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Coagulation Impairment in Type 2 Diabetes Mellitus

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Abstract

Background: Complication of diabetes mellitus (DM) includes coagulation impairment. Hypercoagulable state in patient with DM may accelerate thromboembolic risk for cardiovascular disease (CVD). **Objective:** To assess Prothrombin Time and Activated Partial Thromboplastin Time in type 2 diabetes mellitus for observing their coagubility status. **Methods:** This cross sectional study was conducted in the Department of Physiology, Dhaka Medical College, Dhaka from July 2013 to June 2014. One hundred male patients with type 2 diabetes mellitus aged 40-60 years and one hundred age, BMI matched healthy subjects were included as control in this study. Patients were selected from BIRDEM, Dhaka. Prothrombin Time (PT), Activated Partial Thromboplastin Time (APTT) were estimated by auto analyzer. For statistical analysis unpaired student't test was used. **Results:** In this study PT and APTT were significantly (P<0.001) lower in diabetes mellitus than those of control group. **Conclusion:** From this study, it may be concluded that diabetic patients are prone to develop coagulation impairment.

Key words: Prothromin time, Activated partial thromboplastin time, cardiovascular disease, diabetes mellitus.

Introduction

Diabetes mellitus (DM) is characterized by hyperglycemia accompanied with the biochemical alterations in carbohydrate, protein and lipid metabolism[1]. According to WHO, diagnostic criteria of diabetes mellitus are fasting blood glucose e"7.0 mmol/l, and 2 hour after glucose ≤ 1.11 mmol/l and $HbA_{1c} \leq 6.5\%$[2].

Diabetes mellitus is a major global health problem. Prevalence of diabetes in Bangladesh was found 8.3% in the year of 2011, among them 15.2% in urban and 8.3% in rural population[3,4].

Cardiovascular disease (CVD) is the leading cause of disability and premature mortality in patients with diabetes[5]. About 80% patients with diabetes may die due to thromboembolic CVD[6].

Coagulation abnormalities with decreased level of antithrombin III, protein C and protein S has been reported in DM with elevated clotting factors[7]. Moreover, there is also increase in plasminogen activator inhibitor type 1 which decreases fibrinolysis. Together they contribute to hypercoagulability state in DM[8]. Hypercoagulability in diabetes may accelerate atherosclerosis and acts as a risk factor of cardiovascular disease (CVD)[9]. Measurement of prothrombin time (PT), activated partial thromboplastin time (APTT), bleeding time and clotting factor concentration are are usually done

in patients with a suspected abnormal coagulation. Protrombin time (PT) and APTT are the marker for activation of extrinsic and intrinsic pathway respectively[10,11,12]. The hyperco-aguability state demonstrated by shortened PT and APTT in DM may cause occlusive thrombus within a coronary artery[13]. Therefore shortened PT and APTT value is the risk factors for thromboembolic cardiovascular disease in type 2 diabetic patients[14].

Therefore, this study aimed to investigate the importance of routine determination PT & APTT in order to assess the coagulation impairment in DM to prevent the thromboembolic CVD.

Methods

This cross sectional study was done in the department of Physiology in Dhaka Medical College Dhaka in July 2013 to June 2014. Protocol of this study was approved by Ethical review committee of Dhaka Medical College and Diabetic Association of Bangladesh. For this study 100 male, age (40-60 years), type 2 diabetic patients with FBG level ≥ 7.0 mmol/l and $HbA_1c \geq 6.5$ % [2] and also duration of diabetes >3 years were selected from BIRDEM, Dhaka. All the study subjects were on oral hypoglycemic drugs. One hundred healthy age BMI matched apparently healthy male were considered as control. After selection of the subjects, the nature, purpose and benefit of the study were explained to each subject in details. They were encouraged for voluntary participation. Informed written consent was taken from the participants. Before taking blood, detailed family and medical history were taken. Anthropometric measurement of the subjects was done and blood pressure was measured. All the information were recorded in a prefixed data schedule. With aseptic precaution, 5 ml of venous blood was collected from ante-cubital vein by a disposable plastic syringe from each subject for estimation of PT and APTT level by auto analyzer in the laboratory of the Immunology Department of BIRDEM, Dhaka. All

the parameters were expressed as mean ± SD. Statistical analysis was done by unpaired Student's 't' test. P value < 0.05 was accepted as level of significance. Statistical analyses were performed by using a computer based statistical program SPSS (Statistical package for social science) (version 19).

Results

General characteristics are presented in table I. Subjects of two groups were matched in respect of age. BMI and BP. Mean prothrombin time (PT) and activated partial thromboplastin time (APTT) levels were significantly (P<0.001) lower in patients with diabetes mellitus (Table II). Again, in this study abnormally shortened PT and APTT were found in 93% and 91% diabetic patients respectively (Figure 1 & 2).

**Table I:** General characteristics of study subjects(n=200)

Parameters	Control (n=100)	Diabetes (n=100)
Age (years)	53.58±4.75	54.72±5.73
BMI (K/m²)	23.13±2.26	23.15±2.96
SBP (mm of Hg)	110±7.02	108±10.20
DBP(mm of Hg)	65.95±6.34	62.80±4.40

Results are expressed as Mean ±SD. Unpaired Student's 't' test analyzed statistical significance. n = Number of subjects. BMI= Body mass index, SBP= systolic blood pressure, DBP= Diastolic blood pressure.

Table II: PT and APTT in different groups (n=200)

Parameter	Control (n=100)	Diabetes (n=100)
PT(sec)	11.18±0.41	9.54±0.58***
APTT (sec)	31.88±2.20	19.94±0.62***

Results are expressed as Mean±SD. Unpaired Student's 't' test analyzed statistical significance. ***P< 0.001. PT= Prothrombin time, APTT=Activated partial thromboplastin time.
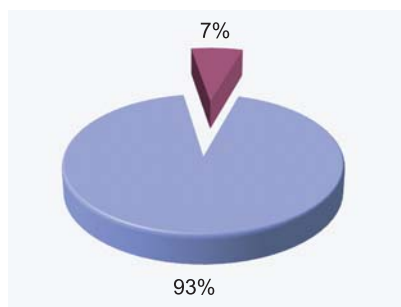
Figure 1: Frequency% of PT in diabetic patients are showing majority of patients had abnormally low prothrombin time (n = 100) Cut point = 11sec
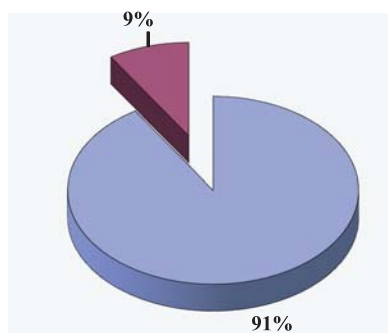
Figure 2: Frequency% distribution of activated partial thromboplastin time in diabetes is presenting that majority of patients had abnormally lower APTT. (n = 100) Cut point 24 sec.

Discussion

In the present study, lower PT level in type 2 diabetic male than healthy male is comparable to others[15,16]. But some studies found no significant changes[17,18,19], whereas few investigators found prolonged PT in type 2 diabetic subjects[20].

Again, in the present study, APTT level was lower in type 2 diabetic male which was similar to others[21,22]. But, some investigators did not find any significant change of APTT in between type 2 diabetic male and adult healthy male[23,24]. Moreover, some researcher found that APTT level was prolonged in type 2 diabetic subjects[25].

It has been suggested that natural anticoagulant antithrombin III keeps the natural procoagulant inhibited. In addition protein C inactivates factors

Va and VIIIa. Hyperglycemia causes non enzymatic glycation of this antithrombin III and depressed it's biological activity and also directly decreases the concentration of protein C. Therefore impaired function of natural anticoagulants activate clotting factors and contribute to the onset of hypercoagulability in DM[26,27]. In this study the abnormally low levels of PT & APTT in 93% & 91% in diabetic patients, in addition to significantly lower mean level of these parameters in DM are suggestive of hypercoagulable state in diabetes which may acts as a risk factor for future cardiovascular disease[28].

Conclusion

From the present study it may be concluded that patients with diabetes mellitus are more prone to develop hypercoagulation state. Therefore, routine examinations of PT & APTT are important to assess coagulation impairment in DM in order to prevent thromboembolic CVD in DM.

Conflict of Interest : None

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