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Study of prothrombin time and activated partial thromboplastin time in type ii diabetes mellitus

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Abstract

Introduction: Diabetes is a major health problem and it is characterized by a high risk of atherothrombotic events. In patient with diabetes mellitus, persistent hyperglycaemia exposes red blood cells (RBCs) to elevated glucose concentration, thus resulting in glycation of haemoglobin, prothrombin, fibrinogen and other proteins involved in clotting mechanisms.

Aim & Objectives: To determine hypercoagulability state of Type 2 Diabetes Mellitus patients by measuring the haemostatic profiles.

Material & Method: The study was an analytical study involving diabetic patients attending S.S.G. Hospital Diabetic clinic. A total of 160 subjects aged 19-71 years participated in the study out of which 80 participants were T2DM patients and 80 were control subjects.

Results & Conclusion: T2DM patients had shortened PT, APTT than the healthy non-diabetic controls. This indicates higher risk of thrombosis in T2DM patients. This study reveals that diabetic patients who had poor glycaemic control were at risk of hypercoagulability than those with good glycaemic control.

Keywords: Diabetes, haemostatic profile, hypercoagulability, PT, APTT

Introduction

Diabetes is a major health problem and it is characterized by a high risk of atherothrombotic events. The number of people with diabetes has risen from 108 million in 1980 to 422 million in 2014 ^[1]. The global prevalence of diabetes among adults over 18 years of age has risen from 4.7% in 1980 to 8.5% in 2014. Almost half of all deaths attributable to high blood glucose occur before the age of 70 years. WHO projects that diabetes will be the seventh leading cause of death in 2030 ^[2].

In patient with diabetes mellitus, persistent hyperglycaemia exposes red blood cells (RBCs) to elevated glucose concentration, thus resulting in glycation of haemoglobin, prothrombin, fibrinogen and other proteins involved in clotting mechanisms. The glycation results in the incomplete activation and function of the clotting cascade. Glycation of intrinsic and extrinsic clotting proteins will decrease the availability of these proteins which affect the clotting capacity ^[3]. Interestingly, stress induced hyperglycemia, which is often transient, has also been associated with poor outcome in thrombotic disease ^[1].

Many mechanisms have been proposed to explain this prothrombotic shift in hyperglycemia ^[4]

- A direct effect on gene transcription of coagulation factors caused by hyperglycemia-induced oxidative stress
- Loss of the endothelial glycocalyx layer, which harbours coagulation factors
- Direct glycation of coagulation factors, altering their activity.

Prothrombin time (PT) is the screening test for coagulation pathway initiated by tissue factor. PT is most sensitive to factor VII (FVII) levels. Factor VII coagulant levels are higher in diabetes patients ^[5]. Standard coagulation screening tests, such as PT and APTT, are important basic examinations in clinical laboratories. Clinical tests for PT, APTT are relatively inexpensive and readily available. Hence we designed this study to examine the relationship of the coagulation parameters PT, APTT with fasting plasma glucose (FPG) in diabetes patients.

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Material & Method

The study was conducted at Sir Sayajirao Gaekwad (S.S.G.) Hospital, a tertiary care hospital at Vadodara district.

Study population and design

The study was an analytical study involving diabetic patients attending S.S.G. Hospital Out-patient department (OPD) Diabetic clinic and healthy adult male and female visiting hospital for blood donation. The study included only consenting adult males and females above age of 18 years who met the inclusion criteria.

Exclusion criteria

- Thrombocytosis
- A history of venous thromboembolism or known inherited coagulation disorder
- Cancer
- Hyperthyroidism
- Recent surgery
- Patients on anticoagulant treatment
- Those not willing to consent

Sample size: Sample size was calculated at standard deviation 1.49, absolute precision 0.5 and at 99% confidence interval using SPSS software. Study group consists of total 160 subjects including 80 cases and 80 controls.

For the purpose of study, individuals were considered to have type 2 diabetes mellitus(T2DM) when fasting plasma glucose was >125mg/dl (>7.5mmol/l) and/or random blood glucose of >200mg/dl (>11.5mmol/l) on more than two occasions and with classic symptoms of diabetes, including polydipsia, polyuria, polyphagia and weight loss. Patients on treatment with glucose lowering medication were also considered to have T2DM.

Potential confounding variables for the study included hypercholesterolemia, cancer, pregnancy and immobility. These variables were controlled by excluding individuals with any of these conditions from the study.

Three (3) ml of venous blood for PT and APTT was collected from each of the study participants in sodium citrate containers and centrifuged at 1500g for 15 minutes. Plasma was then separated and transferred into aliquot and stored at 4°C in a fridge until analysis. The PT and APTT estimation was done using Fully automated analyser.

Results

A total of 160 subjects aged 19-71 years participated in the study out of which 80 participants were T2DM patients and 80 were control subjects.

Haemostatic profile

Table 2.1 Haemostatic profile in T2DM patients and control subjects.

	Status	Number	Mean	Standard deviation	P-Value
PT (seconds)	Control	80	13.2250	0.6185	<0.0001
	Diabetic	80	11.9787	0.5345	
APTT (seconds)	Control	80	31.0975	1.5018	<0.0001
	Diabetic	80	25.4662	1.9338	

To compare the haemostatic profile of T2DM patients and control participants t-test was conducted. Table 2.1 reveals that mean prothrombin time for diabetic patients (11.97±0.53 seconds) was significantly lower than mean of control participants (13.22±0.61 seconds). P-value=

<0.0001.

The mean activated partial thromboplastin time for diabetic patients (25.46±1.93 seconds) was significantly lower than mean of control participants (31.09±1.50 seconds). P-value= <0.0001.

Table 2.2: Haemostatic profile on basis of Fasting blood sugar.

	FBS	Number	Mean	Standard deviation	P-value
PT	<126 mg/dl	39	12.1769	0.4901	0.0004
	>126 mg/dl	41	11.7902	0.5112	
APTT	<126 mg/dl	39	25.0615	1.9624	0.0676
	>126 mg/dl	41	25.8512	1.8481	

As shown in table, patients in both the group were almost equal. The mean Prothrombin time of patients having fasting blood sugar less than 126 mg/dl (12.17±0.49 seconds) was higher than mean of patients having fasting blood sugar less than 126 mg/dl (11.79±0.51 seconds). and the difference between these two was significant. P-value: 0.0004.

The mean activated partial thromboplastin time of patients having fasting blood sugar less than 126 mg/dl (25.06±1.96 seconds) was slightly lower than mean activated thromboplastin time of patients having fasting blood sugar more than 126 mg/dl. But difference between these two was not significant. P-value:0.0676.

Discussion

Patients are considered to have a hypercoagulable state if they have laboratory abnormalities or clinical conditions that

are associated with increased risk of thrombosis; diabetic patients meet these criteria [6, 12]. Hyperglycemia contributes to the hyperfibrinogenemia of diabetic patients and activates the coagulative cascade, thus increasing thrombin formation and fibrinogen degradation products, which may stimulate hepatic fibrinogen synthesis [6, 8]. Diabetic patients have elevated levels of fibrinogen and factors in the intrinsic pathway, which are determinants of APTT [9].

Activated Partial thromboplastin time (APTT) in the diabetic subjects was significantly shorter than that of control participants as well as Prothrombin time (PT) of diabetic subjects was also significantly shorter than that of non diabetic controls. The results are consistent with Acang *et al.*, (2005) & also with Lippi *et al.*, (2009), who also found shortened PT and APTT in T2DM patients than in non-diabetes control subjects [10, 11].

Conclusion

The main aim of study was to determine the haemostatic profile of diabetic patients. It was observed that T2DM patients had shortened PT, APTT than the healthy non-diabetic controls. This indicates higher risk of thrombosis in T2DM patients. Coagulation profile must be considered as a routine test among diabetes patients during their scheduled clinic visit and anti-coagulation measures instituted appropriately.

A cohort study need to be conducted on T2DM patients who participated in this study so as to follow them up and determine those who will develop thrombosis later on in life. The use of aspirin as preventative measure of thrombosis in T2DM should be intensified to prevent cardiovascular complications in these patients.

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