Original Research Article

A study of laboratory parameters prothrombin time and 20 minute WBCT in snake bite patients

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Abstract

Introduction: Since ancient times, snakes have been worshipped, feared and loathed in South Asia. Snake bite is a common occupational hazard of farmers, plantation workers, construction workers, snake charmers and hunters. With urbanization and deforestation, snake bite has become an important public health problem. As the problem is so underrated that, snake bite was finally included in WHO's list of neglected tropical diseases in early 2009.[2] The vast majority of snake bites are accidental in nature. **Aims and Objective:** To study the various Laboratory Parameters like Prothrombin Time and 20 Minute WBCT In Snake Bite Patients. **Methodology:** After approval from institutional ethical committee, this Descriptive study carried out at Tertiary care hospital during 2 years (September 2012-September 2014). Total patients were 112. **Results:** PT was raised in 85 (75.89%) cases and APTT in 77 (68.75%) cases. Out of 85 patients with raised PT, 19 (16.96%) had incoagulable plasma and rest had PT more than 16seconds. Amongst the 77 patients with raised APTT, 19 (16.96%) had incoagulable plasma and remaining had APTT higher than 32seconds but not incoagulable. Patients reaching to hospital between 1 to 6 hours and after more than 6 hours accounted for 67 and 27 respectively, out of them PT was raised in 51 (76.12%) and 24 (88.89%) patients. This was statistically significant. Sensitivity of the20 Minute WBCT test was 50% and specificity was 89.13%. **Conclusion:** 20 minute whole blood clotting test is having low sensitivity for detecting coagulopathy and should not over-ride clinical assessment based decisions about antivenom administration. More attention should be given to standardize the conditions, timing, use and interpretation of the current 20 WBCT.

Keywords: Prothrombin Time, 20 Minute WBCT, Snake Bite.

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INTRODUCTION

Since ancient times, snakes have been worshipped, feared and loathed in South Asia.[1] Snake bite is a common occupational hazard of farmers, plantation workers, construction workers, snake charmers and hunters. With urbanization and deforestation, snake bite has become an important public health problem. As the problem is so underrated that, snake bite was finally included in WHO's list of neglected tropical diseases in early 2009.[2] The vast majority of snake bites are accidental in nature. Homicide may rarely be committed, for instance by throwing a venomous snake on sleeping victim or slipping it under the bathroom door or through a window when a 3 person is bathing.[3] So every case of snake bite is registered as medico legal case (MLC). Snakes have wide range of habitat and prey species. All snakes are predatory carnivores, none is vegetarian. Since snakes are preyed upon by other animals they tend to be secretive and have evolved many survival strategies. Many species are mainly nocturnal (night hunters) e.g. kraits, but other species are mainly diurnal (day-time hunters). By understanding about the habits of snakes, simple precautions can be adopted to reduce the incidence of snake bites.[4] About 2500-3000 species of snakes exist in the world. Most venomous snakes are found in Asia as compared to the other area of the world.[5] India has over 250 species and subspecies, out of which 50 are

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poisonous.[6] The families of poisonous snakes include Elapidae, Viperidae and Hydrophidae[7,8] which are responsible for neurotoxicity, vasculotoxicity and myotoxicity respectively.[9]Viperidae family includes two subfamilies: Viperinae (classic vipers) and Crotalinae (pit vipers).[8]Elapidae family includes cobras and common kraits. Hydrophidae are the sea snakes Viper bites are more common than the other venomous snake bites in human beings.[8] Viper bites are responsible for vasculotoxicity leading to bleeding tendencies and coagulation defects. These bleeding diatheses are 4 mostly caused by consumptive coagulopathy, anti coagulation, fibrinolytic or may be due to direct effect of snake venom on platelet aggregation.[10] Early detection of vasculotoxicity and prompt institution of anti venom therapy can prevent serious complications due to snake envenoming. Presence of coagulopathy is the absolute indication for anti-venom administration, which is the specific treatment of snake bite. Coagulation parameters are also important to monitor the effect of anti snake venom and follow up of the patient. So the study is planned to study the pattern various laboratory profile changes seen in snake bite patients.

AIMS AND OBJECTIVE

To study the various Laboratory Parameters like Prothrombin Time and 20 Minute WBCT In Snake Bite Patients.

MATERIAL AND METHODS

After approval from institutional ethical committee, this Descriptive study carried out at Tertiary care hospital during 2 years (September 2012-September 2014).

Inclusion Criteria

All the patients (irrespective of toxicity) presenting to the emergency ward with history of snake bite, who had not received ASV were included in the study.

Exclusion Criteria

Patients with unknown bite, Pregnant females, Patients with known coagulation disorder, liver disease and patients on anticoagulants. All patients admitted in the emergency ward with history of snake bite were included in the study (regardless of poisonous or non-poisonous snake bite). History of all patients as per preformed Proforma was taken along with detailed clinical examination of the patient. Identification of the species of bitten snake was done on the basis of the dead snake brought to hospital, by the description of the snake provided or identification by showing photographs of the snakes. In case where patient or relative could not see the snake, identification of species and its toxicities were defined for each case by using reference book of toxicology (Parikh's textbook of Medical Jurisprudence, Forensic Medicine and Toxicology). Sensitivity of the test was 50% and specificity was 89.13%.

RESULTS

Table 1: Results of laboratory tests in vasculotoxic bites (n=112)

Interpretation of laboratory tests	Laboratory tests	
	Prothrombin time	Activated partial thromboplastin time
Not raised	27(24.11)	35(31.25)
Raised but coagulable plasma	66(58.93)	58(51.79)
Incoagulable plasma	19(16.96)	19(16.96)
Total	**112(100)**	**112(100)**

Figures in parentheses show percentages To be more precise about the type of coagulation pathway involved prothrombin time (PT) and activated partial thromboplastin time (APTT) are measured. PT was raised in 85 (75.89%) cases and APTT in 77 (68.75%) cases. Out of 85 patients with raised PT, 19 (16.96%) had incoagulable plasma and rest had PT more than 16seconds. Amongst the 77patients with raised APTT, 19 (16.96%) had incoagulable plasma and remaining had APTT higher than 32seconds but not incoagulable.

Table 2: Association between bite to needle time and derangement of prothrombin time

Bite to needle time	Number of cases		Total
	PT raised	PT not raised	
≤1hr	10 (55.56)	08 (44.44)	18 (100)
1hr to 6hrs	51 (76.12)	16 (23.88)	67 (100)
>6hrs	24 (88.89)	03 (11.11)	27 (100)
Total	**85 (75.89)**	**27 (24.11)**	**112 (100)**

Figures in parentheses show percentages, $\chi^2 = 6.56$, df = 2, p = 0.04, Statistically significant

We studied the association between the number of patients showing raised PT and time required for hospitalization of patient after the bite (Bite to needle time).18 patients reached hospital within 1hour, out of them 10 (55.56%) had raised PT while rest had normal PT. Patients reaching to hospital between 1 to 6 hours and after more than 6 hours accounted for 67 and 27 respectively, out of them PT was raised in 51 (76.12%) and 24 (88.89%) patients. When association was studied

it was found that statistically significant correlation was present between bite to needle time and number of patients with raised PT.

Table 3: Determination of sensitivity and specificity of 20 WBCT (by considering INR as standard)

20 WBCT Results	Presence of coagulopathy based on INR range		Total
	Coagulopathy (INR >1.5)	Non-coagulopathy (INR ≤1.5)	
Positive	33	05	38
Negative	33	41	74
Total	**66**	**46**	**112**

Sensitivity = 50%, Specificity 89.13% By considering INR (PT-INR) as a standard test to determine the presence of coagulopathy, the utility of 20 WBCT was assessed to analyse coagulopathy in the vasculotoxic patients. INR >1.5 were taken as cut off for determining presence of coagulopathy. When statistically analysed, sensitivity of the test was 50% and specificity was 89.13%. Sensitivity of the 20 WBCT was 50%, it denotes that, the test can diagnose correctly only 50 % cases that have disease and remaining 50% are shown as negative. In the present study, true positive cases were determined by standard test *viz.* PT-INR. Specificity of the 20 WBCT was 89.13%; it suggests that all the tests diagnosed as positive according to 20 WBCT were not true positive. In our study 38 cases were having positive 20 WBCT, out of them 5 were false positive (i.e. 5 cases were diagnosed as not having coagulopathy by PT-INR test)

DISCUSSION

In the present study, 75.89% of the patients showed deranged PT, which was similar to the Mahmood*et al*[9] (70.00%) studies. Monteiro *et al*[8], Ramamurthy *et al*[11], Harshavardhana *et al*[12] and David *et al*[13] found deranged PT in 32.30%, 40.00%, 56.00% and 47.50% of patients respectively. In our study, deranged APTT was seen in the 68.75% of patients. Mahmood*et al*[9] had similar results with71.30% of patients having deranged APTT. Monteiro *et al*[8], Ramamurthy *et al*[11], Harshavardhana *et al*[12] and David *et al*[13] found deranged APTT in 29.00%, 40.00%, 62.00% and 32.50% of patients respectively. Defects in extrinsic and intrinsic pathways of coagulation lead to prolongation of PT and APTT respectively. Various proteins (like prothrombin activators, thrombin like enzymes, phospholipases, factor X activating proteins etc.) present in the snake venom are responsible for block at different levels of coagulation or it may cause excessive clot formation leading to consumption coagulopathy. In most of the cases PT and APTT both are raised, indicating defect in common pathway or consumption coagulopathy. In present study, these coagulation abnormalities were found in the vasculotoxic snake bites (that were diagnosed clinically), but not in non-vasculotoxic bites. But not all the patients with vasculotoxic bites, showed the deranged coagulation profile tests.

Blood investigation results	Monteir *et al* (2012)	Mahmood *et al* (2010)	Ramamuthy *et al* (2014)	Harshvardhana *et al*[12] (2014)	Devid *et al*[13] (2012)	Present Study
Raised PT	32.30%	70.00%	40.00%	56.00%	47.50%	75.89%
Raised APTT	29.00%	71.30%	40.00%	62.00%	32.50%	68.75%

Association was between bite to needle time and number of patients with raised PT studied it was found that statistically significant correlation was present between bite to needle time and number of patients with raised PT. Sam *et al*[14] studied various parameters among snake bite patients, and they stated that there was a significant correlation between time lapsed to reach hospital and severity index. According to them patients who were admitted late to hospital had high severity score, poor outcome and highernumber of complications like renal failure, breathing difficulty, cellulitis, abnormal PT and APTT. In their study, mortality, morbidity and complications were higher in patients who reached the hospital late. Various parameters of coagulation profile viz. PT, APTT, platelet counts and fibrinogen levels, were one of the determinants of severity index in the study by Sam *et al*[14]. In the other words Sam *et al*[14] reported that there is correlation between bite to needle time and presence of coagulopathy. Similarly, Dharod *et al*[6], Chaudhari *et al*[12], Saravu *et al*[79] and Mathivani *et al*[80] studied various parameters of snake bite separately in different regions, finally all concluding that bite to needle time had significant correlation with complications developed in snake bite patients. Incidence of complications is directly proportional to the duration for which venom was present in the blood, prior to its neutralization by ASV. Increase in complications can be explained by the late arrival of patients to hospital. So the snake venom responsible for all these complications must be neutralised early by anti snake venom (ASV). Furthermore, ASV can neutralize only circulating snake venom and as the time elapses, more and more snake venom is bound to the target tissues, becoming less amenable to neutralization by ASV. So it is important to make people aware of the fact that, seeking early medical help is very important. Moreover medical practitioners should also be sensitised about the early administration of ASV. Number of complications like renal failure,

breathing difficulty, cellulitis, abnormal PT and APTT. In their study, mortality, morbidity and complications were higher in patients who reached the hospital late. Various parameters of coagulation profile viz. PT, APTT, platelet counts and fibrinogen levels, were one of the determinants of severity index in the study by Sam *et al*[14]. In the other words Sam *et al*[14] reported that there is correlation between bite to needle time and presence of coagulopathy. Similarly, Dharod*et al*[6], Chaudhari *et al*[12], Saravu *et al*[16] and Mathivani *et al*[17] studied various parameters of snake bite separately in different regions, finally all concluding that bite to needle time had significant correlation with complications developed in snake bite patients. Incidence of complications is directly proportional to the duration for which venom was present in the blood, prior to its neutralization by ASV. Increase in complications can be explained by the late arrival of patients to hospital. So the snake venom responsible for all these complications must be neutralised early by anti snake venom (ASV). Furthermore, ASV can neutralize only circulating snake venom and as the time elapses, more and more snake venom is bound to the target tissues, becoming less amenable to neutralization by ASV. So it is important to make people aware of the fact that, seeking early medical help is very important. Moreover medical practitioners should also be sensitised about the early administration. Prothrombin time is a simple test which can detect defect in the extrinsic pathway of coagulation cascade. PT will be prolonged if the plasma levels of any of the requisite factors are below 10% of normal. PT is relatively more sensitive and it can be prolonged even before the onset of clinical manifestations. So in our study we studied the sensitivity and specificity of the 20 WBCT by considering INR (PT-INR) as a standard test for determining coagulopathy. Patients with INR more than 1.5 were considered as having coagulopathy. An INR cut-off of 1.5 was chosen because this was above the normal range and higher than any non-envenomed patients. According to present study sensitivity of the 20 WBCT was 50% and specificity was 89.13%.Out of 38 patients with positive 20 WBCT, 33 had INR more than 1.5. There were 5 false positive cases when compared to the results of INR. While out of 74 patients with negative 20 WBCT, 33 had coagulopathy and indicating that there were 33 false negative cases.

Study	Sensitivity of 20 WBCT	Specificity of 20 WBCT
Isbister *et al*[18](2013)	40%	100%
Present study	50%	89.13%

According to Isbister *et al*[18], sensitivity and specificity of 20 WBCT was 40% and 100% which does not match our study. This may be due to the differences in the procedure according to which the test was carried out. Number of factors affect the results of the test which include different volumes of blood samples used, use of bottle or syringe for test, use of different sizes of test tubes/ bottles and tests done by trained investigator or not.20 WBCT is the simple, relatively inexpensive, bedside test. It is routinely done in all snake bite patients in developing countries, especially in rural areas, where expensive tests like PT and APTT are not available and not affordable. It is done to determine the clinically significant coagulopathy and for the decision regarding the administration of ASV. Sequential testing is also useful for determining repeat dose of ASV. Sensitivity of the test was 50% (in the present study), so there will be more false negative cases, which delays ASV administration in approximately half of the patients. Due to the low sensitivity of test, the purpose of test to determine coagulopathy and in turn ASV administration was not fulfilled. Hence, whenever possible more sensitive tests like PT should be used. Though sensitivity of the 20 WBCT is low, the test could play a pivotal role in remote areas and developing countries. In order to increase the sensitivity and specificity of the test, special attention should be given for standardizing the test. Clinicians should be made aware about the limited sensitivity of the test and all the patients with clinical features of envenomation should receive antivenom.

CONCLUSION

Traditionally an abnormal 20 minute whole blood clotting test is taken as marker of coagulation abnormality. But it has low sensitivity for detecting coagulopathy and should not over-ride clinical assessment based decisions about antivenom administration. More attention should be given to standardize the conditions, timing, use and interpretation of the current 20 WBCT. Further work is required to develop such a test that performs to an acceptable standard in the field and delayed administration of antivenom is minimised.

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