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Original article

Evaluation of Prothrombin and Activated Partial Thromboplastin Time in Patients with Diabetes Mellitus

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ABSTRACT

Diabetes mellitus (DM) is a metabolic disease accompanied by high blood glucose due to a defect in insulin secretion, insulin activity, or both. High blood glucose levels may lead to serious damage to some organs of the body, mainly blood vessels and nerves. Therefore, this study was conducted to evaluate prothrombin time (PT) and activated partial thromboplastin time (APTT) in diabetic patients. 100 venous blood samples were collected from diabetic patients attending the diabetes clinic in Sebha. Of them, 57 were males and 53 were females, and their ages ranged between 15-88 years. out of 100, 48 Were treated with insulin-regulating tablets and 52 Were treated with insulin injections. 34 blood samples were collected from healthy people (15 females and 19 males). They were used as a control group, aged between 14-55 years. 4 ml of venous blood was drawn, and 2 ml was placed in containers containing the anticoagulant sodium citrate to perform the PT and APTT. Place 2 ml of sample in tubes containing sodium fluoride anticoagulant to perform a fasting blood sugar (FBS). Place the tubes in a centrifuge at 3000 rpm to obtain plasma. The results showed the mean of PT in patients was (19.4 ± 3.6), the mean APTT was (35.9 ± 1.5) and the Mean FBS was (229.7 ± 80.39), whereas the mean PT, APTT, and FBS in control were (12.8 ± 1.6), (25.4 ± 2.1), and (91.9 ± 12.5) respectively. there was a significant increase of PT and APTT in patients compared to control ($P<0.05$), PT and FBS were higher in patients who used insulin injection with significant differences($P<0.05$), while no significant differences were in APTT ($P > 0.05$). The present study observed a statistically significant increase in PT and APTT among patients compared to controls, it would be helpful to incorporate coagulation screening as a routine investigation for the better management of diabetic patients.

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INTRODUCTION

Diabetes mellitus (DM) is a metabolic disease accompanied by high blood glucose (Hyperglycemia), resulting from a defect in insulin secretion, insulin activity, or both. High blood glucose is one of the common signs of uncontrolled diabetes, and its continued excessive elevation leads to damage to many organs, mainly blood vessels [1]. Maintaining blood fluidity within the vascular system is an important physiological process for humans. The term "hemostasis" refers to the vessel's natural response to injury by forming a clot that stops bleeding [2]. When injury or damage occurs to the vascular lining, platelets, and fibrin work to close the hole and repair the defect. The stages of blood clotting processes

are divided into a primary stage (mainly involving platelets) and a secondary stage (mainly related to fibrin formation or blood clotting). When blood clots are no longer needed, the fibrinolytic system will dissolve them and remove them. 80% of diabetic patients die from strokes, and 75% of these deaths are due to cerebrovascular and peripheral vascular complications.

Vascular endothelium, which is an important part of preventing abnormal blood clotting, is abnormal in diabetes. Endothelial abnormalities play a role in promoting the activation of platelets and coagulation factors seen in diabetes [3]. Hyperglycemia directly contributes to endothelial cell injury by irreversible glycosylation of collagen and other structural proteins under the endothelium, leading to the formation of advanced glycosylation end products (AGEs) [4]. AGEs accumulate in the subendothelium over time under the influence of high blood glucose level and are directly associated with atherosclerotic disease [5,6]. AGEs cause changes in the structure and biophysical properties of the basement membrane, leading to changes in vascular permeability and dilation [7].

Patients are considered to have a hypercoagulable state if they have laboratory abnormalities associated with an increased risk of thrombosis [3]. Hypercoagulability in diabetes can accelerate atherosclerosis become a risk factor for cardiovascular disease, and increase the incidence of cardiovascular disease because clotting occurs 2-4 times in diabetic patients, and thrombotic complications are the main cause of death in diabetic patients [8,9,3]. PT and APTT are blood screening indicators that provide insight into the coagulation status of patients [10]. Due to the high incidence of diabetes in our society and its contribution to vascular damage and the absence of such a study in Sabha City, this study aimed to evaluate the coagulation process in diabetic patients using PT and APTT in the diabetes clinic in Sabha city.

METHODS

Study setting

The study was conducted on 100 diabetic patients attending the diabetes clinic in Sabha City, southern Libya. About 57 of them were males and 53 were females, and their ages ranged from 15 to 88 years. Out of 100 patients, 48 were treated with insulin-regulating tablets and 52 were treated with insulin injections. 34 blood samples collected from healthy individuals (15 females and 19 males) were used as control samples. Their ages ranged from 14 to 55 years.

Experiment

4 ml of blood were collected from the vein from all patients and control samples, 2 ml were placed in a tube containing sodium citrate (3.0%) for coagulation tests (PT, APTT), the rest were placed in tubes containing sodium fluoride for FBS analysis and the sample was separated by centrifugation at 3000 rpm for 10 minutes to obtain plasma. PT and APTT were performed using the Coatron M1 device from TECO GmbH Germany and the solutions prepared by Biomagrab Tunisia and the fasting blood glucose concentration was measured (FBS) using the kit" solutions prepared by BICON, which is based on enzyme chromatography.

Statistical analysis

Data were statistically analyzed using the Minitab 16.1 program on Windows 10 and the Microsoft Excel 2010 spreadsheet, where the mean and standard deviation were calculated. T-test was also used to determine if there were significant differences between patients and healthy individuals at $P \leq 0.05$.

RESULTS

The results of the present study showed that the mean PT of patients was (19.4 ± 3.6), the mean APTT was (35.9 ± 1.5) and the mean FBS was (229 ± 80.4). While the mean PT of healthy subjects (control) was (12.8 ± 1.6), the mean APTT was (25.4 ± 2.1) and the mean FBS was (91.9 ± 12.5). This result showed a statistically significant increase in PT, and APTT in patients compared to the control group ($P < 0.05$) (Table 1).

Table 1. PT, APTT, and FBS between patients and controls

Test	Patents Mean ±SD	Control Mean ±SD	P values
PT (Sec)	19.4±3.6	12.8±1.6	0.000*
APTT (Sec)	35.9±1.5	25.4±2.1	0.000*
FBS (mg/dl)	229 ±80.4	91.9± 12.5	0.000*

**Significant, SD=standard deviation*

Table 2 showed the mean PT and FBS of patients who were treated with insulin injection were higher than those treated with tablets (P > 0.05), while there were no significant differences in APTT between the two groups,

Table 2. PT, APTT, and FBS between two groups of patients

Test	Patients treated with insulin injections Mean ±SD	Patients taking tablets Mean ±SD	P values
PT (sec)	20.5±4.2	18.3±2.3	0.001*
APTT (sec)	35.9±1.6	35.9±1.5	0.882
FBS (mg/dl)	281±62.5	171±58.6	0.000*

*****Significant, SD=standard deviation*

DISCUSSION

Diabetes is one of the most widespread health problems in the world, which is accompanied by hyperglycemia due to a lack of insulin secretion or ineffective insulin. There are more than 170 million diabetic patients who are more susceptible to vascular thrombosis due to its effect on many proteins of the blood endothelial [10,12,13]. There is a quantitative and qualitative defect (in the number and activity of platelets) in platelets, as well as disorders in the clotting process and weakness in the fibrin degradation system in the clot [14].

The vascular endothelium an essential in preventing bleeding and thrombosis. It works to produce clotting initiators such as von Webrand factor (VWF) and secrete substances that help regulate blood pressure by secreting substances that constrict or dilate blood vessels, nitric oxide, prostaglandins, and platelet activators [15]. Due to changes in the vascular endothelial cells in patients with hyperglycemia, lead to an increase in pressure and blood flow in the capillaries, which leads to blockage and an increase in the thickness of the basement membrane of the blood vessel lining, which causes a malfunction in the function of regulating blood circulation, and also due to changes in the composition of vascular endothelial cells, it leads to the expression of tissue factor (coagulation factor III), von Webrand factor, and other coagulation factors, which increases the adhesion of platelets to the wall of the blood vessel lining, increases the effectiveness of platelets, increases the level of coagulation factor, and decreases the level of fibrinolysis. This leads to the onset of activation of the primary and secondary clotting process and thus leads to an increase in prothrombin time and activated partial prothrombin time as recorded in this study and previous studies [16,17,18].

The results obtained in the present study showed that there was a significant increase in both prothrombin time and activated partial thromboplastin time compared to controls. Some studies indicate that the increase in factor VII in diabetic patients is associated with dyslipidemia that occurs in these patients. One study states that a portion of factor VII in plasma is associated with a very low density, while the increase in factor VII leads to an increase in prothrombin time. Several studies have indicated that controlling glucose concentration reduces prothrombin time to the normal range. The results of the current study showed that APTT and PT values were significantly increased among diabetic patients. Similar results were found in several studies, including Omer, 2020 [19], Boshabor, 2022 in Libya [20], and another study in India conducted by Thukral *et al.*, 2018 [21]. However, some studies have not found any significant changes in coagulation tests among diabetic patients [22,23,24]. Otherwise, a few studies have found a decrease in PT and APTT in diabetic patients [25,26].

CONCLUSION

The present study observed a statistically significant increase in prothrombin time and Activated Partial Thromboplastin Time among patients compared to controls, it would be helpful to incorporate coagulation screening as a routine investigation for the better management of diabetic patients.

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تقييم زمن البروثرومبين وزمن الثرومبوبلاستين الجزئي المنشط لدى مرضى السكري

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المستخلص

مرض السكري هو مرض أيضي يصاحبه ارتفاع سكر الدم بسبب خلل في إفراز الأنسولين أو نشاط الأنسولين أو كليهما. قد يؤدي ارتفاع سكر الدم إلى تلف خطير في بعض أعضاء الجسم، وخاصة الاعصاب والأوعية الدموية. أجريت هذه الدراسة لتقييم زمن البروثرومبين وزمن الثرومبوبلاستين الجزئي المنشط لدى مرضى السكري. تم جمع 100 عينة دم وريدي من مرضى السكري المترددين على عيادة السكري في مدينة سبها. كان منهم 57 ذكور و53 اناث، وتراوحت أعمارهم بين 15-88 سنة. من 100، 48 مريض يعالجوا بأقراص تنظيم الأنسولين و52 يعالجوا بحقن الأنسولين. تم جمع 34 عينة دم من أشخاص أصحاء (15 اناث و19 ذكور). كمجموعة ضابطة. كان متوسط زمن البروثرومبين لدى المرضى (19.4 ± 3.6) ثانية، ومتوسط زمن الثرومبوبلاستين الجزئي المنشط كان (35.9 ± 1.5) ثانية، ومتوسط سكر الصيام كان (229 ± 80.4) ميلجرام لكل ديسليتر, بينما كان متوسط زمن البروثرومبين وزمن الثرومبوبلاستين الجزئي المنشط والسكر في المجموعة الضابطة (12.8 ± 1.6)، (25.4 ± 2.1)، (91.9 ± 12.5) على التوالي. كان هناك زيادة ذات دلالة إحصائية في زمن البروثرومبين وزمن الثرومبوبلاستين الجزئي المنشط في المرضى مقارنة بالضوابط، كان زمن البروثرومبين ومستوى السكر أعلى في المرضى الذين استخدموا حقن الأنسولين مع وجود فروق معنوية، لم تكن هناك فروق معنوية في زمن الثرومبوبلاستين الجزئي المنشط، نستخلص من الدراسة الحالية ان هناك زيادة ذات دلاله إحصائيًة في زمن البروثرومبين وزمن الثرومبوبلاستين الجزئي المنشط بين المرضى مقارنة بالضابطة، سيكون من المفيد دمج فحص التخثر كفحص روتيني لتحسين متابعة مرضى السكري.

الكلمات المفتاحية. مرض السكري، زمن البروثرومبين، زمن الثرومبوبلاستين الجزئي المنشط، سبها