Contents lists available at ScienceDirect

Toxicology Reports

journal homepage: www.elsevier.com/locate/toxrep

Incidence and treatment of snakebites in West Bengal, India

Kaushik Mana^a, Rituparna Ghosh^b, Kripasindhu Gantait^a, Kanchan Saha^a, Poulami Parua^a, Upasana Chatterjee^a, Sumana Sarkhel^{a,*}

^a Department of Human Physiology with Community Health, Vidyasagar University, Paschim Medinipur, 721102, West Bengal, India
^b Department of Medicine, Midnapur Medical College, Paschim Medinipur, 721102, West Bengal, India

ARTICLE INFO	ABSTRACT		
<i>Keywords:</i> Snake envenomation Russell's viper	<i>Objective:</i> Snake envenomation is a major cause of death and disability in the developing countries. In India and neighboring countries, the four venomous snakes of concern include – Indian cobra(<i>Naja naja</i>), Common Krait (<i>Bungarus caeruleus</i>); Russell's Viper (<i>Daboia russelli</i>); Saw Scaled Viper (<i>Echis carinatus</i>). We describe the management protocol for snakebite treatment in a tertiary care hospital of <i>Paschim Medinipur</i> district, West Bengal based on case reports of subjects admitted and treated in Ghatal Subdivisional Hospital(GSH) during 2013–2016. <i>Methods &materials:</i> We developed a structured data collection form to record demographic and clinical details of patients hospitalized at GSH between 1 January 2013 through 31 December 2016. <i>Results:</i> Snake bite cases in Ghatal Subdivisional hospital(GSH) were assessed during the period 2013–2016. A total 18 deaths due to snakebite has been reported from this tertiary care hospital during the period. Total patients admitted in this hospital with snakebite is 1160 during the period 2013–2016. In 80% of the cases the lower extremities were affected. Preliminary first aid was provided in 45% cases. About 65% of the affected victims suffered snakebite in the morning hours. Some of the recommended drugs that were prescribed by the physicians of GSH were neostigmine, atropine, adrenaline, hydrocortisone, Amoxicillin. WBCT ₂₀ and Urea, Creatinine level were routinely performed. <i>Conclusion:</i> Hospital studies are a key source of information about snake bites. The ready availability and appropriate use of AVS, close monitoring of patients, the institution of ventilator support and if required, early referral to a larger hospital all help to reduce the mortality. Thus knowledge of the varied clinical manifestations of snake bite is important for effective management in hospitals by a complete health care team.		

1. Introduction

Snake bite which is an important cause of death in rural patients in developing countries, is a neglected public health problem [1]. The fear of snakes is an old, deeply entrenched form of prejudice, born of ignorance and perpetuated through superstition and myth. The presence of some species generates this fear. Morbidity and mortality resulting from snakebite envenomation also depends on the species of snakes involved, since the estimated "fatal dose" of venoms varies with species. In India, 216 species of snakes are found of which 52 species are venomous. World Health Organization (WHO 1963) reports 10,000 annual deaths in tropical countries. In India, the number of snake-bite fatalities has long been controversial. Estimates as low as 61,507 bites and 1124 deaths in 2006 and 76,948 bites and 1359 deaths in 2007 and

as high as 50,000 deaths each year have been published [2]. Most of snakebite statistics are based on hospital records and the majority of snakebites occur in the remote, inaccessible rural areas where they remain unreported. The polyvalent antivenom (Haffkine® India) was available at the study hospital throughout the study period. Serum obtained from the plasma contains purified, enzyme-refined and concentrated specific heterologous immunoglobulins. Most rural hospitals lack the intensive care facilities required for care of patients with multiorgan dysfunction. Also, inappropriate use of antivenom in rural hospitals is common [3]. Earlier a study was conducted in Midnapore Medical College and Hospital which reported the case- fatality rate of snakebite for the hospital during the period 2012–2016 [4]. We describe the management practices of snakebite in Ghatal Subdivisional Hospital(GSH) of *Paschim Midnapore* district along with trends of

* Corresponding author.

https://doi.org/10.1016/j.toxrep.2019.02.008

Received 31 October 2018; Received in revised form 20 February 2019; Accepted 24 February 2019 Available online 01 March 2019 2214-7500/ © 2019 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/BY-NC-ND/4.0/).





Abbreviations: AVS, Antisnake venom; MSVP, Medical superintendent cum Vice Principal

E-mail addresses: koushik.lifescience@gmail.com (K. Mana), rituparnaghosh0491@gmail.com (R. Ghosh), gkripasindhu@yahoo.in (K. Gantait), kanchansaha31@gmail.com (K. Saha), poulamiparua1993@gmail.com (P. Parua), upasana.chatterjee85@gmail.com (U. Chatterjee), sumana.sarkhel@yahoo.in (S. Sarkhel).





Fig. 1. The study area under Paschim Midnapore district.

medications(including antibiotics) and other management strategies used for snakebite treatment.

2. Methods & materials

A **retrospective study** was conducted in the medicine ward of Ghatal Subdivional hospital(GSH) (Fig. 1) during the period 1 January 2013 through 31 December 2016. A prior consent was obtained from Chief Medical Officer of Health(CMOH) of Paschim Midnapore district and Superintendent of Ghatal Subdivional Hospital(GSH) for assessing the record room of the hospital. We developed a structured data collection form to record demographic and clinical details of patients hospitalized at GSH between 2013 and 2016. Clinical data about age, sex, clinical manifestations, complications and outcome were obtained from case records and were analyzed. All cases of suspected snake bite admitted to the medicine wards of the hospital between January 2013 and December 2016 were on the basis of the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes for

Table 1

Summary of species-specific severity of Indian snake envenomation based on clinico-laboratory profile. Source: Kumar et al. [7]

Snake species	Clinico-laboratory severity grading(Grade I-IV/mild-severe)parameters
Cobra (Naja naja) Krait(Bungurus caeruleus) Saw Scaled viper(Echis carinatus) Russell's viper(Daboia russelli)	Local symptoms/ signs of inflammation, papillary response, ophthalmic signs, cardiorespiratory and neurological manifestations Pupillary response, hypokaelemia, abdominal colic, cardio-respiratory and neurological manifestations. Local symptoms/signs of inflammation, laboratory and clinical evidence of coagulopathy, renal failure and cardiorespiratory manifestations. Local symptoms/signs of inflammation, laboratory and clinical evidence of coagulopathy, blisters and necrosis, renal failure and cardio- respiratory manifestations.

venomous snakes.

Anti-venom dosing recommendations were based on the quantity of particular venom (in mg, dry weight) that can be neutralized by each milliliter (ml) of antivenom. In India, each milliliter of polyvalent antivenom is supposed to neutralize 0.6 mg of Indian cobra venom, 0.6 mg of Russel viper venom, 0.45 mg of common krait venom, 0.45 mg of saw scaled viper venom. Skin testing is done prior to AVS administration [5]. According to the severity of symptoms 50–150 ml of ASV was diluted with 200 ml of normal saline and administered as a bolus dose. Blood clotting time was the only laboratory test available to confirm systemic envenomation [6].

Clinical symptoms of snakebite were assessed with (Table 1).We have used the following variables- bite-to-hospital time (time taken by the patient to be brought to the hospital after the bite), home-to-hospital distance (distance from the patient's home to hospital, recorded in km and derived by measuring the radial distance of the patients' residence from the hospital),diurnal variation (day or night), the site of snake bite, use of tourniquet, local swelling, symptoms (vomiting and neurotoxicity) and WBCT₂₀. Neurotoxicity was defined as documented ptosis, external ophthalmoplegia, weakness of neck or bulbar muscles, use of neostigmine or ventilator support. The trends of medications prescribed for treatment of snakebite along with the contraindications of antivenom were also recorded.

3. Results

Ghatal Subdivision Hospital treated 1160 patients(after excluding dry bites) with snakebites with 18 (7 male and 11 females) deaths during the study period. The female to male ratio of the admitted cases was 1.07:1. The case-fatality rate(CFR) of this hospital for the given period was 1.5. 82% of the envenomation were haemotoxic bites. About 65% cases were detected in the interval between 7.30 a.m. to 11:30 am. The snakebite cases registered in the hospital were reported by the villagers and the type of snakebite was identified by the fang marks(poisonous). Generally, the presence of two puncture wounds indicates a bite by a poisonous snake. In the case of a non-venomous snakebite, small puncture wounds are seen arranged in an arc. The snake bite related deaths in the study occurred due to kidney failure(8 patients), coagulopathy leading to fatal haemorrahage(7 patients), respiratory failure(3 patients). The median bite to hospital time was 30 mins(IQR: 26.5-37.5)(55% cases) and bite to AVS injection time was 125 min(IQR:110-128) (45% cases). The median bleeding time for haemotoxic bites was 12 (IOR:8.5-17.5)(40% cases) and the mean clotting time was found to be 19 min(IOR:15.5-22.5) (40%). The symptoms of envenomation included local signs of inflammation, blisters and necrosis, renal failure, coagulopathies, ptosis, dysphagia and respiratory distress (Fig. 2). Concomitant medications prescribed by the physicians of GSH were Paracetamol (fever), Diclofenac (inflammation), Tramadol (Pain reliever), Metoclopramide (nausea), Ondansetron (nausea and vomiting), Cetrizine (relieve allergy), Deriphylline (chest tightness and shortness of breath), Ranitidine (ulcers and stomach acid), Omeprazole (gastrointestinal bleeding), Pantoprazole (swallowing difficulty), Rabeprazole (stomach problems), Glycerine Magnesium sulphate(oedema dressing) (Table 2). Assessment of haemotoxic bites involved the 20 min whole blood clotting time (WBCT₂₀). Patients

with blood that failed to clot received 10 vials of polyvalent antivenom with repeat WBCT₂₀ in 6 h. Patients with blood that again failed to clot received another 10 vials of AVS. This cycle continued until the patient had clotted blood on two consecutive WBCT₂₀ tests. Neurotoxic bites received 10 vials of polyvalent AVS. The symptoms associated after AVS administration were early anaphylactic reactions **(11% cases)** and pyrogenic reactions **(25% cases)**. A preparation of trypsin-chymostrysin were given in **10% cases** to overcome the inflammation after envenomation. The median duration of stay of patients in the hospital was 12 days(IQR:6.0–15.0).

4. Discussion

Snake bite is an important occupational and rural hazard because India. Accurate statistics of the incidence of snakebite and its morbidity and mortality throughout the world does not exist; however, it is certain to be higher than what is reported. Poor outcome of antivenom treatment is associated with delayed initiation of treatment, associated complications rather than total dose of AVS. According to an epidemiological survey among 19,000 individuals living in 26 villages in Burdwan district (West Bengal), there was an annual incidence of snakebite of 0.16% and a mortality rate of 0.016% per year [8]. Clinico - toxicologically, nature of snake envenomation is categorized into hemotoxic, neurotoxic, and myotoxic syndromes. According to WHO guidelines, recommended first-aid methods for snakebite are reassurance, immobilisation of the bitten limb and movement of the patient to a place where they can receive medical care as soon as possible. Pressure immobilisation technique (PIT) which is recommended by WHO was used in one of the patients in our study [9].

AVS can be administered either by slow intravenous injection at a rate of 2 ml/min or by intravenous infusion (antivenom diluted in 5–10 ml per kilogram body weight of normal saline). Sharma et al. [10] found that the average dose of antivenom was 51.2 vials (512 cc) for elapid bites and 31 vials (310 cc) for viper bites. Punde et al. [11] found that dose of AVS required in treating neurotoxic envenomation was 10–320 ml and for viper bites it was 20–250 ml. In our study, 15% cases received more than 20 vials for viper bites. In the present study (10 + 10) vials of AVS was given in viper bites and 10 vials for neurotoxic bites.

Antivenom should be ideally administered within 4 h of the bite, but is effective even if given within 24 h. The dosage required varies with the degree of envenomation. In the present study, the median bite to hospital time was 30 mins(IQR: 26.5–37.5)(55% cases) and bite to AVS injection time was 125 min(IQR:110-128) (45% cases).Snake venom contains various procoagulant factors which cause activation of coagulation cascade leading to intravascular coagulation and consumption of various clotting factors and platelets. Thus, thrombocytopenia and hemostatic abnormalities which ultimately result will cause spontaneous bleeding. The presence of spontaneous bleeding is indicative of presence of unneutralized snake venom present in circulation.

In the present study, the symptoms associated after AVS administration were early anaphylactic reactions (11% cases) and pyrogenic reactions (25% cases).Early anaphylactic reactions occurs within 10–180 min of start of therapy and is characterized by itching, urticaria,



Fig. 2. (A)Types of envenomation of patients admitted in Ghatal Subdivisional Hospital with Symptoms of (B) Haemotoxic and (C)Neurotoxic bite.

dry cough, nausea and vomiting, abdominal colic, diarrhea, tachycardia, and fever. Some patients may develop severe life-threatening anaphylaxis characterized by hypotension, bronchospasm, and angioedema. Pyrogenic reactions usually develop 1–2 h after treatment. Pyrogenic reactions to antivenom are caused by pyrogen contamination during manufacture and may include chills, rigors, fever, myalgia, headache, tachycardia and hypotension secondary to vasodilation [12].

We also found that prolonged bite to hospital time i.e., delayed arrival to hospital was associated with mortality. Most of the studies have observed this correlation between bite to hospital time and complications or mortality. Most of the studies have observed this correlation between bite to hospital time and complications or mortality [13]. This can be explained by the fact that incidence of complications is directly proportional to the duration of venom in the blood prior to its neutralization by AVS due to late arrival of patient at hospital [14] and as complications occur mortality will increase. This delay can be attributed to lack of awareness of hazards of snake bite, belief in traditional methods of treatment, lack of proper referral systems and transport facilities [15]. The mean duration of stay of patients is The median duration of stay of patients in the hospital was 12 days (IQR.:6.0–15.0). Ophthalmoplegia was seen in 10 patients of Neuroparalytic bite. Rapid death from krait bite most often comes as a result of the alpha-toxin and diaphragmatic paralysis and airway obstruction could be delayed by early AChEI therapy. Anticholinergic agent such as atropine would potentially be administered with neostigmine to blunt untoward muscarinic effects of an AchEI [16,17]. Omogbai et al. [18] studied 433 patients of snake bite with a mean duration of stay in hospital of 5.7 \pm 5.1 days. (Range 1–23 days) as compared to our study.

5. Conclusion

Snakebite morbidity is common in Paschim Midnapore. Majority of snakebite in the study area were inflicted by Russell's viper. Coagulation profile should be tested 6 hourly (especially for viper bites). A useful test for venom-induced defibrinogenation is the 20minute whole blood clotting time. The anti-venom available in the Ghatal Subdivisional Hospital is a polyvalent equine antiserum. The

Table 2

		• · · ·		
Funne of Snakobitor	cumptome and druge	used in its treatment in	Chotal Subdivicional	Uccrital of Daschim Midnaporo
I VDES UI SHAKEDHES.	symptoms and drugs	i useu ili ils ueaunent il	i Gilalai Subulvisiolla	

Type of snake species	Total number of affected individuals $(n = 1160)$	Symptoms	Prescribed drugs
Daboia russelii	951 (82%)	Inflammation, Coagulopathies, Blisters and necrosis, Renal failure, fatal haemorrhage, black urine	Paracetamol Diclofenac, Glycerine Magnesium sulphate, Chlorpheniramine maleate ; Amoxicillin
Naja kaouthia	128 (11%)	Local inflammation, Ptosis, Dysphagia, Respiratory distress, chest tightness, External ophthalmoplegia	Neostigmine, Atropine, Deriphylline, Tramadol
Bungarus caeruleus	23 (2%)	Ptosis, Respiratory distress, Chest tightness, Abdominal pain	Neostigmine, Atropine, Tramadol, Deriphylline

emphasis should be on early and adequate medical management for snakebite.

Conflict of interest

None.

Acknowledgements

Authors are grateful to Dr Kripasindhu Gantait; Associate Professor, Department of Medicine, Midnapur Medical College for his support for obtaining hospital data. Authors are indebted to Department of Science and Technology Govt of West Bengal (Ref:607(Sanc)/ST/P/S&T/5G-3/ 2016 dated 17/10/2016) for the financial support.

References

- C.J. Murray, A.D. Lopez, D.T. Jamison, Global Burden of Disease and Injury Series, Harvard School of Public Health, Cambridge, MA, 1996 Global health statistics.
- [2] State/UT Wise Cases and Deaths Due to Snake Bite in India, Government of India, Central Bureau of Health Intelligence. Health Status Indicators, National Health Profile, 2007, pp. 107–108 and 2008 (Provisional).
- [3] D.A. Warrell, Injuries, envenoming, poisoning and allergicreactions caused by animals, in: D.A. Warrell, T.M. Cox, J.D. Firth (Eds.), Oxford Text Book of Medicine, 4th edn, Oxford University Press, Oxford, 2003, pp. 923–947.
- [4] R. Ghosh, K. Mana, K. Gantait, S. Sarkhel, A retrospective study of clinico-epidemiological profile of snakebite related deaths at a tertiary care hospital in midnapore, West Bengal, India, Toxicol. Rep. 5 (2018) 1–5.
- [5] H.S. Bawaskar, P.H. Bawaskar, Profile of snake envenoming in western Maharashtra

India, Trans. R. Soc. Trop. Med. Hyg. 96 (1) (2002) 79-84.

- [6] J. Tiballs, Diagnosis and treatment of confirmed and suspected snake bite, Med. J. Aust. 156 (1992) 270–274.
- [7] V. Kumar, R. Maheshwari, H.K. Verma, Toxicity and symptomatic identification of species involved in snakebites in the Indian subcontinent, J. Venom. Anim. Toxins incl. Trop. Dis. 12 (2006) 3–18.
- [8] A.K. Hati, M. Mandal, M.K. De, H. Mukherjee, R.N. Hati, Epidemiology of snake bite in the district of Burdwan, West Bengal, J. Indian Med. Assoc. 90 (1992) 145–147.
- [9] D.A. Warrell, Injuries, envenoming, poisoning and allergic reactions caused by animals, in: D.A. Warrell, T.M. Cox, J.D. Firth (Eds.), Oxford Text Book of Medicine, 4th ed., Oxford University Press, Oxford, 2003, pp. 923–947.
- [10] N. Sharma, S. Chauhan, S. Faruqi, P. Bhat, S. Varma, Snake envenomation in a north Indian hospital, Emerg. Med. J. 22 (2005) 118–120 (PMC free article PubMed.).
- [11] D.P. Punde, Management of snake-bite in rural Maharashtra: a 10-year experience, Natl. Med. J. India 18 (2005) 71–75 (PubMed).
- [12] G. León, M. Herrera, Á Segura, M. Villalta, M. Vargas, J.M. Gutiérrez, Pathogenic mechanisms underlying adverse reactions induced by intravenous administration of snake antivenoms, Toxicon 15 (2013) 63–76.
- [13] S. Kalantri, A. Singh, R. Joshi, S. Malamba, C. Ho, J. Ezoua, et al., Clinical predictors of in-hospital mortality in patients with snakebite: a retrospective study from a rural hospital in central India, Trop. Med. Int. Health 11 (2006) 22–30.
- [14] K. Narvencar, Correlation between timing of ASV administration and complications in snake bites, J. Assoc. Phys. India 54 (2006) 717–719.
- [15] B.B. Gaitonde, S. Bhattacharya, An epidemiological survey of snake-bite cases in India, Snake. 12 (1980) 129–133.
- [16] S. Rajpal, G. Mittal, R. Sachdeva, Development of atropine sulphate nasal drops and its pharmacokinetic and safety evaluation in healthy human volunteers, Environ. Toxicol. Pharmacol. 27 (2) (2009) 206–211.
- [17] A. Anil, S. Singh, A. Bhalla, N. Sharma, R. Agarwal, I.D. Simpson, Role of neostigmine and polyvalent antivenom in Indian common krait (bungarus caeruleus) bite, J. Infect. Public Health 3 (2) (2010) 83–87.
- [18] E.K. Omogbai, A.M. Zuleikha, M.A. Imhafidon, A.A. Ikpeme, D. Ojo, C.N. Nwako, et al., Snake bites in Nigeria: a study of the prevalence and treatment in Benin City, Trop. J. Pharm. Res. 1 (2002) 39–44.