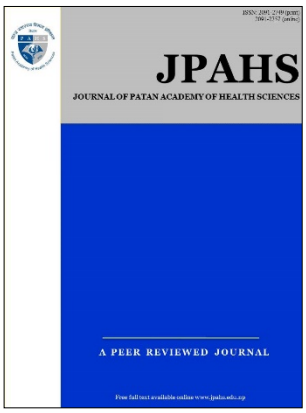

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Factors associated with treatment outcomes in anti-snake venom (ASV) administered snakebite patients

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Abstract

Introduction: Snakebite is a neglected tropical disease causing many deaths and serious consequences in Asia and Africa. Anti-snake Venom (ASV) is effective to prevent or reverse the venomous effects of snakebites. The aim of this study was to identify the prevalence of venomous snakebites and factors associated with treatment outcomes in a district hospital of Western Terai in Nepal.

Method: A single health facility-based retrospective cross-sectional study was conducted with collection of information from the record section of Bhim Hospital, Rupandehi, Nepal. All snakebite cases treated during July 2013 to July 2018 were included. The data on prevalence of snakebite and treatment outcomes were analyzed. Fischer's exact test and exact logistic regression were performed to identify factors associated with treatment outcomes of venomous snakebites.

Result: The prevalence of venomous snakebites was 3.71% (163/4399). Among cases with complete information (N=120), two-third were cured, and one-fourth were referred. Median number of ASV vials used was 12. Age and ASV vials used showed significant positive moderate correlation (r=0.38, p-value<0.001). Year of treatment showed significant association with treatment outcomes. In multivariate analysis, though insignificant, higher adjusted odds of cure was present with one unit increase in ASV vial (AOR= 1.16) and when the bite was in extremities (upper extremities AOR = 11.46 and lower extremities AOR= 21.68).

Conclusion: Snakebite cases require urgent management with administration of ASV, and proper recording of the cases in order to provide tangible evidence for policy and guideline formulation.

Keywords: anti-snake venom (ASV), district hospital, prevalence, snakebite, treatment outcomes

Introduction

Snakebite was reinstated as a neglected tropical disease by World Health Organization on 9th June 2017.[1] Annually, nearly two million people are envenomed by snakes in Asia and an estimated 435,000 to 580,000 snakebite cases need treatment in Africa. Out of these, most deaths and serious consequences are preventable by Anti-snake Venom (ASV), the only effective treatment to prevent or reverse the venomous effects of snake bites.[2]

Vipers, Kraits and Cobras are the venomous snakes found in Nepal which are distributed as per geography and climate.[3] In developing countries, identification of snake species is primarily made from the snake brought by the victim's relatives.[4] Traditional health seeking behavior as well as non-optimal access to health care decreases the true reporting of envenomation cases in developing countries.[5] This study aimed to identify the prevalence of venomous snakebite cases arriving in a district hospital of Western Terai of Nepal and factors associated with their treatment outcomes.

Method

The study was a single health facility-based retrospective cross-sectional study done at Bhim hospital, Rupandehi. Data was collected from the record section of Bhim hospital. All snakebite cases treated during July 2013 to July 2018 were included.

Ethical approval for the study was obtained from Institutional Review Committee of Patan Academy of Health Sciences, Lalitpur, Nepal [Ref: std1903011245]. Written consent for the study was acquired from Bhim hospital administration. Anonymity was ensured during data collection by not including the name of patients and collected information was saved in a password-protected folder of the researcher's password protected laptop to maintain privacy.

Snakebite cases who were administered ASV in the hospital and had complete data were included in the study.

Operational definitions used for analysis in this study, include-

- Cured: Those ASV administered snakebite cases in whom the signs and symptoms of envenomation was reversed and were discharged from the hospital.
- Dead: Those ASV administered snakebite cases who did not survive even after administration of ASV.
- Referred: Those ASV administered snakebite cases who were asked by the health personnel to visit tertiary care centre for further management.
- Anti-snake Venom (ASV): Lyophilized, Polyvalent Enzyme refined Equine immunoglobulin supplied to the public health facilities by Government of Nepal.
- Venomous snakebite cases: All snake bites cases with Anti-snake Venom administered in the hospital.
- Dependent and Independent age group: The age group are divided as dependent (less than 15 years and 60 years and above) and independent (15 to 59 years) as per Population Monograph of Nepal 2014.[6]
- Snake species: Snake species were divided into Cobra, Krait and Unknown based on signs identified in patients, verification mark or killed snake brought by the patient or patient parties that were reported by the health care workers of the hospital.
- Year of treatment: Snakebite cases of 5 years were taken from July 2013 to July 2018 and each 12 months from July 2013 were stratified as year 1, 2, 3, 4 and 5 of treatment.

Data were entered and cleaned in MS Excel for Windows 7 and were analyzed by Stata software version 13.0 and EZR version 1.36. Level of significance was set at 5% with p-value <0.05 being considered as statistically significant. Prevalence of venomous snakebite cases and frequencies for different variables are presented as descriptive analysis. Fisher's exact test was used to find association between independent and dependent variables. Exact logistic regression was performed to find the odds for treatment success (cured) compared to failure (death) for

different independent variables and their subgroups.

Result

There were 163 venomous snakebite cases (3.71% of 4399 bites) in five years, of which 110 (67.8%) got cured, 16 (9.82%) died and 32 (22.7%) had to be referred, Table 1. Complete sets of data for analysis were available in 120 cases, mean±SD age was 30.73±16.79 (male: 28.37±17.11, female: 32.87±16.35) and median number of ASV vials used was 12 (lowest: 3; highest: 29). Age and ASV vials used showed significant positive moderate correlation (r=0.38, p-value<0.001).

In 120 cases with complete data, 88 (73.33%) were of independent age group, females more than males, snake species unknown in more than half, bite on lower extremities nearly half, three-fifth had more than 10 ASV vials, year five had maximum cases, and two-third cases got cured, Table 2.

Table 1. Prevalence and outcome of venomous snakebite cases in a district hospital of Western Terai in Nepal

Year	Total snakebite cases	Venomous cases (% of total)	Cured (% of venomous cases)	Dead (% of venomous cases)	Referred (% of venomous cases)
1	695	30 (4.32)	24 (80)	5 (16.67)	1 (3.33)
2	874	30 (3.43)	20 (66.67)	3 (10)	7 (23.33)
3	1042	36 (3.45)	26 (72.22)	5 (13.89)	5 (13.89)
4	924	29 (3.14)	18 (62.07)	2 (6.90)	9 (31.03)
5	864	38 (4.40)	22 (57.90)	1 (2.63)	15 (39.47)
Total	4399	163 (3.71)	110 (67.48)	16 (9.82)	37 (22.70)

Table 2. Descriptive analysis of venomous snake bite cases in a district hospital of Western Terai in Nepal

Variables		Number	Percentage
Age group	Dependent	32	26.67
	Independent	88	73.33
Sex	Male	57	47.50
	Female	63	52.50
Snake species	Cobra	30	25.00
	Krait	27	22.50
	Unknown	63	52.50
Site of bite	Head and Neck	5	4.17
	Abdomen and Back	2	1.67
	Upper Extremities	54	45.00
	Lower Extremities	59	49.17
Total ASV used	Less than or equal to 10	50	41.67
	More than 10	70	58.33
Treatment year	Year 1	25	20.83
	Year 2	21	17.50
	Year 3	24	20.00
	Year 4	23	19.17
	Year 5	27	22.50
Treatment Outcome	Cured	80	66.67
	Dead	9	7.50
	Referred	31	25.83
Total		120	100

Fisher's exact test was done between independent and dependent variables which showed no association of age group, sex, snake species, site of bite and total ASV used with treatment outcomes, Table 3. Only the variable year of treatment showed significant association (p-value <0.05) with treatment outcomes, Table 3.

As sample size for success (cured cases=1) and failure (dead cases=0) of treatment was less than 100 (N=89) and there were no samples in outcome "dead cases" in sub-groups of different variables, dichotomous treatment outcomes were compared using bivariate and multivariate exact logistic analysis, which provided the Odds Ratio (OR) and Adjusted Odds Ratio (AOR), Table 4. Independent variables with p-value less than or equal to 0.25 in bivariate analysis,[7] and with Variance Inflation Factor (VIF) less than 2 were kept in multivariate analysis, Table 4.

Table 3. Association between Treatment outcomes and independent variables of snakebite cases in a district hospital of Western Terai in Nepal

Variables		Treatment Outcomes			p value
		Cured N (%), Expected Counts	Dead N (%), Expected Counts	Referred N (%), Expected Counts	
Age group	Dependent	18 (22.5%) 21.3	2 (22.2%) 2.4	12 (38.7%) 8.3	0.225
	Independent	62 (77.5%) 58.7	7 (77.8%) 6.6	19 (61.3%) 22.7	
Sex	Male	39 (48.8%) 38.0	3 (33.3%) 4.3	15 (48.4%) 14.7	0.697
	Female	41 (51.2%) 42.0	6 (66.7%) 4.7	16 (51.6%) 16.3	
Snake species	Cobra	20 (25.0%) 20.0	3 (33.3%) 2.3	7 (22.6%) 7.8	0.351
	Krait	17 (21.2%) 18.0	0 (0.0%) 2.0	10 (32.3%) 7.0	
	Unknown	43 (53.8%) 42.0	6 (66.7%) 4.7	14 (45.2%) 16.3	
Site of bite	Head and Neck	1 (1.2%) 3.3	1 (11.1%) 0.4	3 (9.7%) 1.3	0.201
	Abdomen and Back	1 (1.2%) 1.3	0 (0.0%) 0.1	1 (3.2%) 0.5	
	Upper Extremities	36 (45.0%) 36.0	5 (55.6%) 4.0	13 (41.9%) 13.9	
	Lower Extremities	42 (52.5%) 39.3	3 (33.3%) 4.4	14 (45.2%) 15.2	
Total ASVS used	≤10	34 (42.5%) 33.3	6 (66.7%) 3.8	10 (32.3%) 12.9	0.182
	> 10	46 (57.5%) 46.7	3 (33.3%) 5.3	21 (67.7%) 18.1	
Year of treatment	Year 1	21 (26.2%) 16.7	3 (33.3%) 1.9	1 (3.2%) 6.5	0.009*
	Year 2	15 (18.8%) 14.0	1 (11.1%) 1.6	5 (16.1%) 5.4	
	Year 3	17 (21.2%) 16.0	3 (33.3%) 1.8	4 (12.9%) 6.2	
	Year 4	13 (16.2%) 15.3	2 (22.2%) 1.7	8 (25.8%) 5.9	
	Year 5	14 (17.5%) 18.0	0 (0.0%) 2.0	13 (41.9%) 7.0	

*Significant at p<0.05

Table 4. Exact logistic regression, bivariate and multivariate analysis (dependent variable- outcome: cured=1, dead=0) of snakebite cases in a district hospital of Western Terai in Nepal

Independent Variables	Odds Ratio (95% CI)	P*	Adjusted Odds Ratio	p* value
Age	1.01 (0.97-1.06)	0.642		
ASV vials used	1.15 (0.99-1.39)	0.076**	1.16 (0.99-1.40)	0.060
Sex		0.604 (overall)		
Male	Ref			
Female	0.53 (0.08-2.69)	0.604		
Site of bite		0.176(overall)**		
Head and neck	Ref		Ref	
Abdomen and back	0.50* (0.01-Infinity)	1.000	0.49*(0.01-Infinity)	1.000
Upper extremities	6.66 (0.08-580.18)	0.525	11.46 (0.10-1341.86)	0.424
Lower extremities	12.27 (0.13-1123.22)	0.329	21.68 (0.18-2616.57)	0.253
Species of snake		1.0 (overall)		
Cobra	Ref			
Krait	3.05* (0.31-Infinity)	0.359		
Unknown	1.07 (0.16-5.67)	1.000		
Treatment year		0.566 (overall)		
First	Ref			
Second	2.11 (0.15-119.87)	0.941		
Third	0.81 (0.10-6.88)	1.000		
Fourth	0.93 (0.09-12.54)	1.000		
Fifth	2.39*(0.24-Infinity)	0.480		

Significant at p<0.05, *=Median Unbiased Estimate, ** = Go to multivariate analysis

Discussion

The study identified the prevalence of venomous snake bite in patients visiting a district hospital of Western Terai in Nepal with suspicion of snake bite as 3.71% and the mortality of 9.82% among the envenomed patients after treatment. This outcome is similar to the range reported in studies from Southern India.[8] Independent age group populations were bitten more often which corresponds to the results from different studies done in India and elsewhere.[4,9,10] This study showed that more females (52.5%) were bitten by venomous snakes that contradicts the findings of a survey conducted in Nepal,[12] which may be because of increased migration of males from Nepal in recent times.[6] Snake species being unknown and common site of bite being extremities matches with the findings from different studies.[8,10] A clinico-epidemiological study of snakebite done in Nepal has identified that high prevalence of snakebites being from unknown snakes was either due to ignorance of patients who were bitten, poor visibility in the dark or unable to spot the snake when in fields with tall grasses and crops.[13] Three in five venomous snakebite cases were administered more than 10 ASV vials, which is in line with the National Guideline for snakebite management in Nepal. The guideline recommends that 10 vials of ASV should be administered with intravenous infusion at the rate of 2 ml per minute over 40-60 minutes followed by 5 vials of ASV intravenous push at the rate of 2 ml per minute if signs of envenomation do not diminish.[14]

No significant results were identified from bivariate exact logistic regressions, but within the study population there were higher odds of cure (OR= 1.01) with increasing age which opposed the result from study in West Bengal.[9] In present study, as there was significant positive correlation between age and ASV vials used but the amount of venom delivered by a snake is similar in each bite, thus higher odds of cure with increasing age can be justified. A hospital based retrospective epidemiological study on snake bites in two districts of Nepal has also identified higher mortality in lower age group owing to delivery of greater amount of toxin per kilogram body weight.[12] Females had lower odds of cure (OR= 0.53) which was similar to the findings from studies conducted in West Bengal and Maharastra.[9,15] Highest

odds of cure (OR= 3.05) was present when the snake species was Krait which was contrary to the findings from different studies done in India.[16,17] This may be due to absence of mortality of patients bitten by Krait in this study. In this study, highest odds of cure were present in the 5th year (OR=2.39) which may be due to greater number of referred cases, and no reported mortality.

In multivariate analysis, though insignificant, higher adjusted odds of cure (AOR= 1.16) was present with one unit increase in ASV vial controlling for site of bite and when the bite was in extremities (Upper extremities AOR = 11.46 and Lower extremities AOR = 21.68) controlling for number of ASV vials administered. Exact dose of ASV to be administered in cases of snake envenomation is still a matter of discussion, with some studies showing insignificant association between cure and ASV dose administered.[18] However, early administration of ASV to reduce snake bite related morbidity and mortality have been suggested by different studies.[19,20,21,22]

Some of the limitations of present study are- a single health facility-based study, thus the result cannot be generalized. Many variables that could be associated with treatment outcomes such as time of bite, time to reach hospital, status of first aid, use of local measures, signs and symptoms after the bite etc. could not be assessed because they were not mentioned in the record. About one-fourth recorded data were incomplete and could not be included in the analysis which may have affected the results.

Conclusion

Significant association between year of treatment and treatment outcomes, with increased with increased referrals in recent years were identified from the study data. Though insignificant, the study identified different factors like increase in age, male sex, ASV vials used, bite on extremities and bite by Krait to have higher likelihood to be cured. The reasons as “why” the referred rate is increasing from a public hospital and “why” the recording and reporting of snake bite cases are incomplete remains an area for explanations.

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Conflict of Interest

The author declares no conflict of interest in the conduction of this study.

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