RESEARCH REPORT

Outcome determinants of snakebites in North Bihar, India: a prospective hospital based study

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ABSTRACT

Bihar is the state with the third largest number of snakebite deaths per year in India. This prospective, one-year study of 608 snakebites provides the first data from Bihar on determinants of unfavourable outcomes in snakebites. Any delay in reaching hospital raised the risk of a snakebite patient for an unfavourable outcome [OR 8.88, CI 2.04-38.8]. Attending a traditional practitioner prior to presenting to the hospital was the only specific, significant delay [OR 3.52, CI 1.26-9.7]. Prevention of unfavourable outcomes occurred by presenting to hospital in less than 1.5 hours [OR 0.23, CI 0.052-1.0]. Motorbike was the best mode of transport [OR 0.37, CI 0.12-1.1]. Other risk factors were patients aged under 15 years [OR 3.79, CI 1.57–9.12] and bites to the upper limb [OR 2.47, CI 1.01-6.04]. Patients who were envenomated had a higher risk of unfavourable outcome, if referred due to antivenom being unavailable [OR 12.2, CI 1.49-100]. To save lives, it is imperative that measures to reduce delays in getting patients to hospital must be included in snakebite management, alongside continued availability of antivenom and assisted ventilation.

KEY WORDS: Snakebite, unfavourable outcomes, risk factors, delays, traditional practitioners, motorbikes

INTRODUCTION

In Bihar, 4500 deaths are attributed to snakebite each year. Thus, it is the state of India with the third largest number of snakebite deaths after Uttar Pradesh and Andhra Pradesh (David et al, 2012). However, there is little documented evidence regarding the situation of snakebites within the state of Bihar.

Duncan Hospital in East Champaran District of Bihar sees around 500 snakebites per year. Being at the Indo-Nepal border, patients from North Bihar as well as the plains of South Nepal, present to the hospital with snakebites. A retrospective chart audit was carried out of the 367 people who presented to Duncan Hospital, Raxaul, in 2011 with snakebites, bites by unknown agent (but suspected to be a snakebite), and signs of envenomation with no known bite. The highest number of cases was in 11–15 year olds, with neurotoxic envenomation occurring in 13.3%. No coagulopathies were seen. Of those with neurotoxic symptoms, 51% also had local bite site tissue damage or inflammation consistent with a cobra bite (Unpublished data). The venomous snakes in the region were believed to be cobras and kraits.

The closest snakebite research, geographically, is from the Chitwan district, Nepal and (Pandey, 2007) and the Eastern Terai (plains) of Nepal (Sharma et al, 2004a). They have both reported predominantly neurotoxic envenomation due to cobras and kraits. The community study by Sharma et al (2004b) showed 80% of the deaths were occurring prior to reaching hospital. Attending a traditional practitioner prior to hospitalisation was a significant risk factor for mortality and travelling to the hospital on a motorbike, decreased the risk of dying. (Sharma et al, 2004a or 2004b). Due to the similar geography and socioeconomic status to the area the Duncan Hospital services, this data has provided the most useful comparative data.

The envenomation rate in the community study on the Eastern Terai of Nepal showed an envenomation rate of 52% (Sharma et al, 2004a). Duncan Hospital admissions had an envenomation rate of 13.3% in the unpublished, 2011 audit. This marked difference required further investigation. The hypothesis was that there are either many non-venomous snakebites, and/or, many people are dying prior to reaching health facilities. A prospective hospital based study is reported here and a community based study is planned for the near future.

This is a prospective study to look specifically into mortality and unfavourable outcomes in snake bites. The data on issues relating to human–snake conflict and snakebites has been published elsewhere (Longkumer et al, 2016). The information collected in this study will help to provide an evidence-based, community and hospital, education program to reduce the incidence of snakebite deaths.

MATERIAL AND METHODS

This prospective study was carried out at Duncan Hospital from 1 July 2012 to 30 June 2013. Duncan Hospital is a secondary level, 200-bed hospital with 10 Intensive Care beds and at the time of this study had five ventilators available. All patients during this time period who were admitted alive with: a history of snakebite, a bite by an unknown agent, or symptoms of snake envenomation without a known snakebite, were asked to take part in the study. Patients who dead on arrival with a history of snakebite or symptoms of envenomation were also included.

Routine management protocol at the time of the study included:

- Injection of tetanus toxoid for all patients;
- 10 vials of ASV (Snake antivenom) to patients showing signs of neurotoxic envenomation, with a premedication of hydrocortisone and pheniramine maleate;

- Patients with inflammation and swelling at the bite site for more than 24 hours were given ampicillin/cloxacillin and metronidazole.

If the patient was given less than 10 vials of ASV at a prior hospital/clinic, the balance was given on arrival at Duncan Hospital. The ASV used is the Indian manufactured quadrivalent antivenom.

Descriptive information was collected on: the patient; the snakebite – site of bite, time of bite, time to hospital; the environment where the snakebite occurred. Dead snakes brought to the hospital were photographed and then preserved in formalin. At the end of the study these snakes were identified to the species level by a herpetologist. Information was also obtained on delays in reaching the hospital, first aid prior to arrival and any treatment given in a referring hospital. The symptoms on arrival at the hospital were recorded along with the details of management throughout their hospital stay and their outcome on discharge.

Unfavourable outcomes were defined by one of the following; (i) patients who were dead on arrival at hospital; (ii) died in hospital; (iii) referred to other centres due to serious complications that were likely to cause their death; (iv) patients who were discharged from the hospital because they had not regained consciousness after 72 hours, or showed symptoms of brain death, and were expected to die. This composite outcome variable was chosen to capture all the poor outcomes in one variable and was used assess for Odds Ratios for two groups: the set of persons bitten by snakes and the subset of persons who were envenomated. Only univariate analysis has been used as the small size of the outcome variable provided sparse data for many variables.

The study was explained to patients and their relatives in a relevant language and verbal consent was taken. In the situation where the patient was unable to give consent (dead on arrival or intubated), the consent was sought from the attending relative. A written copy of the study explanation was made available in Hindi for those who can read.

The data were collected on a written proforma and then entered in EpiData. Analysis was done in Epi Data Analysis and Vassarstats (www.vassarstats.net). Ethics permission was obtained from Emmanuel Hospital Association Research and Ethics Committee (Proposal number 77).

RESULTS

From 1 July 2012 to 30 June 2013, 608 people were recruited in the study as per Figure 1. The six

excluded cases were: scorpion bite (1); spider bite (1); late presendation-6days (1); snake's blood splashed into the eyes while killing a snake (1); afraid but not actually bitten by a snake (2). The descriptive data of the 608 patients studied is presented in Table 1. The odds ratios for unfavourable outcomes have been included where adequate data was available. The descriptive data of the 76 envenomated patients is presented in Table 2. The odds ratios for unfavourable outcomes have been included where adequate data was available.

Unfavourable outcomes accounted for 21 patients: 14 dead on arrival at hospital; four who died in hospital; and three who left against medical advice at relatives request and were expected to die due to Hypoxic Ischaemic Encephalopathy. The causes of death for those who dies in hospital were: Hypoxic Ischaemic encephalopathy (HIE) [2]; cardiogenic shock (1); Acute Respiratory Distress Syndrome [1]. The overall evenomation rate is 12.6%; case fatality rate is 2.9%; unfavourable outcome rate is 3.4%.

The snakes that were identified in the preserved collection were Common Wolf Snake (*Lycodon aulicus*) – 21, Spectacled Cobra (*Naja naja*) – 11, Common Kukri Snake (*Oligodon arnensis*) – one. Four *Naja naja* were associated with a syndrome of neurotoxic envenomation with local tissue damage as per Figure 2. The *Lycodon aulicus* and *Oligon arnensis* specimens were not associated with any envenomation syndrome.

DISCUSSION

This study provides the first data regarding determinants of unfavourable outcomes in snakebites from the state of Bihar.

The under-fifteen age group had a significantly higher risk of unfavourable outcomes due to snake envenomation. This may be because the snake will inject the same amount of venom in both the adult and paediatric age group, which in children will mean a higher concentration of venom in their smaller body. It may also be related to the need to first inform an adult about the bite and then wait for the adult to bring them to hospital, another factor which increases the risk of unfavourable outcomes.

Bites to the upper limb have a higher risk of an unfavourable outcome. This has not been noted in the literature previously. One possible hypothesis is that venom may reach the central circulation more rapidly from upper limbs than from the lower extremities but no data has been found to support this.

Arrival at hospital within 1.5 hours of the bite appears to be protective against an unfavourable outcome. There was no unfavourable outcome if the patient arrived in less than one hour of the bite. The rapid demise caused by respiratory paralysis requires an even more rapid treatment with both ASV and assisted ventilation. Thus, it is important that any reasons for delay are understood and remedied.

Organising transport was reported to be a much bigger problem than organising money or organising relatives to accompany a snakebite patient. Motorbikes were the most common means of transport and appear to be more protective than other forms of transport. This is in line with the study found from the nearby eastern region of Nepal. (Sharma et al, 2004a). Advising people to come by motorbike, especially if there is no other readily available transport, would be likely to prevent deaths. (Sharma et al, 2013) The advice should involve three people travelling on the motorbike: the driver, the patient, and a person who can hold on to the patient should they become paralysed.

The unavailability of ASV resulted in people travelling longer distances to reach definitive treatment. Although this is not statistically significant in the odds ratios for snakebite patients, it was when the envenomated patients are evaluated for determinants that contribute to unfavourable outcomes. During July/August 2012 there was limited supply of ASV in Nepal and this resulted in extra cases of snakebite presenting to the hospital.

Attending a traditional practitioner prior to attending hospital also increases the risk of an unfavourable outcome. This was the only question asked regarding traditional practitioners so this practice needs to be understood further so that relevant education can be implemented to prevent this delay leading to unnecessary deaths.

The syndromes present; neurotoxic, with or without local tissue damage, match with the species of venomous snakes locally described as being in the region, Cobra and Krait. This study provides evidence of *Naja naja* being responsible for the syndrome of neurotoxicity with tissue damage in North Bihar. Patients have a much better ability to identify cobras than other snakes (Longkumer et al, 2016) and so it is not surprising that 20 out of 45 patients who described being bitten by a cobra, also presented with neurotoxic envenomation and tissue damage. The haemotoxic envenomation is the only one seen in the seven years of the longest serving physician at Duncan Hospital. This patient presented with bleeding from the mouth and nose. He had been given four vials of snake

antivenom (ASV) at a peripheral hospital in Nepal and his clotting parameters were normal on arrival. The patient came from the foothill region in Nepal (3 to 4 hours travel) suggesting the snake may have been one of the pit vipers from that region.

Two non-venomous snakes (Common Wolf Snake and Common Kukri Snake) were brought to the hospital during the study. Ongoing, unpublished work on snakes seen in the area now documents seven other non-venomous species and a recent study from the plains of Nepal also has recorded numerous non-venomous species (Sharma et al, 2016). This may partly explain the low envenomation rate seen at Duncan Hospital.

The other possible reason for low envenomation rates is deaths due to snakebite occurring the community before presentation to hospital. The 14 patients who were dead on arrival at the hospital, may support this. Community studies in Nepal and West Bengal have shown there are many victims of snakebites who never attend hospital facilities. (Sharma et al, 2004a; Majumder et al, 2014).

Unfavourable outcomes were positively associated with the need for mechanical ventilation in analysis relating to the entire cohort. Vellore, in southern India, has a different spectrum of snakes, but there is also an increase in mortality associated with mechanical ventilation (David et al, 2012). Neurotoxic envenomation management requires not only ASV, but also timely intubation and appropriate ventilation to prevent hypoxia, which is the ultimate killer.

Limitations and further directions

Despite working in a resource-limited setting, this study begins to provide data on an unstudied problem in Bihar. As a hospital based study, there will always be a bias in the data collected and so a community study would be important, especially to discover information on patients that never reach hospital. The available health facilities and the skill of their staff, needs to be assessed.

This study was only designed to collect data for one year and so there are limitations due sample size of the data. A larger study, which allowed for multivariate analysis of data, could assist in clearly pinpointing the problems causing delays.

No data were collected on the practices of traditional practitioners and the reasons why people seek care from them. During this study, Nepal ran out of ASV and so the data collection for this study became a larger than expected. However, this may have provided evidence that the unavailability of

ASV has contributed to unfavourable outcomes.

CONCLUSIONS

This study provides a basis to pursue further the neglected problem of snakebite among the huge, rural population of Bihar, India. Delays in seeking the definitive treatment (ASV and assisted ventilation) are the major contributors and need to be better understood to provide the necessary education, training and resources. The practice of attending traditional practitioners needs to be better understood to prevent this delay in seeking definitive treatment increase the risk of an unfavourable outcome. Arrival at hospital in less than one hour from the bite is the determinant that eliminates the risk of an unfavourable outcome. 72% of patients completely recovered from their envenomation but this percentage needs to approach 100%, for this very treatable incident.

COMPETING INTERESTS

None declared.

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Figure 1. Flow chart of study participants

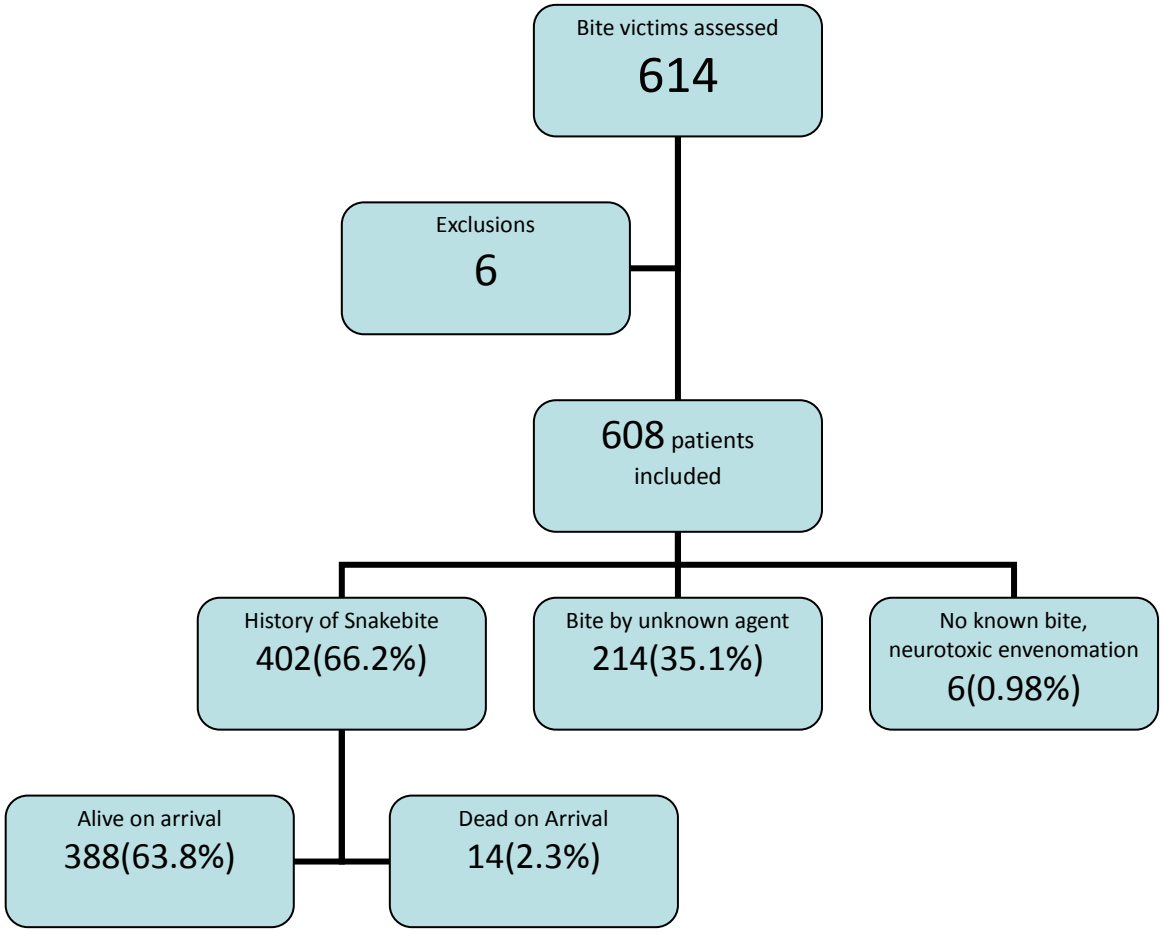

Figure 2. Flow chart of Envenomation syndromes seen in the patients who showed signs of envenomation.

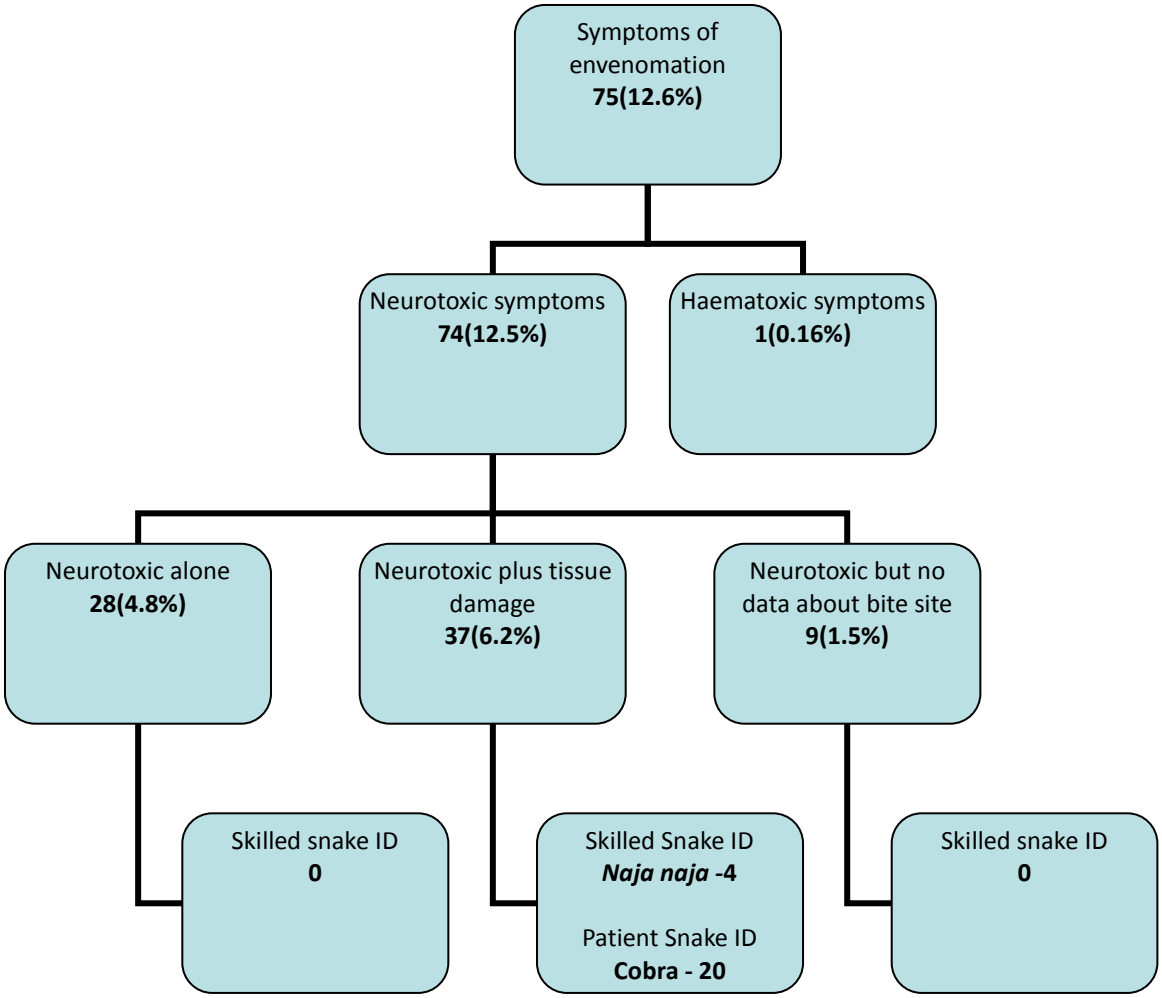

Table 1. Descriptive data of snakebites and determinants for unfavourable outcomes of snakebite in Duncan Hospital, North Bihar, India. [N = number of patient for whom data were available. # = Patients/relatives were first asked if they had any delay in reaching hospital. Then they were asked what the delays were; there may have been more than one specific cause for the delay.]

Variable (N)	n (%)	OR	CI
Gender **(608)**			
Male	321	1.2	0.46-3.28
Female	277	-	
Age **(608)**			
<15	143	3.79	1.57-9.12
15+	465	-	
Country **(605)**			
India	351	1.09	0.40-3.12
Nepal	254	-	
Time to hospital **(580)**			
<1.5 hour	200	0.23	0.052-1.0
>=1.5 hour	380	-	
Bite site part **(576)**			
Upper Limb	178	2.47	1.01-6.04
Lower Limb	391	0.28	0.11-0.71
Trunk	1	-	
No known site	6	-	
Transport **(533)**	#		
By foot	13	7.5	1.5-37
Motorbike	314	0.37	0.12-1.1
Cycle rickshaw	25	undefined	
Four wheeled vehicles	212	1.45	0.52-4.06
Tanga	11	3.83	0.46-32
Other	14	-	
Delays **(505)**			
Any Delay #	262	8.88	2.04-38.7
Organising money	0	-	
Org Transport	82	0.44	0.12-1.56
Floods	1	-	
Traffic Jam	0	-	
Bad roads	0	-	
No ASV	47	3.77	0.49-29.1
Distance	59	1.93	0.68-5.47
Org relatives	8	2.08	0.24-17.9
Traditional Practitioner	47	3.52	1.26-9.7
Other	45	-	
Management **(60)**			
Assisted Ventilation	33	7.05	0.72-354

Table 2. Descriptive data of envenomated patients and determinants of unfavourable outcomes of snakebite in Duncan Hospital, North Bihar, India. [N = number of patient for whom data was available # = Patients/relatives were first asked if they had any delay in reaching hospital. Then they were asked what the delays were; there may have been more than one specific cause for the delay. * = All were unfavourable outcomes]

Variable (N)	n (%)	OR	CI
***Gender* (75)**			
Male	39(52)	1.75	0.62-4.9
Female	36(48)	-	
***Age* (75)**			
<15	28(37)	2.39	0.85-6.7
15-30	25(33)	0.57	0.18-1.8
30+	23(30)	0.62	0.19-1.9
***Time to hospital* (64)**			
<1.5 hour	11(17)	0.56	0.17-2.4
>=1.5 hour	54(84)	1.77	0.34-9.1
***Bite site part* (72)**			
Upper Limb	29(40)	1.7	0.57-4.98
Lower Limb	36(50)	0.74	0.25-2.17
Trunk	1(1.4)	-	
No known site	6 (8.3)	-	
***Transport* (66)**			
Motorbike	22(33)	0.87	0.25-3.01
Four wheeled vehicle	44(67)	2.05	0.62-6.81
Delays			
Any Delay **#**	58	0.49	0.09-2.5
Org Transport	9	1.6	0.29-8.58
No ASV	19	12.2	1.49-100
Distance	19	0.96	0.29-3.14
Traditional Practitioner	19	0.69	0.21-2.24
***Management* (75)**			
Assisted Ventilation	28(37)	0.12	0.014-1.08
Surgical debridement	13(17)	-	
***Syndrome* (75)**			
Neurotoxic alone	28(37)	0.78	0.27-2.27
Neurotoxic plus tissue damage	32(43)	0.21	0.06-0.67
Neurotoxic but no data about bite site	9(12)	*	
Haemotoxic	1(1.3)	-	