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Research Article

Management and Outcome Study of Snake Bite Cases in Central India

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Abstract: Snake-bite is a life-threatening medical emergency & major public health problem throughout the World, especially in tropical countries like India. The annual death rate due to snake bite in India is estimated to be 4.1 per 1,00,000 population while in Maharashtra, it is 3.0 per 1,00,000 population. The objective of this study is to observe the management of snake bite and their outcome in central India. It was a prospective observational study of 203 patient of snake bite from June 2011 to September 2013. Inclusion criteria: all the adult patients of poisonous snake bite admitted in medical wards and intensive care unit. Exclusion criteria: patient of non-poisonous snake bite & scorpion bite. Most important investigation to be performed in vasculotoxic snake bite was 20 minute whole blood clotting time which helped in early detection of coagulopathy and subsequent acute renal failure. Complete blood count, liver function test, renal function tests, urine examination to rule out haematuria, coagulation profile (PT and INR) were also done. Primary outcome was defined in the form of survival or non-survival. Prognostic factors were compared in survived and non survived groups. Variable clinical presentations were noted starting from cellulitis (90.6%) followed by nausea and vomiting (70.4%), ptosis (19.2%), colour changes in form of bluish discoloration of bite site (12.8%), respiratory failure and haematuria (7.4%) to Hypotension (6.9%). Out of 203 cases studied 30, patients were died during the study period and overall mortality was 14.8%. Mortality in patients who received ASV more than 300 ml was higher than those who received anti-snake venom (ASV) less than 300 ml (p value < 0.001). To conclude, it was found that in order to reduce the mortality by snake bite, it is important for the patient to reach to the hospital as early as possible so as to get appropriate and adequate treatment with anti-snake venom to prevent the development or progression of complications with proper intervention. Those patient who developed dreadful complications like renal failure requiring dialysis may not be benefited only by giving more amount of ASV (ASV>315 ml) and same is true with coagulopathy.
Keywords: Snake bite, Anti-snake venom.

INTRODUCTION

Snake-bite is a life-threatening medical emergency & major public health problem throughout the World, especially in tropical countries like India. Snake bite is known to the mankind from antiquity and has been described in some of the oldest myths and medical writings.

Snake bite is one of the commonest causes of morbidity and mortality in India, particularly in rural areas. All the snakes are generally considered as poisonous, in the sense that venom in their saliva is sufficient to kill or paralyze their prey. Fact is that majority of them are non-poisonous. There are about 3000 species on the earth and they are predominantly in warm climate and bushy regions of the tropics.

In India, there are 216 species, out of which 52 are poisonous [1].

The annual death rate due to snake bite in India is estimated to be 4.1 per 1,00,000 population while in Maharashtra, it is 3.0 per 1,00,000 population. The annual snake bite deaths were greatest in the states of Uttar Pradesh, Andhra Pradesh, Madhya Pradesh and Bihar [2]. India has the highest number of deaths due to snake bites in the world with 35,000–50,000 people dying each year [3, 4]. The Registrar-General of India's "Million Death Study" 2001-2003 is expected to provide reliable evidence of substantial mortality (exceeding 50 000 per year) as it is based on Representative, Re-sampled, Routine Household Interview of Mortality with Medical Evaluation (RHIME) [5].

Every year about 2000 deaths occur due to snake-bite in Maharashtra. The majority of them remain unreported because many villagers go to traditional

healers [6]. Delay in seeking medical aid or ignorance among primary care physicians about the correct treatment of snake-bite is also responsible for the high morbidity and mortality [7]. Four species popularly known to be dangerously poisonous to man are spectacled cobra (*Naja naja*), common krait (*Bungarus caeruleus*), saw-scaled viper (*Echis carinatus*) and Russell's viper (*Daboia russelii*) [2]. The most common poisonous snake among them is common krait [8]. Viperine vasculotoxic snake bite is a cause of severe morbidity and mortality in our country. The bleeding diathesis by viperine envenomation can be successfully reversed with anti-snake venom.

It is important to decide not only the proper regimens but also the modality of treatment in complication of snake bite cases. Hence, the objective of this study is to observe the management of snake bite and their outcome with different variables.

MATERIALS AND METHODS

It was a prospective observational study of 203 patient of snake bite satisfying the inclusion and exclusion criteria, admitted to the medical intensive care unit and wards during the period from June 2011 to September 2013. Estimation of sample size was done in reference with assumption of mortality in snake bite cases studied by Kalantri S *et al.* [8] as 11% and absolute precision of 5%. Considering the desired level of confidence as 95%, minimum estimated sample size was found to be 150 while we included 203 cases.

Inclusion criteria: all the adult patients of poisonous snake bite admitted in medical wards and intensive care unit.

Exclusion criteria: patient of non-poisonous snake bite & scorpion bite.

Demographic characteristics of the patients and the snake bite event such as age, gender, time of bite, site of bite, bite-to-hospital time were recorded. Symptoms and signs such as local swelling, nausea, vomiting, ptosis, tachycardia, hypotension, impending respiratory failure by single breath count (SBC), bite to injection time of anti-snake venom (ASV), ASV treatment before referral, total dose of anti-snake venom administered and duration of stay were documented. Most important investigation to be performed in vasculotoxic snake bite is 20 minute whole blood clotting time (20 minute WBCT) which helps in early detection of coagulopathy and subsequent acute renal failure. Complete blood count, liver function test, renal function tests, urine examination to rule out haematuria, coagulation profile (PT and INR) were also done. Primary outcome was defined in the form of survival or non-survival. Prognostic factors were compared in survived and non survived groups.

Statistical analysis

In the present study continuous variables (age, door to needle time, length of stay etc) were presented as mean ± standard deviation. Discrete variables (gender, site of bite, symptoms and signs, complications) were expressed in actual numbers and percentages. Continuous variables were compared by performing un-paired t test. ASV and outcome were compared by performing Wilcoxon-rank-sum test. Discrete variables were compared using chi square test and for small number, fisher extract test was applied whenever applicable. To compare the door to needle time and time of bite with the outcome, chi square for linear trend was applied. Cox proportional regression hazard model was used to identify the independent risk factor of mortality in the management of snake bite. A p value < 0.05 was considered as statistically significant and p value of <0.01 was considered highly significant. Statistical software STATA version 10.0 was used for statistical analysis.

RESULTS

Present prospective observational study was conducted at tertiary level hospital in central India for detection of predictors in the management of snake bite by observing demographic, laboratory parameters and specific treatment with anti-snake venom, correlating them with the outcome in the form of mortality and survival.

Most of the snake bites (30.6%) cases were in age group of 21 to 30 years followed by 31-40 years (22.0%). Out of 203 cases, 126 were males and 77 females with male to female ratio of 1.63:1. Commonest site of snake bite was the lower extremity (65%) and followed by upper extremity (35%). Seasonal variation in the incidence of snake bite was observed in this study with maximum number of bites occurring in rainy season (83.3%) between June to October and highest number of cases during August (28.1%).

Table 1 showed incidence of different symptoms & signs of snake bite. Clinical presentations in decreasing order of incidence were cellulitis (90.6%) followed by nausea and vomiting (70.4%), ptosis (19.2%), colour changes in form of bluish discoloration of bite site (12.8%), respiratory failure and haematuria (7.4%) and Hypotension (6.9%).Table 2 showed outcome of the snake bite management in which out of 203 cases studied 30, patients were died during the study period and overall mortality was 14.8%.

Table 1: Incidence of different symptoms and sign in snake bite patients

Symptoms and Sign	Number (%)
Cellulitis	184(90.6)
A Localized	36(17.7)
b. Crossing near joint	81(39.9)
c. Whole limb	67(33)
Colour changes	26(12.8)
Nausea/vomiting	143(70.4)
Neuroparalysis	39(19.2)
a. Ptosis	39(19.2)
b. Respiratory failure	15(7.4)
Hematuria	15.(7.4)
Hypotension	14(6.9)

Table 2: Outcome of snake bite management

Outcome	Number (%) (n = 203)
Death	30(14.8)
Survived	173(85.2)

Table 3 showed the correlation between the door to needle time and mortality. Most of the cases were reported within 6 hrs of bite (47.4%). Mortality was highest in cases reported after 24 hrs of bite (66.7%). Mean door to needle time was 20.49 ± 45.87 with median of 6 hrs. X^2 for linear trend applied with p value< 0.001 which was statistically significant.

The parameters shown in table 4 were evaluated in terms of outcome (mortality), It was found that haemoglobin less than 7 g%, total leukocyte count >11000/µl, WBCT more than 20 minute, INR more than 1.5, raised SGPT were statistically significant with mortality and can be used as predictors of mortality. Hyponatremia is not found to be statistically significant with mortality.

Table 3: Correlation between door to needle time and mortality

Time(Hours)	Number (%) (n = 203)	Mortality (%) (n = 30)
<6	96(47.2)	7(7.2)
6-12	48(23.6)	5(10.4)
13-24	23(11.3)	4(17.4)
25-36	06 (2.9)	4(66.6)
>36	30(14.7)	10(33.3)
TOATL	203(100)	30(14.7)
Mean time of site to hospital 20.49 ± 45.87, Median (Range) 6(1-480), x^2 for trend =15.93, p < 0.001,HS; HS= Highly significant		

Table 4: Comparison of laboratory parameters in management of snake bite with mortality

Parameter	Number (%)	Mortality (%)	P-value
Hb<7g/dl	5 (2.5)	2 (40)	<0.001, **HS**
TLC>11000/µl	51 (25.1)	21 (41.1)	<0.001, **HS**
20 Minute WBCT	122 (60.1)	27(22.1)	<0.001, **HS**
INR	64 (31.5)	22 (34.4)	<0.001**, HS**
Hyponatremia	3 (1.5)	1 (33.3)	0.362, **NS**
Raised SGPT	10 (4.9)	4 (40)	0.021,**S**

HS= Highly significant, NS = Non significant, S= significant, Hb= haemoglobin, TLC= Total leucocyte count, 20 WBCT= 20 minute whole blood clotting time, INR= International normalized ratio, SGPT= serum glutamic-pyruvic transaminase

Table 5 showed the complication of snake bite and mortality. It was found that cellulitis (90.6%) was the most common complication observed followed by acute renal failure (43.3%), coagulopathy (22.2%) and neuroparalysis (19.2%). Reverse was true with mortality which was high in coagulopathy (42.2%) followed by acute renal failure (28.4%), neuroparalysis (20.5%) and cellulitis (15.8%).

Table 5: Complication of snake bite and mortality

Complication	Number (%)	Mortality (%)	P-value
Celluliitis	184(90.6)	29(15.8)	0.172, NS
Neuroparalysis	39(19.2)	8(20.5)	0.262, NS
Acute renal failure	88(43.3)	25(28.4)	<0.001,HS
Coagulopathy	45(22.2)	19(42.2)	<0.001,HS

HS= Highly significant, NS = Non significant

Table 6 showed group of patients who first received ASV treatment at PHC/RH, then referred to higher centre. Out of 203 cases of snake bite, 188 (92.6%) patient received ASV treatment at PHC/RH before referral to higher centre. They had statistically significant less mortality (9.6%) as compared to 15 patients (7.4%) who didn't received ASV treatment (80%).

Table 6: ASV Treatment at PHC/RHC.

ASV Treatment	Number (%)	Mortality (%)	P-value
Yes	188(92.6)	18(9.6)	<0.001,HS
No	15(7.4)	12(80)	

HS= Highly significant, PHC=Primary health care center, RHC= Rural health center

As shown in table 7, the dose of anti-snake venom in all patients of snake bites was compared with outcome. It was observed that mortality in patients who received ASV more than 300 ml was higher than those who received ASV less than 300 ml (p value < 0.001).

Table 7: Dose of ASV and mortality

Dose of ASV (ml)	Number (%) (n=203)	Mortality (%) (n=30)	Hazard ratio 95% CI	P-Value
>300	66(32.51)	20(30)	11.7(4.39-31.84)	< 0.001HS
≤300	137(67.48)	10 (7)		

C I = Confidence interval, HS= highly significant

Table 8 showed the comparison of dose of ASV in mortality and survived group. It was observed that patients of mortality group received more ASV than those of survived group (Mean 392.66 ml vs. 310.98 ml and median 315 ml vs. 220 ml). It was also observed that maximum duration of hospital stay was between 5 to 7 day (34%) followed by 2 to 4 days (33%) with mean of 6.45 days.

Table 8: Mean ASV and outcome

ASV Dose (ml)	Mortality	Survived
Mean	392.66	310.98
SD	275.81	297.39
Median	315	220
Range	50-1200	50-1200
Z-VALUE = 4.921	P<0.001, HS	

HS = highly significant

Table 9 showed Cox proportional hazard regression analysis for factors associated with snake bite management. The risk of mortality was 6.19 times more among the study subjects who had door to needle time more than 24 hrs as compare to those who had door to needle time less than 24 hrs. This was statistically significant (P-value -0.010,**S**) If Whole blood clotting time was more than 20 minutes then the risk of mortality was 6.50 times more as compared to group of patient who's WBCT less than 20 minute. (P value -0.046,**S**). The risk of mortality was 94% less among the study subjects who had received ASV treatment at PHC/RH as compare to those who didn't get ASV (P value - 0.001, HS). The risk of mortality was 3.35 times higher among the patient who had developed acute renal failure than those who didn't have acute renal failure. (P value -0.032,S). The risk of mortality was 6.13 times more among the study subjects who had duration of stay less than 7 days as compare to those whose duration of stay more than 7 days, those who died had severe systemic envenomation and complication which allowed less time take adequate intervention and even after intervention they had less response to the treatment (P value -0.013, S).

Table 9: Cox proportional hazard regression analysis for factors associated with snake bites management.

Factor	Hazard ratio	95 % C.I.	P-value
Door to needle time (24hrs)	6.19	1.55 - 24.78	0.010,S
20 WBCT	6.50	1.03-40.83	0.046,S
Dose of ASV (300ml)	3.35	1.26-18.43	0.021,S
ASV treatment at PHC/RHC	0.06	0.01-0.29	<0.001,HS
Acute renal failure	3.35	1.10-10.17	0.032,S
Duration of stay (7days)	6.13	1.46-25.60	0.013,S

C.I. = Confidence interval, HS=highly significant, S= significant, PHC=Primary health care centre, RHC= Rural health centre, ASV = Anti-Snake venom, 20 WBCT= 20 minute whole blood clotting time.

DISCUSSION

The present study comprised of 203 cases who presented with history of snake bite with signs of envenomation during the study period. A meticulous history, clinical examination and laboratory investigations were carried out on the day of admission and regularly thereafter. Cases were followed till the final outcome in form of discharge or death. Data records include the patient's characteristics such as symptoms and signs complications, dose of ASV, duration of stay and final outcome. This data was analyzed for predicting survival using statistical analysis.

Age and gender wise distribution of study subjects is in corroboration with previous studies. In present study, most of snake bites were in age group of 21 to 50 years comprising of 75.86% with mean age of 37.73 ±13.31 years, range being 12 to 70 years. Individuals in this age group are actively involved in farming and outdoor activity, with male to female ratio of 1.63:1. Hansdac SG *et al*. [10] and Wanje sudhir *et al*. [11] observed that 11 to 40 years and 10 to 39 years was the most common age group in their study respectively with male predominance. Bhavesh Jarwani *et al*. [12] noted 15 to 45 years as most common age.

Seasonal variation in incidence of snake bite was in accordance to I F Inamdar *et al*. [13], D. P. Punde [14]. Most of the snake bites occurred in July to October which is the monsoon season, with increased agricultural activity and also the time of increased activity of snakes as they come out of their shelters. Some variation may be due to geographic variation in rainy season.

In hospital-based studies, mortality rates ranged from 3% in northern India [15] to 20% in Nepal [16, 17]. The case-fatality rate in our study was 14.8% (30/203), most common cause of mortality in our study was coagulopathy 42.2% (19/45) followed by ARF 28.4% (26/88), neuroparalysis 20.5% (8/39) and cellulitis 15.8% (29/184). Mortality rates in other studies varied from 3-11%. Apparently high mortality rate in our study may be due to delay in arriving at the hospital after the snake bite or external factors which increase the chances of mortality are not receiving first aid, unavailability of anti-snake venom (ASV) at health centres, no transport facilities and lack of public awareness about the urgency and need of treatment.

Incidence of complications was directly proportional to the duration of venom in the blood prior to its neutralization by ASV due to late arrival of the patient at hospital [18]. Correlation between door to needle time and mortality is similar to those observed by by Kavitha Saravu *et al*. [19] and I F Inamdar *et al*. [20]. A study by Ko Ko Naing *et al*. [21] in Nepal showed that the delay in receiving treatment was significantly longer for victims with a fatal outcome. It was found that the mortality was high in patients with door to needle time more than 24 hours, as compared to patients whose door to needle time was less than 24 hours.

Laboratory parameters in management of snake bite were similar to those found in previous studies. Butt KZ *et al*. [22] in his study notified that leukocytosis was most common followed by WBCT > 20 minute, raised SGPT and INR >1.5. A significantly higher mortality was observed in cases with WBCT more than 20 minute as compared to those with normal WBCT (20.4% *vs.* 3%, p <0.001HS). Myo-Khin *et al*. [23] in his study noted that unclotted blood after 20 minute associated with higher incidence of mortality. Haemostatic disturbances are known to be the pathological mechanism causing fulminant disease in hematoxic snake bite and bleeding tendency is well recognized as an indicator of greater risk of mortality.

Most of vasculotoxic bites were associated with cellulitis (90.60%) and coagulopathy (19%). Bhat RN *et al*. [24] and Saini *et al*. [25] in their study recorded haemorrhagic manifestations in 65% and 47.80% respectively. Another study by Dhannya *et al*. [26] reported the same in 76%. Neuroparalysis was encountered in 19.20% cases. The common symptoms were ptosis and blurring of vision in all patients of which 7.4% cases developed respiratory failure. Acute renal failure was observed in 43.3% cases. Incidence of acute renal failure in 14.4% was noted by Halesha BR *et al*. [27]. These differences in the complication of different studies imply differences between the venoms of the sub species around that geographic area. The dose of ASV was studied in relation to complication and found that dose of ASV was more in mortality

group of patient as compare to survived group which was not statistically significant.

As stated earlier, incidence of complications was directly proportional to the duration of venom in the blood prior to neutralization by ASV due to late arrival of patient at hospital [18]. Hence, infusion of more ASV may not be helpful once dreadful complications like renal failure and coagulopathy developed.

The correlation between dose of ASV and outcome had similar results as that in Srimannarayana J *et al*. [28], Soyed Moied Ahmed *et al*. [29], Kavitha Saravu *et al*. [19] which state that the mean dose of ASV in mortality group was high as compared to survived group. Saravu *et al*. [19] found that overall less dose of ASV in survived group. Median dose of ASV in survived and mortality patients were 220 and 315 ml respectively with range being 50 ml to 1200 ml. Similar dose range of 150 to 1600 ml were observed by Agarwal *et al*. [30]. The outcome of snake bite and treatment by anti-snake venom is influenced by host and environmental factors. Still it is recommended to use adequate and appropriate dose of anti-snake venom as soon as possible after the bite, within 4 hour of administration to get better outcome.

During the study on management of snake bite, it was discovered that outcome of snake bite depends upon multiple factor. Univariate analysis of the following risk factors was done and found significantly associated with mortality: Vomiting, door to needle time more than 24 hrs, WBCT more than 20 minute, ASV treatment at peripheral centre, acute renal failure, duration of stay, while Age and gender, neurotoxicity were not significant. By using Cox proportional hazard regression analysis, it was concluded that the door to needle time more than 24 hrs, WBCT more than 20 minute, development of acute renal failure, duration of stay less than 7 days were associated with significant increase in risk of mortality while ASV treatment at PHC/RH had protective effect on outcome of snake bite patients. In group of patients with duration of stay less than 7 days had severe systemic envenomation and complications which allowed less time for adequate intervention. This resulted in less response to the treatment and finally to increased mortality.

CONCLUSION

In order to reduce the mortality by snake bite, it is important for the patient to reach to the hospital as early as possible so as to get appropriate and adequate treatment with anti-snake venom to prevent the development or progression of complications with proper intervention. Those patient who developed dreadful complications like renal failure requiring dialysis may not be benefited only by giving more amount of ASV (ASV>315 ml) and same is true with coagulopathy.

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