



Evaluation of Whole Blood Clotting Time in Snake Bite Patients

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Type of Publication: Original Research Paper

Conflicts of Interest: Nil

Abstract

Introduction: Numerous species of snakes are found in the tropical and subtropical countries including India, out of which some of the species are known to be poisonous. High rate of morbidity and mortality are associated with snake bites due to local and systemic complications. The snake venom has a toxic effect which triggers enzymatic pathways causing vascular endothelium injury and coagulopathy. Whole blood clotting time helps in detection of coagulopathy.

Aims and Objectives: To compare the outcome of WBCT evaluation at both 20 and 30 min after collection in snake bite patients.

Materials and Methods: A prospective study was conducted on 50 patients with history of snake bite who came to Mahatma Gandhi Mission's Hospital, Navi Mumbai. WBCT results at both 20-min (WBCT20) and 30-min (WBCT30) were assessed serially.

Results: The mean age of the study population was 39 years. Male to female ratio was 1.78. In the present study, WBCT interpretation showed that 18 cases at 20 minutes and 16 cases at 30 minutes indicated coagulopathy. Deranged PT and INR were noted in 21 and 19 cases. In five cases WBCT was prolonged though INR was less than 1.5 and WBCT was normal in 2 cases in spite of INR more than 1.5. Five patients presented with severe bleeding manifestation.

Conclusion: WBCT sequential evaluation will help in bedside diagnosis and monitoring of venom-induced coagulopathies. There is also a possibility of discrepancy in the sensitivity of WBCT20 and WBCT30 in timely detection of coagulopathy and hence correlation with clinical symptoms, prothrombin time, International normalized ratio (INR) and Activated partial thromboplastin time (APTT) is necessary.

Keywords: NIL

Introduction

Snakebite is a universal emergency encountered in day-to-day medical practice, especially in the tropical and sub-tropical countries. Morbidity and mortality due to snakebite is a preventable health hazard if the patient is investigated and treated on time. Cobra bite can cause death of the patients within minutes to few hours. However, the patient may recover if adequately supervised on time and treated with antsnake venom. More commonly seen are viper

bite, which are known to cause death occurs over few days. Even in the absence of death, the morbidity in these cases could be high. Therefore, there is a need for precise and quick initiation of treatment.

Around 300 varieties of snakes which include 67 varieties of Elapidae (cobras and kraits) and Viperidae (Russel viper, pit viper and green pit viper) have been identified in Asia [1]. Every year around

1.2 million- 5.5 million cases of snakebite occur worldwide, which include 421,000-1,841,000 cases of poisoning and 20,000-94,000 deaths [2, 15].

Four major species of toxic snakes found in India are accountable for life-threatening envenomation. These include: Indian cobra (*Naja naja*), common krait (*Bungarus caeruleus*), Russell's viper (*Daboia russelii*) and saw-scaled viper (*Echiscarinatus*) [3]. Patients with Viperidae envenomation present with clinical feature of ecchymosis, oliguria, pulmonary edema, and bleeding whereas those with Elapidae group and Russell viper envenomation present with neurological signs and symptoms, such as, altered sensorium, cranial nerve involvement and peripheral motor weakness [4, 5].

Some of the local effects of snake bite can vary from mild local pain to extensive tissue necrosis. The most common clinical manifestation of snake bite is coagulopathy resulting in death [6]. Snake bite is a well known cause of disseminated intravascular coagulation (DIC). The snake venom affects the clotting factors of the human clotting cascade, and either activates or inhibits a specific reaction in the pathway. Neurotoxic snake bite can lead to block in neurotransmission at synapses [7]. Hemorrhagic snake bite leads to an increase in the vascular permeability as a result of the hemorrhagic toxins. Myotoxic snake bites act on the skeletal muscle membrane and cause destruction [8]. Renal injury can be as a result of direct action of the toxins or secondarily due to myotoxicity.

Whole Blood Clotting Test (WBCT) helps to monitor hemotoxicity in snake bite patients and also to calculate the dose of antivenom. In the year 1903, Lee and White were the ones to introduce the WBCT20 test [9].

The WBCT acts as an indicator of envenomation in patients with history of snake bite and points towards the possibility of coagulopathy [13, 14]. It is a simple test which involves collection of a few mL of blood in a clean and dry glass test tube and leaving it undisturbed for 20 minutes followed by 30 minutes to discover whether the blood has clotted. This test can be extremely helpful when the patient presents with only mild symptoms in the early phase or before the onset of the hemorrhagic syndrome.

Grading scale for WBCT interpretation is as follows:

1. Grade 0: Stable, solid clot (normal coagulation);
2. Grade 1: Unstable or friable clot that disintegrates rapidly upon inversion of the test tube (abnormal coagulation);
3. Grade 2: No clot formation or coagulation

The clot formed can be graded accordingly for evaluation of WBCT. [10]

WBCT is a simple and effective, low cost procedure that can be performed bedside and is helpful in initial assessment as well as prognosis throughout the course of treatment. It can also aid in evaluation of efficacy of antivenom therapy.

Material and Methods:

A prospective study was conducted in the Central Laboratory, Department of Pathology of M.G.M Hospital, Kamothe, Navi Mumbai where 50 cases of snake envenomation were analyzed for WBCT over a period of 6 months. The aim of the study was to evaluate the Whole Blood Clotting Test (WBCT) at intervals of 20 minutes and 30 minutes in snake bite patients for detection of coagulopathy.

Inclusion Criteria:

1. Patients with history of snake bite in the age group - 10 to 75 years
2. Snake bite patients willing for blood collection.

Exclusion Criteria:

1. Uncooperative patients, not willing for blood collection.
2. Patients who are already undergoing treatment after diagnosis.
3. Patients presenting after 72 hours of snake bite.
4. Patients with coagulopathy due other causes such as sepsis, chronic liver disease, or bleeding diathesis –thrombocytopenia.
5. Patients who are already receiving anti-coagulants.

Disposable 10 mL plain red top vacutubes of NIDOVAC, 16 × 100 mm were used. Approximately 2 mL of fresh venous blood was collected in a fresh,

clean and dry glass tube and kept undisturbed at room temperature for 20 minutes. Later the tube should be tilted gently to check if blood is still liquid and if so then 20WBCT was noted as positive. The observation was repeated and tube gently tilted again at 30 minutes. If the blood was still liquid then 30WBCT was also considered positive. The grading scale used for serial WBCT interpretation was as follows:

1. Grade 0: normal coagulation(solid, stable clot);

2. Grade 1: abnormal coagulation (unstable or friable clot that disintegrates rapidly upon inversion of the test tube);
3. Grade 2: no coagulation

Results:

In the present study, out of the 50 patients who came to the casualty with history of snake bite, 18 cases (36%) were females and 32 cases (64%) were males. Male to female ratio in the patients was noted as 1.78:1.

Table 1: Age - wise distribution of the patients (n=50)

Age (Years)	Number of Cases	Percentage (%)
15-24	9	18
25-34	5	10
35-44	12	24
45-54	18	36
55-64	6	12

Majority of the patients were seen in the age group of 45-54 years, i.e., 18 cases (36%) followed by 12 cases (24%) in the age group 35- 44 years. The mean age of the study population was 39 years.

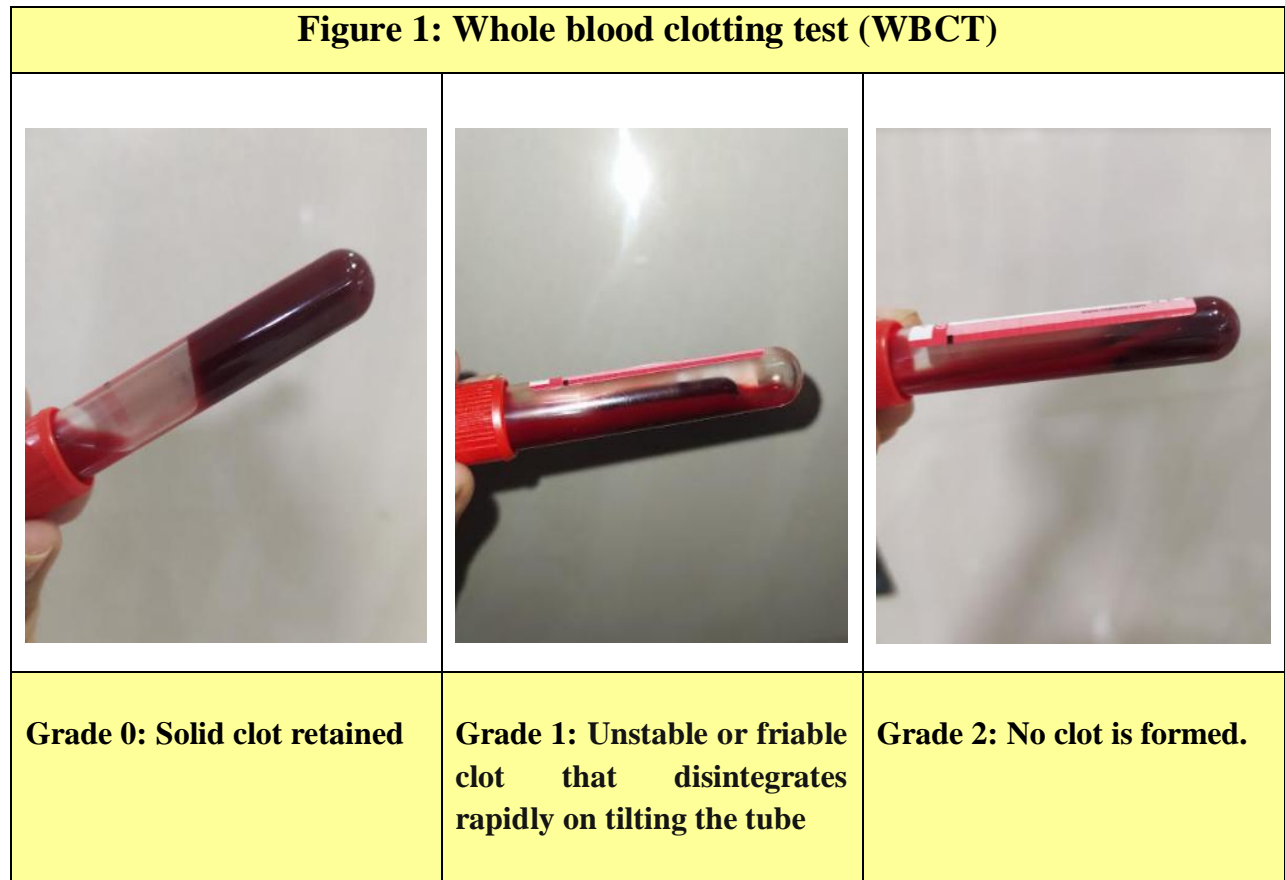


Table 2: Grading of WBCT (Whole blood clotting time) in minutes of patients studied

WBCT	Grade 0	Grade 1	Grade 2	Total
WBCT 20	28	4	18	50
WBCT 30	31	3	16	50

On serial assessment of Whole blood clotting time at 20 and 30 minutes, i.e., WBCT20 and WBCT30, we observed that 28 cases presented normal coagulation at 20 minutes and 31 cases at 30 minutes. Four cases at WBCT20 and three cases at WBCT30 were found to have a friable clot with delayed coagulation. It was found in the present study that 18 cases at 20 minutes and 16 cases at 30 minutes showed no coagulation at all. In one case, WBCT was noted as Grade 1 at 20 minutes and Grade 0 at 30 minutes. Two cases that

were grade 2 at WBCT20 turned out to be grade 0 at WBCT30.

Maximum number of patients showed normal coagulation (Grade 0), 56% at 20 minutes and 62% at 30 minutes. These patients may have had snake bite injury due to non-venomous snake. Least number of cases were seen in Grade 1 category which included only 4 cases at WBCT20 and 3 cases at WBCT30. It was observed that no coagulation was found in 36% of the patients at 20 minutes and in 32% cases at 30 minutes indicating urgent need of therapy.

Table 3: Hematological Parameters in patients of Snake bite (n=50)

Hematological Parameters	Number of Patients	Percentage
Hb less than 10 g/dL	5	10
Wbc count > 10,000/ cumm	25	50
Platelet count < 1 lakh/cumm	18	36
PT > 15 sec	21	42
INR > 1.5	19	38
APTT > 30 sec	16	32

On evaluating the hematological parameters in these 50 patients, only 5 patients (10%) had low hemoglobin value of less than 10 g/dL, 25 patients (50%) showed a total leucocyte count of more than 10,000/cumm and 18 patients (36%) were reported to have thrombocytopenia with decreased platelet count of less than 1 lakh/cumm. It was observed that prothrombin time was more than 15 seconds in 21 cases (42%) and International normalized ratio was more than 1.5 in 19 cases (38%). It was also found

that raised APTT of more than 30 seconds was noted in 16 cases (32%) of all the patients.

Out of 50 patients, 12 patients presented with vasculotoxic snake bite and 2 patients with neurotoxic snake bite. In case of three patients, the relatives gave history of snake bite by russel viper species. Five patients with severe bleeding manifestation were transfused with Fresh frozen plasma.

Discussion

The snake venom contains toxins which interact with the fibrinolytic system and clotting mechanism in the human body. Local and systemic complications in snake bite that occur are linked to toxins in snake venom [17, 18]. Acute kidney injury, neurological complications requiring ventilator support, infarction and disseminated intravascular coagulation are some of the serious adverse effects seen in cases of envenomation. Mortality rate due to snake bites in developing countries like India with large number of farmers working in rural areas is more than the developed countries [16].

In the present study, a disparity was observed in the results of WBCT and other coagulation parameters in seven cases out of 50(14%). Five cases showed prolonged WBCT though INR was less than 1.5 and in two cases WBCT was normal in spite of INR more than 1.5. Three cases showed difference in results at 20 and 30 minutes. In one case, WBCT was noted as Grade 1 at 20 minutes and Grade 0 at 30 minutes. Two cases that were grade 2 at WBCT20 turned out to be grade 0 at WBCT30. Other 47 cases showed similar result at both times.

In a study by Benjamin *et al.*, WBCT results were alike at both the reading times similar to our study. 14 patients out of 17 patients showed discrepancies between WBCT20 and WBCT30 results at the time serial evaluation. Completely contradictory results, such as normal clot at WBCT20 and no clot formation at WBCT30 or a marked difference in the quality of the clot, for example, no clotting activity at WBCT20 and an unstable partial clot at WBCT30 were the observations in cases where inconsistency was noted. In three situations WBCT discrepancies were observed to occur most commonly. These are initial normalization of hemostasis following antivenom therapy, detection of a secondary resumption of coagulopathy and final restoration of hemostasis after a secondary resumption [10].

A study done by Isbister *et al.* showed that WBCT20 evaluation was done in 140 Russell's viper bites with coagulopathy and was positive in 56/140 [sensitivity 40%]. Delayed antivenom administration occurred in case of a negative WBCT20. Initial WBCT20 was negative in nine non-envenomed patients and 48 non-venomous snakebites [specificity: 100%] [11].

A study conducted by Rajeswari G *et al.* showed that the population had a mean age of 42.58 years and the male to female ratio was found to be 3.85:1. Local symptoms occurred in all the patients, systemic symptoms in 94%, bleeding manifestations in 82%, acute renal failure in 51.9%. It was observed that WBCT was prolonged with an INR of less than 1.5 in 10 cases whereas in seventeen patients WBCT turned out to be normal in spite of INR more than 1.5. This is in accordance with results of our study [12].

Conclusion

WBCT sequential evaluation will help in bedside diagnosis and monitoring of venom-induced coagulopathies. Evaluation at both 20 and 30 minutes of WBCT was included to reduce the number of false negatives or false positives. There is also a possibility of discrepancy in the sensitivity of WBCT20 and WBCT30 in timely detection of coagulopathy and hence correlation with clinical symptoms, prothrombin time, International normalized ratio (INR) and Activated partial thromboplastin time (APTT) is necessary. Hematological parameters are of paramount importance in evaluating snake bite coagulopathy and reducing the morbidity and mortality rate following envenomation. Those patients detected with coagulopathy require close monitoring while providing therapeutic management and adjusting dose of antivenom to prevent complications. WBCT can always be used as an easily accessible and inexpensive bedside test with rapid results especially and more importantly in remote areas where a tertiary care center is not available nearby.

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