite of other studies mentioned above.

3. Mean Bite to ASV time is more in Group B patients (5.7 hours) as compared to Group A (3.6 hours). This may be the single and dominant predictor of respiratory paralysis in neurotoxic envenomation. Though 69% of patients presented within 6 hours, yet 52.6% of patients developed respiratory paralysis. This suggests that neuro-paralysis develops earlier in Krait and Cobra bites. In this study, those patients who received loading dose of ASV within 3 hours, their outcome was better than those received ASV after 3 hours.

4. Predictor of respiratory paralysis based on clinical feature at admission- In this study the clinical features which were statistically significant were found to be more common in Group B patients (dysphagia, ophthalmoplegia, pain abdomen, others including neck, limb weakness and unconsciousness and hypotension). This type of study, highlighting the above parameter has not been reported in West Bengal in last 10 years. Hence the results are not comparable. This study is unique in that sense and picked up few clinical predictors of acute respiratory failure from neurotoxic snake envenomation. Further, studies with larger population are required to test the validity of this result.

5. Based on laboratory profile:

- Mean WBC count in Group B (11980cells/mm³) patients is more than Group A (10160cells/mm³) patients. The increase in WBC count is due to polymorphonuclear leukocytosis.

- Mean SpO₂ level in Group B patients is low as compared to Group A patients, whereas mean Con. Bil. concentration in Group B is more than Group A patients. No studies have been conducted in West Bengal, highlighting this finding. Logical explanation to this finding is due to development of respiratory paralysis, which cause hypoxia and decreases SpO₂. Hepatotoxicity of snake neurotoxins has not been reported yet.

6. Positive Neostigmine challenge test is a good predictor of efficacy of neostigmine in a given case. Post-synaptic neurotoxicity is easily reversed by neostigmine therapy. In the present study percentage of Cobra bites and Russell's viper bite (post-synaptic neurotoxin) are very less (9.5%). Outcome has been predominantly influenced by Krait bungarotoxin (pre- synaptic neurotoxin).

7. Type of snake is not significantly associated with development of poor outcome. It has been documented that ASV can prevent further deterioration and poor outcome. There is a suggestion that neurotoxicity can improve (although minimal) by ASV therapy. Efficacy of ASV is time dependent. However, in the study mean bite to ASV time is 4.6 hours which is far beyond than preventive action of ASV. Post-synaptic neurotoxicity can be treated by neostigmine therapy and thus poor outcome can be prevented. In our study Cobra bitten population was comparatively lesser than Krait bitten subjects. Hence this result may be applicable to situation when both patient groups are equal and statistically comparable in terms of number and Bite to ASV time.

Studies on predictive factors of acute respiratory failure in neurotoxic envenomation are very few in last 10 years. This study is unique original study in this local population in that sense. Although study population is small and statistical significance is not strong enough, this study identified some of the pre- selected parameters of research interest. Further study with large study population is required to work out validity of this result.

CONCLUSION

This prospective observational analytical study on neurotoxic snake envenomation revealed the following results-

Snake bite Parameters- Bite to ASV time (>3 hours), site of bite (upper limb) were found to be statistically associated with development of respiratory paralysis.

Clinical parameters on Admission- Presence of dysphagia, pain abdomen, ophthalmoplegia, hypotension and others (neck weakness, limb weakness and unconsciousness) were found to be statistically associated with development of respiratory paralysis.

Laboratory parameters on Admission-

- Mean WBC count was statistically significantly higher in poor outcome group as compared to good outcome group.
- Mean SpO₂ level was statistically significantly lower in poor outcome group as compared to good outcome group.
- Mean Con.Bil. concentration was statistically significantly higher in poor outcome group as compared to good outcome group.

Hence, WBC count, SpO₂ level and Con.Bil. are statistically associated with outcome.

Neostigmine challenge test was found not to be statistically associated with outcome.

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Table no: Distribution of study population according to type of snake(n=116).

Type of snake	Frequency (n=116)	Percentage (%)
Cobra	11	9.5
Krait	80	69.0
Unknown	25	21.5
Total	116	100.0

Table: Distribution of study population according to clinical features at presentation (n=116).

Clinical feature	No. Of (n=116)	Percentage (%)
Local features	13	11.2%
Hemotoxic features	1	0.9%
Ptosis	116	100%
Dysphagia	111	95.7%
Pain abdomen	78	67.2%
Ophthalmoplegia	98	84.5%
Respiratory paralysis	51	44%
Neck, limb weakness and Unconsciousness	51	44%
Hypotension	33	28.4%

Type of snake	Outcome		Total(n=116)	p value	d f
	A(n=55)	B(n=61)			

1.	Cobra		6	5	11	0.215	2
			54.5%	45.5%	100%		
2.	Krait		41	39	80		
			51.25%	48.75%	100%		
3.	Unknown		8	17	25		
			32%	68%	100%		