



SNAKE BITE; VASCULOTOXIC EFFECTS IN PATIENTS

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ABSTRACT... Snake bites are increasing amongst those who unlawfully keep snakes as pets worldwide. The rural population active in agricultural works, laborers, herders, professional snake handlers, trekkers, snake charmers and fishermen are at risk for snake bites. **Objectives:** To determine the frequency and pattern of vasculotoxic effects in patients with snake bite. **Design:** Case Study. **Period:** Six Months **Setting:** Liaquat University Hospital Hyderabad. **Patients and methods:** All the patients who initially present in casualty department of hospital with the history of snake bite were enrolled in the study. The vasculotoxic effects were evaluated by whole blood clotting time (WBCT) test, bleeding time, PT/APTT, hypofibrinogenemia, DIC and thrombocytopenia. Relevant information would be entered in specifically designed proforma for this study. The data was entered, saved and analyzed in SPSS. So no test of significance would be applied. **Results:** Out of 140 patients 112(80%) had vasculotoxic effects, of which 80(72%) were males and 32(28%) were females. The mean age \pm SD of the overall patients was 37.53 ± 8.72 whereas the mean age \pm SD of male and female population was 38.98 ± 7.44 and 34.88 ± 4.32 respectively. The systemic bleeding was observed in 99% patients, the fang marks in 94 patients, the prolonged bleeding time, WBCT and PT/APTT in 103, 96 and 101 patients, thrombocytopenia in 93 patients, hypofibrinogenemia in 81 patients and DIC in 76 patients. The hamaturia (22%), hamoptysis(16%) and hametemesis (11%) was predominant features. The gangrene was observed in 02 patients, vomiting was observed in 60% of patients had haematemesis in 11%, bleeding gums in 03 cases and haemoptysis in 16%. Renal failure was observed in 12 cases. **Conclusions:** The coagulation tests disturbed as venom increases the clotting time. Proteins digesting enzymes or thrombin like activity of venom may be one of the causes for prolongation coagulation tests (vasculotoxic effects)

Key words: Snake bite, vasculotoxic, bleeding, prothrombin, thrombocytopenia, DIC, Hypofibrinogenemia

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INTRODUCTION

Snake bites are increasing amongst those who unlawfully keep snakes as pets worldwide.¹The rural population active in agricultural works, laborers, herders, professional snake handlers, trekkers, snake charmers and fishermen are at risk for snake bites¹. A study conducted, by Kasturiratne A et al based concluded that at least 4, 21,000 envenomations and 20,000 deaths occur globally from snakebite each year². The highest number of envenoming were estimated to be from South Asia (1,21,000) which was followed by South East Asia (1,11,000) and East Sub-Saharan Africa (43,000) annually.²Among the Asian countries, Pakistan had 40,000 snake bites annually with 8,200 fatalities and Nepal was

estimated to have more than 20,000 envenomings with 1,000 fatalities². Chippaux JP³ estimated that in Asia with 3500 million population, four million snake bites may occur each year of which 50% are envenomated with 1,00,000 mortality. The data regarding the incidence of snake bite, the mortality and morbidity due to snake bite are unreliable due to poor and improper reporting system as majority of the snake bites (80% of all reported cases) occur among rural population³. A national mortality survey conducted by Mohapatra B, et al⁴ estimated 45,900 deaths to occur annually.

The vasculotoxic effects of snake bite include; increase whole blood clotting time (WBCT > 10 minutes, bleeding from recent wounds and from

old partly healed wounds, spontaneous systemic bleeding from gums, vaginal bleeding, epistaxis, bleeding into tears, bleeding into the skin (purpura, ecchymosis, petechiae and mucosae)^{5,6}. This study was purposed to calculate the frequency and pattern of vasculotoxic effects in patients admitted with history of snake bite. The study raised concern and awareness regarding various vasculotoxic complications of snake bite.

PATIENTS AND METHODS

This descriptive case series study of six months was conducted at Liaquat University Hospital Hyderabad / Jamshoro. All the patients aged ≥ 12 years of age, of either gender who did not receive antisnake venom before admission in the hospital were enrolled and entered in the study. The exclusive criteria of the study were pregnant patients, patients suffering from liver, cardiac disease or clotting disorder and the patients receiving aspirin or anticoagulants. A thorough history was taken for the presence of bleeding at bite site, recent wounds, epistaxis, bleeding from tears, hemoptysis, hematemesis, rectal bleeding, hematuria, vaginal bleeding, bleeding from the skin in the form of petechiae, bruises. Clinical examination included confirmation of site of bleeding (at the skin or mucosal orifices). Whole Blood Clotting Time (WBCT) test was performed. In this test a standard 5ml sized syringe was filled with blood and the contents were shifted to glass test tubes (standard size). After every minute the content were gently tilted. If the whole column of blood moves as a single unit then the sample was considered as clotted. A lab technician who has at least 5 year experience of doing this test was engaged for such task. If WBCT is prolonged (>10 min) then the test was repeated after every six hours until the result becomes normal (this is routine practice in medical units to observe therapeutic effects of anti-snake venom). The highest value of WBCT was noted. The pattern of vasculotoxic effects includes bleeding from bite site and spontaneous systemic bleeding (manifested as epistaxis, bleeding from tears, hemoptysis, hematemesis, rectal bleeding, hematuria, vaginal bleeding, bleeding from the skin in the form of petechiae, bruises) while the

protocols used to identify vasculotoxic effects were prolonged bleeding time: Bleeding time (BT) >6 min, prolonged Whole Blood Clotting Time (WBCT) >10 min, thrombocytopenia: Platelet count $< 1,50,000/\text{cmm}$, prolonged PT / APTT : PT > 12 sec, APTT > 32 sec, hypofibrinogemia: Fibrinogen $<200\text{mg/dl}$ and DIC: d-dimer of <250 ng/ml, along with evidence of microangiopathic hemolysis (broken RBCs on microscopy). Relevant information was entered in specifically designed proforma for this study. The primary outcome variables was the value of WBCT (>10 min was considered as prolonged) and the frequency of the vasculotoxic effects. Statistical Package of Social Sciences (SPSS) version was used for data analysis. Descriptive statistics included continuous variables; age and duration of whole blood clotting time, bleeding time, clotting time (WBCT), PT, APTT, platelets counts, fibrinogens and d-dimer levels presented as mean and standard deviations. Categorical variables such as sex, bleeding from site of bite, bleeding from wounds, and systemic bleeding (as described previously) were presented as frequencies and percentage. As this study is a case series, so no test of significance was applied.

RESULTS

During six month study period, out of 140 patients 112(80%) had vasculotoxic effects, of which 80(72%) were males and 32(28%) were females. The mean age $\pm\text{SD}$ of the overall patients was 37.53 ± 8.72 whereas the mean age $\pm\text{SD}$ of male and female population was 38.98 ± 7.44 and 34.88 ± 4.32 respectively. The mean pulse rate for overall patients was 83.54 ± 4.31 , whereas the mean $\pm\text{SD}$ pulse rate in male and female population was 85.82 ± 2.98 and 80.21 ± 3.53 respectively. The mean $\pm\text{SD}$ systolic blood pressure of overall patients was 100.82 ± 08.62 , whereas the mean $\pm\text{SD}$ systolic blood pressure of male and female patients was 110.72 ± 05.21 and 100.72 ± 5.42 respectively. The mean diastolic blood pressure $\pm\text{SD}$ of overall patients was 70 ± 02.32 , whereas the mean diastolic blood pressure $\pm\text{SD}$ of male and female patients was 60.21 ± 04.43 and 80.71 ± 1.72 respectively. The mean temperature $\pm\text{SD}$ of overall patients was

100.62±1.21, whereas the mean temperature ±SD of male and female population was 101.77±1.42 and 101.12±2.0 respectively. The mean respiratory rate ± SD of overall patients was 25.81±2.32, whereas the mean respiratory rate ± SD of male and female population was 26.54±2.32 and 22.87±1.42 respectively. In this study 70 cases reported within 6 hours of bite, 20 cases reported between 6-24 hours, 35 cases between 24-48 hours and 15 cases after 48 hours of bite. Pain at the site of bite was a common symptom 90%, local swelling was present in 78% of cases, and blister formation was seen in 5% of cases. The gangrene was observed in 02 patients, vomiting was observed in 60% of patients had haematemesis in 11%, bleeding gums in 03 cases and haemoptysis in 16%. Renal failure was observed in 12 cases, all of these 12 cases were subjected to haemodialysis, out of which all recovered. The distribution of systemic bleeding, clinical presentation, bleeding time, WBCT, PT-APTT, thrombocytopenia, hypofibrinogemia and DIC in relation to gender is shown in Table I-VIII.

Gender	Systemic Bleeding		
	Yes	No	Total
Male	74(74.7%)	06(46.2%)	80(71.4%)
Female	25(25.3%)	07(53.8%)	32(28.6%)
Total	99(100%)	13(100%)	112(100%)

Table-I. Gender distribution in relation to system bleeding

Symptoms	Gender		Total
	Male	Female	
Gums	04 (5.4%)	01 (4.0%)	05 (5.1%)
Epistaxis	07 (9.5%)	03 (12.0%)	10 (10.1%)
Haemoptysis	14 (18.9%)	02 (8.0%)	16 (16.2%)
Hemetemesis	07 (9.5%)	04 (16.0%)	11 (11.1%)
Rectal bleeding	06 (8.1%)	00 (00%)	06 (6.1%)
Haematuria	14 (18.9%)	08 (32.0%)	22 (22.2%)
Vaginal bleeding	00 (00%)	02 (8.0%)	02 (2.0%)

Petechaie	06 (8.1%)	02 (8.0%)	08 (8.1%)
Purpura	07 (9.5%)	01 (4.0%)	08 (8.1%)
Bruises	09 (12.2%)	02 (8.0%)	11 (11.1%)
Total	74 (100%)	25 (100%)	99 (100%)

Table-II. Gender distribution in relation to clinical presentation

Gender	Bleeding time		
	Prolonged	Normal	Total
Male	76(73.8%)	04(44.4%)	80(71.4%)
Female	27(26.2%)	05(55.6)	32(28.6%)
Total	103(100%)	09(100%)	112(100%)

Table-III. Gender distribution in relation to bleeding time

Gender	WBCT		
	Prolonged	Normal	Total
Male	72(75%)	08(50%)	80(71.4%)
Female	24(25%)	08(50%)	32(28.6%)
Total	96(100%)	16(100%)	112(100%)

Table-IV. Gender distribution in relation to WBCT

Gender	PT/APTT		
	Prolonged	Normal	Total
Male	75(74.3%)	05(45.5%)	80(71.4%)
Female	26(25.7%)	06(54.5%)	32(28.6%)
Total	101(100%)	11(100%)	112(100%)

Table-V. Gender distribution in relation to PT/APTT

Gender	Thrombocytopenia		
	Yes	No	Total
Male	70(75.3%)	10(52.6%)	80(71.4%)
Female	23(24.7%)	09(47.4%)	32(28.6%)
Total	93(100%)	19(100%)	112(100%)

Table-VI. Gender distribution in relation to thrombocytopenia

Gender	Hypofibrinogemia		
	Yes	No	Total
Male	62(76.5%)	18(58.1%)	80(71.4%)
Female	19(23.5%)	13(41.9%)	32(28.6%)
Total	81(100%)	31(100%)	112(100%)

Table-VII. Gender distribution in relation to hypofibrinogemia

Gender	DIC		Total
	Yes	No	
Male	60(78.9%)	20(55.6%)	80(71.4%)
Female	16(21.6%)	16(44.4%)	32(28.6%)
Total	76(100%)	36(100%)	112(100%)

Table-VIII. Gender distribution in relation to DIC

DISCUSSION

Snake bite is a major problem and in Pakistan it is common in agriculture areas, it has been estimated that atleast 40,000 episodes of snake bite occur every year in Pakistan⁷⁻⁹. Alteration of whole blood clotting time have been observed in 48% of patients suffering from snake bite, whereas coagulopathy was a prominent feature in 38% in the same study done by Jorge et al¹⁰. In another study done by Amaral et al some patients presented with virtually no detectable fibrinogen levels¹¹.

The present study evaluated the vasculotoxic effects in patients with snake bite presenting at Liaquat University Hospital Hyderabad / Jamshoro. The highest frequency was observed in the age group of 12 to 40 years (82%) in that 72% were males and 28% were females. The predominance of male victims is due to frequent outdoor activities. This predominant male population also observed in the study by Hati AK, et al¹². Time interval between bite and admission in the hospital carries a prognostic importance, lesser the time interval better the prognosis¹³. The delay in seeking medical help is mainly due to home remedies and faith in local and regional health care practitioners before visiting to tertiary care medical centre and due to delay several victims undergo complications and die during transit to the hospital. In this study 70 cases reported within 6 hours of bite, 20 cases reported between 6-24 hours, 35 cases between 24-48 hours and 15 cases after 48 hours of bite. In current series 07 subjects expired and had complications like compartmental syndrome, ARF, intracranial bleed and those who required ventilatory support had presented after 12 hours of bite. This pattern of presentation was also found in the study by Jeyarajah R¹⁴. Present study showed that maximum cases of bites

occurred on lower extremity (37.14%) followed by upper extremity (28.57%), 42% incidence of bite on lower extremities was reported by Bhat RN study.¹⁵ Probably the higher incidence of snake bite on lower extremity is because people move around without any protection to their feet¹⁶.

In this study 90% of the cases are from rural areas. This correlates with study of Bhat RN (92%)¹⁵, Kulartne SAM (96%)¹⁷. This shows snake bite remains a major public health problem in rural population¹⁹. In present study 39% patients saw snake but none of them brought snake for identification. Pain at the site of bite was a common symptom 88%, while 90% and 85% pain was reported by Rodney E et al & Saini RK et al^{18,19}. Local swelling was present in 57% of cases, whereas it was 60% in the study by Virmani SK et al study²⁰. Blister formation was seen in 5.71% of cases, which is 3.9% in study of Rodney E et al study¹⁸. One patient had gangrene in a limb other than that bitten by the snake while it was 3% reported by Sathyanathan VP et al study²¹. Vomiting was observed in 22% of patients, haematemesis in 11%, Bleeding gums in 3 cases and haemoptysis in 16%. Virmani SK²⁰ in his study reported haematuria as the commonest (67.2%) presentation followed by bleeding from gums (36.2%), bleeding from injection site (38.7%), haemoptysis (18.1%), haemetemesis (28.4%), malena 52 (25.4%) and epistaxis (12.5%)². In present study epistaxis was observed in 10% cases. Renal failure was observed in 12 cases, all of these 12 cases were subjected to haemodialysis, out of which all recovered, Vermani SK, et al²⁰ reported 09 cases of acute renal failure, Saini et al¹⁹ has reported 11 cases of acute renal failure in their study. Mortality rate in Bhatia S, et al study²² was 1.96%, whereas our study showed a slightly higher mortality (07 cases). In this study, 65% cases needed 03 to 07 days of hospitalization while it was 3-5 days in the study conducted by Bhatia S, et al.²² Mean duration of Hospital stay was less in the study conducted by Lal P et al. (2001) at JIPMER Hospital Pondicherry as compared to this study²³. In present study most of snake bite victims were agriculture workers. Tropical countries snake

bites is an occupational disease affecting farmers plantation workers, hunters. Because agriculture is the main occupation of most rural dwellers they are at increased risk.

Coagulopathy is a clinically significant issue responsible for bleeding and fatal diseases. Snake venom forms fibrin venom causes unstable fibrin polymer vulnerable to fibrinolysis and phagocytosis by the reticuloendothelial system. As a result, venom leads to different types of coagulopathy, from defibrination, thrombocytopenia to DIC. The prevalence of coagulopathy was reported to be up to 38%²⁴. The prevalence of coagulopathy observed in this study (80%) was consistent with that in the previous research ((82.5%) and the prevalence of DIC in current series (76%) was also observed by other studies (74% and 70%)^{25,26}. Although the previous studies suggested that serious coagulopathy such as DIC rarely happened because venom was absorbed into the blood in only a small number of cases, in this study, the prevalence of DIC after poisonous snake bite was not considered to be low. In present study the PT/APTT was prolonged in 101 (90%) subjects, thrombocytopenia in 93(83%) patients and hypofibrinogemia in 81 (72%) individuals, the findings are consistent with they study by Khadwal A, et al and Li QB, et al^{27,28}. The coagulation tests disturbed as venom increases the clotting time and proteins digesting enzymes or thrombin like activity of venom may be one of the causes for prolongation coagulation tests (coagulopathy). The late presentation following snakebite is due to various social, cultural and biological factors like poor awareness, regional healing methods and lack of transport and late onset of symptoms. This has a significant impact on outcome. Therefore, it should be recognized that vasculotoxic effects due to snake bite can leads to various complications and early evaluation, appropriate management can save the patients to acquire life threatening complications induced by snake bite.

CONCLUSIONS

Snakebite is a major problem that can be easily

treated provided adequate knowledge is given to general population and anti-snake venom is administered timely. The government should try to inculcate knowledge to the general population, especially in rural areas about this health problem and its management thru health care providers and by the use of media.

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PREVIOUS RELATED STUDY

Kamran Zaheer Butt, Faheem Anwar, Mohammad Rizwan. SNAKE BITE; EXPERIENCE IN A FIELD HOSPITAL (Original) Prof Med Jour 17(2) 263-268 Apr, May, Jun 2010.

Manzoor Ahmed Faridi, Talat Bashir, Muhammad Farooq, MANAGEMENT OF COBRA SNAKE BITE; THE ROLE OF ANTICHOLINES-TERASE (Case Report) Prof Med Jour 11(1) 99-101 Jan, Feb, Mar, 2004.



ABILITY
is what you are capable of doing.
MOTIVATION
determines what you do.
ATTITUDE
determines how well you do.

Lou Holtz



AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Dr. Mohammad Asif Ansari	Contribution to conception and design, acquisition of data, analysis and interpretation of data	
2	Dr. Ahmed Hussain	Drafting the article and shares its expert research opinion and experience in finalizing the manuscript	
3	Dr. Nisar Ahmed Shah	Contributed in conception and interpretation of data and give his expert view for manuscript designing	
4	Dr. Syed Zulfiqar Ali Shah	Collection and acquisition of data analysis and interpretation of data and make it suitable for final revision and a corresponding author	
5	Dr. Zulfiqar Ali Qutrio Baloch	Analysis and interpretation of data Contributed in conception and shares its expert research opinion	