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Research Article

Evaluation Of PT And APTT among Diabetes Mellitus Type2 Patients in Atbara City, Sudan

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Abstract:

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. To evaluation of PT and PTT among diabetes mellitus type 2 patients. This is a cross-sectional study with a control group based conducted in Atbara hospital during the period from March to July 2018. The patients were interviewed according to a questionnaire prepared for this purpose. A total of 50 samples were from patients with type2 diabetes mellitus and 50 samples were from healthy persons as control. PT and APTT were measured using semi-automated coagulometry (TECO- COATRON M1, GERMANY). The data was analyzed by SPSS software using an independent t-test. The results show that the mean level of prothrombin time in type 2 diabetic patients was (16.64±3.09 Sec) and of control was (16.7±1.24 Sec), it was none significantly correlated (P value = 0.832) and the mean level activated partial thromboplastin time APTT in type 2 diabetic patients was (38.3±8.7) Sec and of control was (36.2±2.7 Sec), it was none significantly correlated (P. value =0.111). Our study concluded that patients with type 2 diabetes mellitus had no hypercoagulable state due to PT and APTT. Another study with large sample size and many variables to reach another fact.

Keywords: Diabetes mellitus, PT, APTT, Evaluation, Bleeding profiles.

Background:

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Hyperglycemia is an increase in plasma glucose levels. In healthy patients, during a hyperglycemia state, insulin is secreted by the β - cells of the pancreatic islets of Langerhans. Insulin enhances membrane permeability to cells in the liver, muscle, and adipose tissue. It also alters the glucose metabolic pathways. Hyperglycemia, or increased plasma glucose levels, is caused by an imbalance of hormones. An intermediate stage, in which the fasting glucose is increased above normal limits but not to the level of diabetes, has been named impaired fasting glucose. Use of the term impaired glucose tolerance to indicate glucose tolerance values above normal but below diabetes levels was retained. Also, the term gestational diabetes Mellitus was retained for women who develop glucose intolerance during pregnancy [1]. 80% of patients with diabetes mellitus die a thrombotic death, 75% of these deaths are due to Cerebrovascular and peripheral vascular complications [2]. In Nigeria and the world at large, Diabetes is a major health problem with about 90% of diabetic patients having non-insulin type 2 while about 10% have insulin-dependent [3]. Diabetes is divided into two broad categories: type 1, insulin-dependent diabetes mellitus (IDDM); and type 2, non-insulin-dependent diabetes mellitus (NIDDM). Type 1 diabetes is characterized by inappropriate hyperglycemia primarily a result of pancreatic islet β -cell destruction and a tendency to ketoacidosis type 1 diabetes mellitus is a result of cellular mediated autoimmune destruction of the β cells of the pancreas, causing an absolute deficiency of insulin secretion. Upper limit of 110 mg/dL on the fasting plasma glucose is designated as the upper limit of normal blood glucose.

Type 1 constitutes only 10% to 20% of all cases of diabetes and commonly occurs in childhood and adolescence. This disease is usually initiated by an environmental factor or infection (usually a virus) in an individual with a genetic predisposition and causes the immune destruction of the β cells of the pancreas and, therefore, increased production of insulin. Characteristics of type 1 diabetes include abrupt onset, insulin dependence, and ketosis tendency. This diabetic type is genetically related. One or more of the following markers are found in 85% to 90% of individuals with fasting hyperglycemia let cell autoantibodies, insulin autoantibodies, glutamic acid decarboxylase autoantibodies, and tyrosine phosphatase-2 and IA-2B autoantibodies. Signs and symptoms include polydipsia (excessive thirst), polyphagia (increased food intake), polyuria (excessive urine production), rapid weight loss, hyperventilation, mental confusion, and possible loss of consciousness (due to increased glucose in the brain. an individual's resistance to insulin with an insulin secretory defect. This resistance results in a relative, not an absolute, insulin deficiency. Type 2 constitutes the majority of diabetes cases. Most patients of this type are obese or have an increased percentage of body fat distribution in the abdominal region. This type of diabetes often goes undiagnosed for many years and is associated with a strong genetic predisposition, with patients at increased risk with an increase in age, obesity, and lack of physical exercise. Characteristics usually include the adult onset of the disease and milder symptoms than in type 1, with ketoacidosis, seldom occurring. However, these patients are more likely to go into a hyperosmolar coma and are at an increased risk of developing macrovascular and microvascular complications [1]. Multiple mechanisms are found to be involved in it, but the most likely mechanism is that the insulin resistance syndrome be central to the development of

diabetic endothelial dysfunction. The hemostatic abnormality and endothelial dysfunction are responsible for the generation of a hypercoagulable state in type 2 diabetes mellitus individuals [2]. Body of evidence suggests that certain hematological indices are altered in patients with diabetes mellitus [4]. In patient with diabetes mellitus, persistent hyperglycemia exposes red blood cells (RBCs) to elevated glucose concentration, thus resulting in the glycation of hemoglobin, prothrombin, fibrinogen, and other proteins involved in clotting mechanisms. [5]. The glycation results in the incomplete activation and function of the clotting cascade [6]. Glycation of intrinsic and extrinsic clotting proteins will decrease the availability of these proteins which affects the clotting capacity. [7]. Complication of diabetes mellitus type 2 Microvascular complications such as (neuropathy, retinopathy, and nephropathy) are strongly related to hemoglobin A1c Concomitant atherosclerosis and occult macrovascular disease may follow an accelerated course in type 2 diabetes [8].

Materials and methods:

Study design:

A cross-sectional study with the control group, prospective.

Study area:

Atbara city, Sudan.

Study duration:

From March to July 2018.

Study population:

Diabetes type 2 patients in Atbara city.

Sample size:

100 samples were collected, 50 of them were collected from diabetes mellitus type 2 patients, and the other 50 were collected from healthy persons as a control.

Data collection:

The data was collected by using questionnaires and will be excluded the patients who use anticoagulant drugs and other drugs that affect the bleeding profile, those who have liver and kidney disease, and other diseases that can affect the bleeding profile in the diabetic Mellitus type 2 patients.

Sample processing:

The samples collected from the diabetes type 2 patients and healthy persons were centrifuged and assessed the prothrombin time (PT) and activated partial thromboplastin time (APTT).

Test procedure:

The COATRON M1 is designed to carry out coagulometric tests such as PT, PTT, fibrinogen, single factor tests, chromogenic and immune-turbidimetric tests (for instance antithrombinIII D -dimer, etc.). Use only citrated plasma for test analysis runs: mix 9 parts venous blood with 1 part 3.2 % (0.105m) sodium citrate and centrifuge the mixture at 1500g for approximately 10 minutes, plasma must be used within 4h. All tests are performed with a quarter of the regular volumes. the micro cuvette can be run with a minimum of 75 μ l = 25 μ l sample +50 μ l thromboplastin for PT. Incubation area for 6 samples and 2 reagent positions. The COATRON M1 needs 3-5 min to warm up to 37.0 C. Green signal light indicates the correct temperature. Automatic start at reagent addition [9].

Theory of operation:

The COATRON M1 is a highly sensitive single-channel photometer. A very intensive

laser LED-Optic at 400 nm ensures accurate and precise results, even when icteric or lipemic samples are used. The receiver signal is detected and converted to an electrical current. During the actual test, the system is searching for the best amplification. The software algorithms are based on optical density (extinction), which absorbs outside light effects [9].

Detection principle:

Plasma /blood and reagent absorb the transmitted laser light. The rate of absorbance is obtained by the detector and sent to the microcontroller. Here a program analyses the signal and sends the result to the display and printer (optional) [9].

Test selection:

To alternate between the tests, press the key "TEST" to activate selection, cursor keys to change, and key ENTER to confirm [9].

Stopwatch:

A stopwatch function helps the operator to control the correct incubation times the timer stops after 999s automatically, to start the stopwatch press key "TIMER", to stop and rest press key "TIMER" again [9].

Measurement:

Before activating the channel, the cuvette must be inserted into the measurement position and ready to add the start reagent. press key "OPTIC" to activate the channel message "WAIT" indicates that the measurement calibrates the optic to the actual optical value. If "ACTIVE" is displayed on the screen the measurement is ready to start. The actual result ID is also displayed. If the optical value changes from the "TRIGGER" value (e.g., by adding a reagent), the measurement will start. The start can be also triggered by pressing the key "OPTIC". Once

started a small Deeping noise is followed by a scrolling arrow. The current light absorbance (OD) can be read on the display. Avoid contact with the cuvette while this message is shown. A Deeping noise will sound again when a clot reaction was detected and the result will be displayed. If the clot reaction needs more than the maximum reading time of 300s the optic will stop and display "+++.", which means "no clot detected".[9].

Quality control:

Control plasma should be tested in conjunction with the patient sample, it is recommended that at least one normal and one Subnormal be run at least each shift and a minimum of once per 20 patient samples. A control range should be established by the laboratory to determine the allowable variation in day-to-day performance on each control plasma [9].

PTT Determination:

The APTT test measures the clotting of test plasma after the addition of the APTT reagent. then allowing an "activation time", followed by the addition of calcium chloride, deficiencies of approximately 40% and lower of factors VIII, IX, XI, and XII will result in a prolonged APTT. Heparin in the presence of adequate amounts of anti-thrombin III will also result in a prolonged APTT [9].

Data analysis:

Data were analyzed by SPSS version 22 using an independent T-test.

Ethical considerations:

Permission to carry out the study was obtained from the college of health, Elsheikh Abdallah Elbadri University, and permission of the ministry of health.

Results:

Table-1: Distribution of study group according to Gender

Gender	Frequency	Percent
Male	23	46%
Female	27	54%
Total	50	100%

Table-2: Distribution of study group according to age

Age group	Frequency	Percent
Less than 30 years	3	6%
31 - 40 years	3	6%
41 - 50 years	12	24%
51 - 60 years	10	20%
61 - 70 years	14	28%
71 - 80 years	8	16%
Total	50	100%

Table-3: Distribution of study group according to physical exercising activities:

Exercise activities	Frequency	Percent
Yes	21	42%
No	29	58%
Total	50	100%

Table-4: Distribution of study group according to duration

Duration	Frequency	Percent
1-5 years	22	44%
6 - 10 years	15	30%
11 - 15 years	8	16%
16 - 20 years	2	4%
21 - 25 years	3	6%
Total	50	100%

Table-5: Comparison of means of PT, APTT and INR in healthy individuals' and diabetic patients

Variable	Healthy individuals	Diabetic patients	P value
PT	16.7 ± 1.24 (14.6 - 19.2)	16.64 ± 3.09 (12.9 - 28.1)	0.832
APTT	36.2 ± 2.7 (30 - 42)	38.3 ± 8.7 (26 - 61)	0.111
INR	1.158 ± .091 (1 - 1.34)	1.15 ± .227 (.88 - 2)	0.844

Table-6: Comparison between exercise and PT, APTT, INR in diabetic patients

Variable	Yes N=21	NO N=29	P value
PT	16.9 ± 3.5	16.4 ± 2.8	0.609
APTT	38.21 ± 9.4	38.3 ± 8.35	0.956
INR	1.1695 ± .25814	1.1379 ± .2055	0.632

Table-7: Comparison between age and PT, APTT, INR in diabetic patients

		Sum of Squares	Df	Mean Square	F	Sig.
PT	Between Groups	22.977	5	4.595	0.453	0.808
	Within Groups	445.901	44	10.134		
	Total	468.878	49			
INR	Between Groups	.125	5	.025	0.458	0.805
	Within Groups	2.403	44	.055		
	Total	2.528	49			
PTT	Between Groups	133.373	5	26.675	0.326	0.895
	Within Groups	3605.507	44	81.943		
	Total	3738.880	49			

Discussion:

Diabetes Mellitus is associated with an increased risk of atherosclerosis, so diabetes is a procoagulant state. Is characterized by a high risk of athero-thrombotic complications affecting the coronary, cerebral and peripheral arterial trees. It is a syndrome characterized by the presence of chronic hyperglycemia due to defective insulin secretion, insulin action, or both affecting metabolism of various compounds including carbohydrates, lipids, and proteins and it also impairs various biological processes such as coagulation and fibrinolytic alteration. Therefore, the present study evaluated some Bleeding profile tests in diabetes mellitus type2 individuals. The results show that the mean level of prothrombin time in type 2 diabetic patients was 16.64 ± 3.09 Sec and of control was 16.7 ± 1.24 Sec, it was none significantly correlated (P value = 0.832) and the mean value of APTT in diabetes mellitus type2 was 38.3 ± 8.7 seconds while in healthy individuals it was 36.2 ± 2.7 seconds, no significant difference in APTT was found in the diabetes mellitus type2 and healthy individuals (P value as 0.111). The study done by acang N1 jalil FD, University of andalas general hospital in 1993. Hypercoagulation in diabetes mellitus. That result was significantly high fibrinogen and short PT and APTT in diabetic patients which disagrees with our study [10]. Another study was done by Fayez Karim, et al, from July 2013 to June 2014. Coagulation impairment in type 2 diabetes mellitus. As a result, in this study, PT and APTT were significantly ($P < 0.001$) lower in diabetes mellitus than those of the control group, which disagrees with our study [11]. In the study done by Fathelrahman Mahdi Hassan, Prothrombin time and activated partial thromboplastin time among type 2 noninsulin-dependent diabetes mellitus the results show that the mean level of prothrombin time in 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), which disagrees with PT in our study, however, the APTT agrees with our study [12]. Another study was done by Amal S. elhassadelet al, the effect of diabetes

mellitus type 2 on activated partial thromboplastin time and prothrombin time. That result shows the mean value of APTT in diabetes mellitus type2 individuals was significantly lower (28.95 ± 7.54) seconds as compared 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 diabetes mellitus type2 individuals ($P \geq 0.05$) which the APPT of their study disagreed with our study, however, the PT of their study agree with our study [13].

Conclusion:

Our data concluded that patients with type 2 diabetes mellitus had no hypercoagulable state due to PT and APTT.

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