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Research article

EFFECT OF DIABETES MELLITUS TYPE II ON ACTIVATED PARTIAL THROMBOPLASTIN TIME AND PROTHROMBIN TIME

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ABSTRACT

Diabetes mellitus contributes for initiation and progression of micro vascular and macro vascular complications. Complication includes coagulation impairment however Shortened activated partial thromboplastin time (aPTT) values may reflect hypercoaguable state, which is associated with increased thrombotic risk and adverse cardiovascular events. **Objective**: The present study was conducted to study the aPTT and PT levels in patients with diabetes mellitus type II. **Material and method**: A sample of 50 persons were selected, 30 patients suffering from DM as type II from Al-wahda teaching hospital, Derna-Libya. At the same time a group of 20 randomly selected healthy adults to participate in the study as control group. **Result**: The mean value of APTT in T2DM individuals was significant lower (28.95 ±7.54) seconds as compare with control, (34.12±2.82) seconds (P = 0.06). The mean value of prothrombin time (PT) among T2DM individuals was (14.04 ±2.96) seconds and the mean value of PT among healthy individuals was (13.5 ± 1.54) seconds. There was no significant difference in PT of T2DM individuals P ≥ 0.05. **Conclusion:** From this study, it may be concluded that shorted APTT confirms that T2DM is a hyper-coagulable state due to which there is increased risk of thrombotic events

KEYWORDS: Prothrombin time, Activated partial thromboplastin time, hypercoagulable, Diabetes mellitus.

INTRODUCTION

Diabetes mellitus (DM) is one of the most common serious metabolic disorders, it describes as metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbance of carbohydrate, fat and protein metabolism resulting from defect in insulin secretion, action or both.[1]

There are two general types of diabetes mellitus, type 1 diabetes, also called insulin-dependent diabetes mellitus (IDDM), is caused by lack of insulin secretion and type 2 diabetes (T2DM) also called non-insulin-dependent (NIDDM), is caused by decreased sensitivity of target tissues to the metabolic effect of insulin.[1] 80% of patients with diabetes mellitus die a thrombotic death, 75% of these deaths are due to Cerebrovascular and peripheral vascular complications.[2]

It is well known that the vascular endothelium plays an essential role in the regulation of (local) haemostatic processes. Endothelial dysfunction has also been shown to occur in T2DM [2]. Multiple mechanisms are found to be involved in it; but most likely mechanism is that of the insulin resistance syndrome may be central to the development of diabetic endothelial dysfunction.

The hemostatic abnormality and endothelial dysfunction are responsible for the generation of hyper-coagulable state in T2DM individuals [2]. Coagulation tests like prothrombin time (PT) and the activated partial thromboplastin time (APTT) are global tests used to assess the coagulation system in a clinical setting [3].

Patients are considered to have a hypercoagulable state if they have laboratory abnormalities associated with increased risk of thrombosis.

The aim was conducted to study the aPTT and PT levels in patients with diabetes mellitus type II T2DM.

MATERIAL & METHOD

Study Design: A case control comparative **analytical** study.

Ethical approval: Approval was granted from the Research and Ethics Committee of the faculty. Consent was gotten from all participated patients at Alwahda hospital.

Sample size and sampling method: A sample of 50 person were selected, 30 patients suffering from DM as type II , from Al-wahda teaching hospital, Derna-Libya. At the same time a group of 20 randomly selected healthy adults were invited to participate in the study as control group.

Inclusion criteria

1. T2DM individuals of either sex between the age group of 31 to 72 years. For this study, diabetic individuals who attended to alwahda hospital at medicine department; and were diagnosed previously as T2DM were selected.

Diagnostic criteria for DM issued by the National Diabetes Data Group and WHO was applied as: [1]

1) Symptom of diabetes plus random blood glucose> 200mg% OR

2) Fasting plasma glucose >126mg% OR

3) Two hour plasma glucose >200mg% during oral glucose tolerance test

All individuals were maintained on anti-diabetic treatment like oral hypoglycaemic

2. Healthy individuals of either sex between the age group of 21 to 50 years.

Exclusion criteria:

1. H/o clinical conditions associated with increased risk of thromboembolic diseases, like venous thrombosis, cerebrovascular diseases, peripheral vascular diseases.

2. Past H/o predisposition to hyper-coagulability like known inherited coagulative disorders, cancer, recent surgery, pregnancy, hyperthyroidism etc.

3. H/o heart diseases like myocardial infarction, hypertension, angina pectoris, positive electrocardiographic changes etc.

Grouping:

Group I: It consisted of 20, healthy individuals.

Group II: This group consisted of 30, T2DM individuals.

Sample collection:

Five ml of venous blood specimen were collected from all patients and control in medical laboratory at Alwahda-hospital, plasma was separated for testing prothrombin time and activated partial thromboplastin time.

Methodology:

Study Procedure:

The objective and detailed procedure were explained to each individual, before collection of the blood sample following coagulation parameters were studied,

a) Prothrombin time (PT)

b) Activated partial thromboplastin time (APTT)

Procedure for coagulation tests: Collected samples from both the patients and controls in clean container or a tube having 3.2% trisodium citrate.

- Immediately mixed the blood with anticoagulant avoiding foam formation. Centrifuge the sample for 15 min at approximately 3000 rpm and collect the plasma in separate tube.
- Fresh plasma is preferred for testing as it performs best when tested immediately.
- Sample may be tested within 2 hours at 25 to 30° C and within 3 hours at 2 to 8° C.
- Take haemostatic reagent into a test tube; add patient plasma into test tube or reaction cuvette.
- Incubate the test tube containing plasma and reagent, PT and APTT were measured on coagulometer model.[4]
- Our laboratory reference ranges of coagulation tests were; PT (11-14 seconds) and APTT (30 seconds).

Statistical analysis: Data were analyzed by t test using. Results are expressed as mean values ± SD. Significant difference was considered to exist at P value less than 0.05.

RESULTS

A total of 50 sample were included in this study, 20 normal healthy persons were included in the study as control subject mean age (24.06 ±3.73) with a range 20-33 year and they were clinically healthy and free of any serious illness.

Thirty patient as T2DM were selected from Al-wahda Teaching Hospital, Derna, ge mean age (51.13 ± 11.52) with a range (35- 65) year.

The mean value of APTT in T2DM individuals was 28.95 seconds with standard deviation ±7.54 seconds while mean value with standard deviation in healthy individuals was 34.12±2.82 seconds.

By applying unpaired t test, we found that, there were significantly decreased value of APTT among T2DM individuals than healthy individuals (p =006) as in table 1.

The mean value of prothrombin time (PT) among T2DM individuals was 14.04 seconds with standard deviation ±2.96 seconds and the mean value of PT among healthy individuals was 13.5 seconds with standard deviation ± 1.54 seconds.

By applying unpaired t test, we found no significant difference in PT of T2DM individuals P ≥ 0.05 as in table 2.

Table 1: **Comparison of APTT, PT between Group I (healthy individuals) and Group II T2DM**

	Group I	**Group II**	P value
Activated partial thromboplastin time (in second)	34.12±2.82	28.95±7.54	**0.006***
Prothrombin time (in second)	13.5±1.54	14.04±2.96	0.25

DISCUSSION

Diabetes mellitus is associated with increased risk of atherosclerosis, so diabetes is a pro coagulant state. DM is characterized by high risk of atherothrombotic complications affecting the coronary, cerebral and peripheral arterial trees. It is a syndrome characterized by presence of chronic hyperglycaemia due to defective insulin secretion, insulin action or both affecting metabolism of various compounds including carbohydrate, lipids, and proteins and it also impairs various biological processes such as coagulation and fibrinolytic alteration.

Therefore in the present study we evaluated some of coagulation tests in T2DM individuals.

The mean value of APTT in T2DM was 28.95 seconds while in healthy individuals it was 34.12 seconds. We found statistically significant difference in p value as 0.006, which shows that, T2DM is associated with shorter APTT. Our results are supported by similar findings of Zhao *et al* [5] and Chan *et al.*[6] Their results also showed that DM is associated with shortened activated partial thromboplastin time. In contrast, Abdulraheman & Dallatu [7] and Alao *et al.*[8] found increased APTT in their study results.

The mean value of PT in T2DM was 14.04 seconds and in healthy individual it was 13.5 seconds. no significant difference in PT was found in the T2DM and healthy individuals. Similar findings were observed in Soltani *et al*. [9] and Madan *et al*. [10] studies in which they had reported normal PT in T2DM individuals. While Zhao *et al.* [11] and Acang & Jalil [12] found shorter PT in T2DM individuals. Raised PT in T2DM individuals was found by Hassan [13] and There are various factors that promote the coagulation while others inhibit coagulation, whenever there is imbalance between these two factors, blood will coagulate. Enhanced activation of clotting system has been implicated as contributing factor for the occurrence of vascular complications. The endothelium contributes for maintaining the blood flow by preventing platelet aggregation, by its anticoagulant properties and by stimulating the fibrinolytic system. The endothelium consists of a single layer of cells lining the inside surface of blood vessels, hence establishing a barrier between the blood and the vessel. [14]

The most important factors for preventing clotting in the normal vascular system are the

smoothness of the endothelial cell surface, which prevents contact activation of the intrinsic clotting system; a layer of glcocalyx on the endothelium (glycocalyx is a mucopolysaccharide adsorbed to the surfaces of the endothelial cells), which repels clotting factors and platelets, thereby preventing activation of clotting and a protein bound with the endothelial membrane, thrombomodulin which binds thrombin. [15]

Endothelial dysfunction is the earliest event that precedes the development and progression of diabetic vascular complications. The pathogenesis of endothelial dysfunction in diabetes is complex. Multiple cellular and molecular mechanisms are involved in the development of diabetic dysfunctional endothelium. Along with hyperglycemia insulin resistance, impaired lipid metabolism and lipoproteins, oxidative stress, all these factors lead to endothelial dysfunction in T2DM.

The APTT assay is traditionally used for identifying abnormalities in the contact (factor XII, prekallikrein, and high-molecular-weight kininogen), intrinsic (factors XI, VIII, IX) and common (factors X, V and II and fibrinogen) pathways of coagulation. Hence there was shortened APTT in T2DM. [17]

The laboratory result of shorted APTT confirms that T2DM is a hyper-coagulable state due to which there is increased risk of thrombotic events. Clinical tests for APTT relatively inexpensive and are readily available. The results shown in our study indicated that shortened APTT levels might be useful haemostatic markers in diabetic patients, especially in those at high-risk for thrombotic complications.

CONCLUSION

APTT in which used for identify abnormalities in intrinsic and common coagulation pathway was shorter in T2DM than healthy individuals, shorted APTT confirm that T2DM is a hyper-coagulable state which increases risk of thrombotic events.

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