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Amended prothrombin time as a diagnostic perceptive in HIV infected patients

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Abstract

Background: HIV infection is a serious disorder of the immune system and is associated with a wide range of haematological abnormalities including coagulation defects. Basic coagulation parameters like prothrombin time, partial thromboplastin time and thrombin time gets altered in HIV infected patients.

Objective: The objective of the study is to analyze prothrombin time among HIV infected patients.

Methods: Study group consisted of 15 HIV infected patients and control group consisted of 15 healthy volunteers. Blood sample of 2ml was collected into sodium citrate anticoagulant containers from both the groups by venepuncture. The blood samples were processed and evaluated for prothrombin time. The results were tabulated and analyzed using unpaired t-test.

Results: Results showed a significant increase in prothrombin time values in the study group when compared to the control group.

Conclusion: Since the basic coagulation test like prothrombin time is prolonged in HIV infected patients, it can be used as a prospective screening test to measure the quality of coagulation and to assess the possibility of complications in HIV infected patients.

Keywords: coagulation defects, hematopoesis, HIV infection, prothrombin time

Introduction

Human immunodeficiency virus infection is a serious disorder of the immune system in which the normal immunity against infection breaks down leading to fatal conditions [1]. HIV infection is caused by human deficiency virus which was first identified in 1983. Globally the phenomenon of HIV is best viewed as a pandemic affecting nearly all the countries of the world [2]. HIV infection is notorious to have been related to a wide range of haematological abnormalities including coagulation defects. As HIV infection progresses, the coagulation abnormalities would increase since they have impact on endothelial dysfunction and liver damage which may result in clotting impairment [4]. Also, there exist some abnormalities in the fluid phase of the coagulation cascade that may lead to bleeding in the HIV patient [9]. Prothrombin time is a haematological test that measures the quality of extrinsic pathway of coagulation which detects deficiency or inhibition of clotting factors. Therefore, it may get altered in HIV infected patients and has a specific diagnostic role in assessing the severity in HIV patients [3]. Our study aimed to analyze prothrombin time among HIV infected patients and to implicate prothrombin time as screening test to measure the quality of coagulation.

Materials and Methods

Study Design and Subjects: The study was conducted on patients with HIV infection compared with controls that were age and sex matched normal healthy individuals.

Selection Criteria

Inclusion criteria: Study group included 15 confirmed HIV seropositive patients in the age group 35-75 years and control group included 15 age and sex matched healthy subjects.

Exclusion criteria: Patients with complications like hemophilia, liver diseases, renal diseases and inflammatory conditions that interfere with hemostatic mechanism and patients undergoing HAART treatment and those who are smokers and alcoholics, pregnant and lactating women were excluded from this study.

Sample collection

2ml of venous blood was drawn using sterile disposable syringe under aseptic conditions from antecubital vein of all the subjects and dispensed into sodium citrate anticoagulant containers. The plasma was separated by centrifugation at 3000 rpm for 3 minutes. The samples were processed and evaluated for prothrombin time by photo optical clot

detection method using fully automated analyser, 'Robonik Prietest' by Robonik India PVT. LTD.

Statistical Analysis

Mean values of prothrombin time in both the groups were analysed using statistical software SPSS version 17. The unpaired t-test was applied and results were tabulated and analyzed with statistical package. The data was expressed as mean and in the entire tests P (probability) value ≤ 0.05 was taken to be statistically significant.

Results

Results showed a significant increase in prothrombin time values in the study group when compared to the control group. The difference between prothrombin time values in both the groups was statistically significant (p<0.0001) [Table 1] [Graph 1].

Discussion

HIV infection is a complex infectious disease that causes a serious disorder of immune system in which normal immunity against infection breaks down [1]. Heterosexual transmission remains the dominant mode of transmission and accounts for 85% of all HIV infections [8]. It is also associated with a wide range of haematological abnormalities including coagulation defects. The origin of haematological disorders in HIV infection remain incompletely understood, but has been endorsed to dysfunctional hematopoiesis in bone marrow caused by several factors. These incorporate severe nutritional stress in HIV infection, suppression of marrow by invading opportunistic infections and chronic diseases associated changes [2]. It is well established that 20-80% of the people in different parts of the world who have HIV infection do not know their HIV status [7]. The most important biomarkers of disease stage and progression in HIV infected patients are CD4 count and HIV RNA concentration. However, there are other factors like total lymphocyte count, white blood cell count, hematocrit and coagulation tests have been proposed as alternative markers of the disease [6].

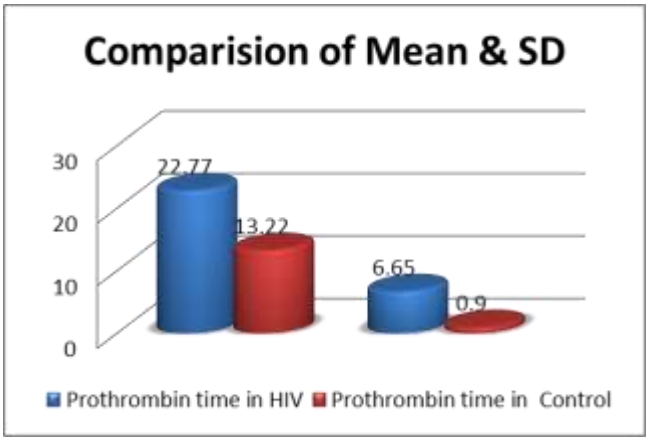
Prothrombin time is a haematological test that measures factors II, V, VII, X and fibrinogen. It is the time taken by the plasma to clot after addition of tissue factor [5]. It measures the quality of extrinsic pathway of coagulation which detects deficiency or inhibition of clotting factors [4]. The cause for defect may be due to host, drug and viral factors. Host factors include age, intravenous drug abuse, CD4 count, presence of opportunistic infections, associated malignancies, acquired hypercoagulable state and endothelial dysfunction [3]. As HIV infection progresses, endothelial dysfunction and liver damage will increase and may result in severe clotting impairment. In HIV infection, the liver gets affected. The liver is the major organ responsible for the synthesis of most coagulation factors and infection of the liver by HIV can lead to abnormal production of coagulation factors.

High levels of plasma von Willebrand factor have been reported in HIV disease and might be indicative of activated endothelium. Endothelium is involved in important homeostatic mechanisms of non-thrombotic vascular surfaces, vascular tone regulation and immunomodulation. Injured endothelium leads to localized inflammatory response of which the direct consequence is the occurrence of occlusive thrombotic events mediated between leucocyte recruitment and platelet adhesion and aggregation, blood clotting activation and fibrinolysis derangement. HIV infection associated endothelial dysfunction may therefore result in activation and consumption of coagulation factors and ultimately coagulation defect [4]. The results in our study showed a significant increase in prothrombin time values when compared to the control group. The difference between prothrombin time values in both the groups was statistically significant (p<0.0001). This indicates that endothelial activation is mainly responsible for the increased PT. Another possible reason might be due to disturbance in coagulation cascade. Factor VII is the only coagulation factor defect that PT detects. Baker *et al* (13) reported that tissue factor (TF) released by subendothelial cells during vascular damage, binds to circulating factor VII with formation of VIIa. The TF: VIIa complex activate X to Xa and this proceeds through the usual coagulation cascade. Since endothelial cell dysfunction is observed in HIV infection and the function of factor VII is disturbed, the coagulation cascade gets altered. It also seems likely that PT could be used as a means of HIV disease progression in places where financial resources are limited to afford for CD4 count, just as anaemia is used as a marker of disease progression [4].

Table 1: Mean and standard deviation values of prothrombin time in both groups.

Parameter	Study group Mean±SD	Control group Mean±SD	P value
Prothrombin time	22.77±6.65	13.22±0.9	<0.0001S*

S*- Significant, NS – Not Significant



Graph 1: Mean and standard deviation values of prothrombin time in both groups.

Conclusion

HIV infection is notorious to have been related to a wide range of haematological abnormalities including coagulation defects. HIV infected individuals can be screened for those defects which may become more severe as the disease advances. Since the results showed a significant increase in

prothrombin time values in the study group, the basic coagulation tests like prothrombin time can be used as screening test to assess severity and to measure the quality of coagulation.

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