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Original Research Article

Haemostatic Profile in Saudi Patients with Type II Diabetes Mellitus

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ABSTRACT

Study Design and Objective: This was a descriptive case control study aimed to identify the haemostatic profile in Saudi patients with Type II Diabetes Mellitus.
Material and Methods: During the period between August and December 2012, fifty Saudi type II diabetic patients and fifty gender/age matched healthy persons from western Riyadh hospitals were included in this study. The patients and controls were tested for Activated Partial Thromboplastin Time, hemoglobin A1c, fibrinogen, and prothrombin time.
Results: Prothrombin time was 16.5 seconds; activated partial thromboplastin time was 27.6 seconds; fibrinogen was 3.7 g/l; tissue-type plasminogen activator was 14.9 mg/dL; and HbA1c was more than 48 mmol/ mol.
Conclusion: This study concluded that diabetic patients have the risk of activation of coagulation and atherothrombosis.

Key words: Haemostasis; Type II Diabetes.

INTRODUCTION

Diabetes mellitus (DM) is a group of disorders characterized by hyperglycemia associated with vascular complications, mainly affecting retinal, renal, coronary, and peripheral vessels. Hyperglycemia results from lack of endogenous insulin (due to an inadequate response by the pancreatic beta cells) or resistance to the action of insulin in muscle, fat and liver.[1] Diabetes leads to a hypercoagulable state. The hypercoagulable state is broadly defined as encompassing two clinical situations: i) the presence of laboratory abnormalities, such as thrombocytosis or antithrombin III deficiency, or clinical conditions, such as cancer, pregnancy, or the postoperative state, that have been considered to be associated with an increased risk of thromboembolic complications; and ii) recurrent thrombosis in patients who have no recognizable predisposing factors (thrombosis-prone patients).[2] It is associated with increased production of tissue factors by endothelial cells and vascular smooth muscle cells, as well as increased plasma concentrations of the coagulation factor VII. Hyperglycemia is

also associated with decreased concentrations of antithrombin and protein C, impaired fibrinolytic function, and excess production of plasminogen activator inhibitor-1 (PAI-1).[3]The etiology of atherosclerosis, including lower extremity arterial disease (LEAD), is multifactorial. Major risk factors are hyperglycemia, smoking and hypertension.[4]

The fibrinolytic system includes a broad spectrum of proteolytic enzymes with physiological and pathophysiological functions in several processes such as haemostatic balance, tissue remodeling, tumor invasion and angiogenesis.[5] The main enzyme of the plasminogen activator system is plasmin, which is responsible for the degradation of fibrin into soluble degradation products. The activation of plasminogen into plasmin is mediated by two types of activators, urokinase –type plasminogen activator (uPA) and tissue-type plasminogen activator (t-PA). The activity of both is regulated by specific plasminogen activator inhibitors (PAIs).[6]The fibrinolytic system is primarily an interaction between plasminogen activators and inhibitors; any response to vascular injury is an activation of t-PA. Increased t-PA-activity may therefore be a potential indicator of an early ongoing vascular damage and, possibly, a compensatory mechanism. Both t-PA and PAI-1 mass levels have been suggested as indicators of vascular damage.[7]

In diabetic patients, vascular endothelial cells are exposed to high glucose levels, leading to elevation of t-PA in the plasma accompanied by impaired fibrinolysis.[8] High plasma levels of tissue plasminogen activator in diabetic patients with lower extremity arterial disease (LEAD) can be used as an early marker for diagnosis of these cases.[9]

MATERIAL AND METHODS

From western Riyadh hospitals and during the period between August and December 2012, a total of 50 patients with type II diabetes were selected for this study. These patients included adult males and females aged between 40 – 70 years. Definition of DM in this study was based on laboratory findings as a fasting plasma glucose levels greater than 7.0 mmol/L on two or more occasions (WHO, 1999). Their medical history and personal data were obtained via a comprehensive questionnaire after due approval from the ethnical committee of the hospitals. Fifty age and sex – matched non diabetic persons attended the family medicine outpatient clinic of the hospitals were used as controls in this study. Informed consent was obtained from all the participants.

Twenty milliliters (20 ml) of venous blood was collected from each subject using aseptic procedure after 12 hours of fasting. Nine ml of the collected blood was dispensed into a specimen bottle containing 1ml of trisodium citrate to make a ratio of one volume of anticoagulant to nine volumes of venous blood (1/9) for determination of PT, APTT, and fibrinogen weight. Plasma was separated from the blood after centrifugation at 2000 rpm for 10 minutes to obtain platelet- poor plasma required for these coagulation assays. Tests were performed in duplicates within 3 hours of sample collection. Standard methods of Dacie and Lewis (1996) were employed for the determination of PT, APTT, and fibrinogen weight. For all participants, HbA1c was determined on a Bio-Rad Variant II HbA1c analyzer (Bio-Rad, California, USA). All the study patients underwent APTT, PT, fibrinogen, t-PA, and HbA1c measurements. Patients were excluded if they had a past history of a predisposition to hypercoagulability, including thrombocytosis, venous

thromboembolism, known inherited coagulation disorders, cancer, pregnancy, recent surgery, hyperthyroidism, or patients who were taking standard anticoagulant treatment with either coumarin derivatives or heparin at the time of admission. Patients with type I diabetes were also excluded from the study.

RESULTS

The mean of fasting blood glucose (FBG) in patients was 6.8 mmol/L; in controls, it was 5.3 mmol/L.

The mean of random blood glucose (RBG) was 32.3 mmol/L in patients and 8.7 mmol/L in controls.

Prothrombin time(PT) was 16.5 seconds in patients and 15 seconds in controls. Activated partial thromboplastin time (APTT) was 27.6 seconds in patients and 25.3 seconds in controls.

Fibrinogen was 3.7 g/l in patients and 2.2 g/l in controls. Tissue-type plasminogen activator (t-PA) was 11.2 mg/dL in patients and 14.9 mg/dL in controls.

HbA1c was 48 mmol/ mol or more in diabetic patients and it was less than 48 mmol/mol in controls.

DISCUSSION

In the present study, HbA1c was significantly higher in the study group. These results coincide with the results of Elizabeth et al., who found significant increase in levels of HbA1c in type II DM compared to control group due to chronic elevation of the blood glucose level.[10] These results indicate that exposure to hyperglycemia for long periods results in increased and accelerated glycosylation of hemoglobin A within the red blood cells throughout its life span in the circulation (120 days).

Our results are also in agreement with Stegenga et al., who found that t-PA was significantly lower in type II diabetes because fluctuating hyperglycemia lead to protein glycation that induce oxidative stress, endothelial cell dysfunction, extracellular matrix formation and apoptosis. This lead to vascular damage, thrombotic formation, stimulation of the fibrinolysis system, increased PAI-1 and decreased t-PA in late stages.[11]

Increased plasma levels of PT and decreased APTT in this study are consistent with abnormal coagulation mechanism that may be interpreted as a tendency to thrombosis with cardiovascular disease in diabetic patients.

The significant increase of fibrinogen in the study group coincides with the results reported by Andreas et al., who reported that fibrinogen levels in diabetic patients were higher than those in the control group due to increased synthesis and turnover of fibrinogen in diabetes that was related to insulin deficiency.[12] These results were explained by Meigs et al., who suggested that diabetes complicated by vascular disease and multiple vascular damages was responsible for the high fibrinogen level.[13] On the other hand, the study of Pandolfi et al. found and reported no significant differences in fibrinogen between control group and diabetic patients.[14]

CONCLUSION

From this study, it is concluded that chronic type II diabetic patients have a significant risk of vascular damage and thrombus formation.

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