



PROTHROMBIN TIME AND ACTIVATED PARTIAL THROMBOPLASTIN TIME AMONG TYPE 2 NONE INSULIN DEPENDENT DIABETES MELLITUS (T2DM) PATIENTS

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Abstract

Objective: To determine the prothrombin time and activated partial thromboplastin time among type 2 none insulin dependent Diabetes Mellitus Patients.

Materials and methods

Descriptive, prospective analytical case-control based study conducted in Abdelrahman Elsedari Hospital, Sakaka city, Aljouf Region, Saudia Arabia during the period of March to July 2009. Fifty patients and ten normal controls were studied. Patients were those who fulfilled the clinical diagnosis of type II none insulin dependent Diabetes Mellitus of either sex in all age groups, on or off treatment. The controls were normal, non- Diabetes Mellitus individuals of either sex.

Results

The results Show that the mean level of prothrombin time type 2 diabetic patients was 12.0 Sec and of control was 11.1 Sec, it was significantly correlated (P value = 0.02) and the mean level activated partial thromboplastin time (APTT) was 30.7 Sec and of control was 31.2 Sec. This result was none significant (P. value = 0.826).

Conclusion

Our data further demonstrated that patients with type 2 diabetes mellitus had hypercoagulable state and hypofibrinolysis thereby indicating that the activation of coagulation and reduced fibrinolytic activity may contribute to the increased risk of vascular disease in type 2 diabetic patients.

Key Words: Diabetes Mellitus; Type 2 none insulin dependent Diabetes Mellitus; PT; APTT.

Introduction

Abdominal (android) obesity was first proposed to be a risk factor for the development of atherosclerosis and type 2 diabetes mellitus (T2DM) over 40 years ago^[1]. Metabolic alterations accompanying the visceral distribution of fat lead to arterial hypertension, dyslipidemia, insulin resistance and subsequently to T2DM^[2]. This phenomenon is associated not only with classical atherosclerotic risk factors but also with coagulation and fibrinolysis abnormalities^[3]. Hypercoagulation in abdominal obesity is thought to be caused primarily by the synthesis of factors activating coagulation and inhibiting fibrinolysis (for example factor VII activator and the fibrinolytic inhibitor PAI-1) in adipose

tissue^[4]. Hemostatic abnormalities may also result from the synthesis in adipose tissue of cytokines that are mediators of inflammation and insulin resistance, such as interleukin 6 and TNF-alpha^[5]. In addition to this direct effect, the metabolic and lipid alterations that accompany obesity and T2DM are likely to indirectly influence coagulation properties in these patients. Other factors that may be implicated in the generation of hypercoagulation state in visceral obesity and T2DM are endothelial injury and dysfunction^[4]. The purpose of the present study was the assessment of the relationship of some hemostatic factors (PT and APTT) in patients with T2DM.

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Materials and methods

This is a descriptive, prospective analytical case-control based study conducted in Abdelrahman Elsedari Hospital, Sakaka city, Aljouf Region, Saudia Arabia during the period of March to July 2009 to determine the prothrombin time and activated partial thromboplastin time among type II none insulin dependent Diabetes Mellitus Patients.

Fifty patients and ten normal controls were studied. Patients were those who fulfilled the clinical diagnosis of type II none insulin dependent Diabetes Mellitus of either sex in all age groups, on or off treatment. The controls were normal, non- Diabetes Mellitus individuals of either sex.

Exclusion criteria: patients (male and female) with previous history of venous or arterial thrombosis and hypertensive patients, who received antiplatelet or anticoagulant drugs in the previous 15 days, were excluded from the study.

Consent was obtained from the selected individuals after being informed them with all detailed objectives of the study, blood samples were collected from both patients and controls and proceed to platelet poor citrate plasma (PPP) preparation [6]. Prothrombin time (PT) and Activated partial thromboplastin time (APTT) were determined using Coagulometer model, Fibrin I, Vitallab, The Netherlands. Data from study groups were analyzed by computer using SPSS (statistical Package for Social Science), to measure the mean and standard deviation, p.value of < 0.05 was regarded as statistically significant.

Results and Discussion

Enhanced activation of the clotting system has been previously reported in patients with type 1 or type 2 diabetes [7]. This activation of blood coagulation has recently been implicated as an important contributing factor for the occurrence of vascular complications in diabetes [8]. In large epidemiological studies, the procoagulant factors (fibrinogen and factor VII) have been described as independent predictors of cardiovascular events in diabetic and nondiabetic subjects. Our finding indicated a significant correlation between type 2 none insulin dependent Diabetes Mellitus and family history (**Table 1**), while the duration of diabetes between 1 month up to 5 years was highly incidence among the study group which was explained the increased of diabetes in recent years (**Fig. 1**).

The pathogenetic mechanism of the clotting activation in diabetes is not completely clear. Perturbance of components of the anticoagulant system associated with hyperglycemia may play an important role as exemplified in hyperglycemia inducing depressed

biological activity of the anticoagulant protein AT-III in diabetic and nondiabetic subjects[9]. Structural modification due to no enzymatic glycation was suggested as the causative factor of this AT-III dysfunction[10]. In various studies, it was reported that plasma levels of AT-III were decreased[11] or unchanged[12].

Abnormalities of the extrinsic pathway may also cause hypercoagulability in diabetic patients. The mean plasma PT level was found to be either decreased or increased in various reports depending on the type of diabetes (**Table 2**). While reduced plasma levels APTT have been described in type 1 diabetic patients, they were found to be elevated in those with type 2 diabetes[8]. The Extrinsic or intrinsic pathways did not change in our diabetic patients. Hyperglycemia has been considered to be the causative factor of the abnormalities of the anticoagulant pathway. In our type 2 diabetic patients, we found a significant ($p = 0.02$) correlation between mean PT patients compared to control groups. Increased levels of PT in subjects with type 2 diabetes are associated with macrovascular mortality[13]. Several studies have shown that levels of PT are increased in both type 1 and type 2 diabetic patients[12] and that glycemic control normalizes PT levels in diabetic patients[14]. In our study, we found an increased PT in type 2 diabetics in comparison with the healthy controls. However, the mean values of both groups were within normal ranges of our laboratory. PT did not differ between the diabetic patients with and without vascular complications. Previous studies of the fibrinolytic system in diabetes have provided conflicting results; type 2 diabetes is often associated with profound depression of fibrinolysis[15], while Aso *et al*, 2000[16] reported that both coagulation and fibrinolysis are enhanced concomitantly in patients with type 2 diabetes mellitus. Our findings of increased plasma levels of PT and decreased APTT (but not significant) are consistent with abnormal coagulation mechanism and may be interpreted as a tendency to thrombosis with cardiovascular disease for diabetic patients.

Table 1 Family history of T2DM among patients (n, 69) and controls (n, 10).

Family history	frequency	Percentage	P.Value
Patients			
Positive	44	64	0.005
Negative	25	36	
Total	69	100	
Controls			
Positive	4	40	0.000
Negative	6	60	
Total	10	100	

P.Value statistical significant < 0.05

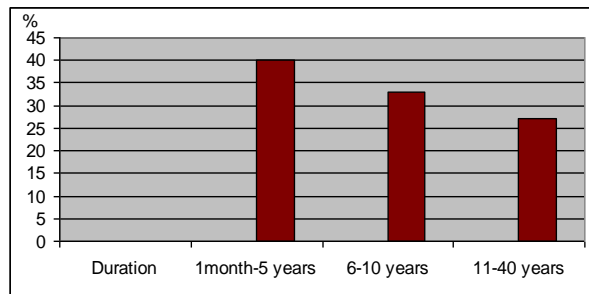
Table 2 The mean level of prothrombin time (PT) and activated partial thromboplastin time (APTT) in T2DM patients (n, 69) and control (n, 10).

	No	Mean	Std. Deviation	P-value
PT				
Patients	69	12.0	2.241	0.02
Control	10	11.1	1.054	
APTT				
Patients	69	30.7	5.571	0.826
Control	10	31.2	2.558	

P-Value statistical significant < 0.05

NS: None Statistical significant

Fig. 1 The duration of T2DM in the study group (n, 69)



Conclusion

Our data further demonstrated that patients with type 2 diabetes mellitus had hypercoagulable state and hypofibrinolysis thereby indicating that the activation of coagulation and reduced fibrinolytic activity may contribute to the increased risk of vascular disease in type 2 diabetic patients. Our study, patients with T2DM showed independent factors determining hypercoagulation which suggested including metabolic control, lipids and haemostatic disorders for subjects with diabetes at risk of developing vascular complications.

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