Evaluation of Common Coagulation Tests in Type 2 Diabetic Patients and Association with Diabetic Pre-cardiovascular Complications, Gezira State–Sudan, 2020-2021

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background and Objectives: Diabetes has an epidemic character because of the huge growth within side the wide variety of human affected in latest years. If laboratory findings display abnormalities connected to an improved threat of thrombosis, diabetes, specifically type 2, can present hypercoagulability symptoms. The aim of this study to evaluate the common coagulation parameters PT, aPTT, and D-dimer in patients suffering with diabetes type 2 and to associate these parameters with the thrombotic complication in those patients.

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Methods: This was a case control study performed on 70 patients with diabetic type 2 from different ages (Their ages ranging from 20 -72 years with an average age of 56.2 years) and different gender (41.4% were males and 58.6% were females) attending the Diabetic Clinic of the Aldaraja Health Center, compared with 50 apparently healthy individual as a control group were enrolled in study and that in Wad Madeni, Gezira State, central of the Sudan in the period between June 2020 to January 2021, Blood were collected from each enrolled subject and the levels of PT, aPTT and D-dimer were measured.

Results: This study showed lower levels of PT and aPTT (patients 13.3 seconds/ control 14.3 seconds and patients 34.3 seconds/ control 36.6 seconds) respectively with highly significance difference (*P. value* = 0.001) respectively when compared with control group, while showed higher level of D-dimer (patients 585.3 ng/ml/ control 178.58 ng/ml) with highly significant difference (*P. value* = 0.000) when compared with control group. In diabetic patients without thrombosis (early onset of occurring thrombosis) had low level of PT with highly significant difference (*P. value* = 0.000) when compared with diabetes plus thrombosis and control groups.

Conclusion: We concluded that the Sudanese diabetic patients had a procoagulant state that would result in thrombosis, so we advocated that diabetic patients, specifically type 2 to take delivery of anticoagulant therapy for as a minimum a quick time as a preventative degree to keep away from thrombus formation, specifically cardiovascular.

1. INTRODUCTION AND BACKGROUND

The prevalence of hyperglycemia in the absence of therapy characterizes and distinguishes a set of metabolic diseases known as diabetes. Defects in insulin production, insulin action, or both, as well as abnormalities in carbohydrate, lipid, and protein metabolism, are among the several aetiopathologies (WHO, 2019). It is one among the top ten causes of mortality in people worldwide, and it was estimated to have caused deaths in about 4 million globally in 2017 [1]. According to the WHO, the eastern Mediterranean area has the world's highest prevalence of diabetes. Seven nations, including Sudan, have a moderate incidence of DM 9–12% [2]. Type 1 and type 2 diseases are the two most common types.

Type 2 diabetes, also known as non-insulin dependent diabetes, is a considerably more common form of the illness, accounting for roughly 90% of all cases [3].

T2DM can induce microvascular and macrovascular problems, the latter of which is linked to an increased risk of atherothrombosis, which is the leading cause of mortality in 80 percent of diabetic patients. More than 75% of these deaths are caused by cardiovascular problems, whereas the remaining 20% are caused by other macrovascular problems [4,5]. Long-term consequences of diabetes mellitus are the leading causes of morbidity [6], death, and high healthcare expenditures [7,8], the latter of which will continue to be a major issue specially in Sudan [9]. Sudan is the largest country in Africa with a total area of 1,886,068 km2, and a total population of about more than 33 million. The annual population growth rate is 2.2% and the rural population constitutes about 60%. The estimated prevalence of diabetes in urban areas of Sudan is 19% and rural areas is around 2.6% [10]. Gezira state is located in the central part of Sudan, with a population of 3,900,000. The imbalance between coagulation and fibrinolysis mainly contribute to excess fibrin deposition in the vascular wall and then result in the pathogenesis of atherothrombosis. The registration of hart center in Wad Medani, 25% of the cardiovascular disease was diabetic patients due to atherothrombosis and the incidence is approximately 200 patients/ year in Medani Heart Center (MHC), Gezira state, Sudan. The diabetic patients have a two- to fourfold higher risk of cardiovascular disease, compared with non-diabetics and there is no protective agents for this complication. In terms of coagulation, the human body's haemostatic system is typically intended to keep blood in a fluid state (normal physiological circumstances).There are three methods for controlling hemostasis: first platelet creation, second thrombin production, and third diffusion of active coagulant proteins. These variables are then taken into account. The fibrinolysis system is the primary mechanism for clot dissolution [11,12]. The occlusive vascular thrombus manly in the condition of hypercoagubility; arterial thrombi consists of fibrin fibers with cellular components present in this network. Many factors contribute to thrombus development, including hyperlipidemia, diabetes,

smoking, lack of exercise, obesity, and hypertension [13]. In this study, we look at hypercoagubility as a thrombosis risk factor rather than a traditional risk factor in diabetic individuals with type 2 diabetes.

2. MATERIALS AND METHODS

This was analytical case control study to estimate the PT, aPTT and D-dimer tests for evaluation of the procoagulant process in Sudanese diabetic patients type 2 and associate this parameters with diabetic complication. A total of 70 patients known diagnosed with diabetes by Glucose Tolerance Test (GTT) and HbA1c attending to the Diabetic Clinic of the Aldaraja health center during Jun 2020 to January 2021, in Wad Medani, Gezira state central of Sudan. Both males and females aged between 28 – 86 years controlled and uncontrolled type 2 diabetic patients was selected by simple random sampling technique. A thorough questionnaire was used to collect their medical history and personal information.

2.1 Patients Selection

Age less than 18 years and other types of diabetes patients were excluded also; pregnancy and women using contraceptive pills; neuropathy and nephropathy; smoking or patients who were taking standard anticoagulant treatment with either Coumadin derivatives or heparins at the time of admission and patients with liver disease and finally patients had hypertensive before diabetes mellitus disease.

2.2 Samples Collection and Laboratory Methods

6 ml of venous blood was collected from each subject using aseptic procedure after a 12 hours fasting, 1.8 ml was dispensed into specimen bottles containing 0.2 ml of tri-sodium citrate to make a ratio 1:9 for the determination of PT, aPTT and level of D-dimer. These tests were performed within 2 hours in duplicates. Standard methods of Dacie and Lewis (2016) were employed for the determination of PT, aPTT by using Coatron M4 coagulometer semi-automated method and level of D-dimer done by i-chroma™ reader by fluorescence immunoassay method. The reminder of blood sample was drown in to lithium heparin tube for estimate FBG used SPINREACT reagent by spectrophotometric method [14].

2.3 Statistical Analysis

Statistical Package for Social Sciences (SPSS) Version 16. Common coagulation assays (PT , aPTT, D-dimer), FBG and HbA1c results were normally distributed and were reported as the mean and standard deviation. The significances of the differences in study parameters between patients and control groups were determined using t-Test for 2 groups, if not met this criteria the Kruskal-Wallis test were applied.

3. RESULTS

120 blood samples were collected, 70 from diabetic patient type 2 from different ages (Their ages ranging from 20 -72 years with an average age of 56.2 years) and different gender (41.4% were males and 58.6% were females) and 50 samples collected from healthy individuals as a control group. In comparison means of the parameters under study common coagulation (PT, aPTT and D-dimer) between diabetic patients and control subjects showed the highly significant difference in all parameters as shown in (Table 1). In compare mean of common coagulation (PT, aPTT and D-dimer) in diabetic patients type 2 according to the gender showed that, there were statistical difference between the groups in (PT and D-dimer), with low mean for female in PT and high in D-dimer as shown in (Table 2). When compare median of study parameters between diabetic patients without thrombosis, diabetic patients with thrombosis and control subjects showed that highly significant difference in PT (P.value = 0.000), other parameters were not significance between the groups(PTT and D-dimer with P. value 0.895 and 0.082) respectively as shown in (Table 3).

Table 1. The significant difference between diabetic patients and control

Parameters	Case / control	N	Mean	Std.	P. value
PT Sec	Diabetic patients	70	13.3	1.4	0.000
	Control	50	14.3	1.1	
a PTT Sec	Diabetic patients	70	34.3	3.6	0.001
	Control	50	36.6	3.4	
D-dimer ng\ml	Diabetic patients	70	585.33	639.162	0.000
	Controls	50	187.58	96.637	

Table 2. Compare means in diabetic patients between the gender group

Study parameters	Gender	N	Mean	Std. Deviation	P. value
PT Sec	Male	29	13.7517	1.53800	**.030**
	Female	41	13.0122	1.24784	
aPTT Sec	Male	29	34.1552	3.93851	.663
	Female	41	34.5439	3.44485	
D-dimer ng\ml	Male	29	364.29	282.55475	**.014**
	Female	41	741.67	767.04148	

Table 3. The significant difference between diabetic patients with, without thrombosis and control group in the study parameters

Parameters	Subjects	N	Median	Range (Min-Max)	P. value
PT Sec	Diabetic patients with thrombosis	5	13.8	12.6-14.8	**0.000**
	Diabetic patients without thrombosis	65	13.6	11.7-21.7	
	Control	50	14.0	12.9-17.1	
aPTT Sec	Diabetic patients with thrombosis	5	34.7	33.4-36.1	0.895
	Diabetic patients without thrombosis	65	35.2	28.5-43	
	Control	50	37		
D-dimer ng\ml	Diabetic patients with thrombosis	5	152	108-315	0.082
	Diabetic patients without thrombosis	65	441	36-3200	
	Controls	50	167	64.9 -550	
FBG mg\dl	Diabetic patients with thrombosis	5	114	79-245	0.006
	Diabetic patients without thrombosis	65	157	48-356	
	Control	50	89	70-133	

4. DISCUSSION

In Sudan, there are limited reports on coagulation screening tests, and there is no information on these parameters in diabetes patients in Gezira state in central Sudan. Many research have found coagulation activation indicators, according to various research. The averages of clot base parameters in this research were modest in time, showed low level with significant differences in PT and PTT (13.3 sec and 34.3 sec, respectively), but the mean of D-dimer was high, at 585.3 ng/ml showed in Table 1.There was a highly significant difference in PT, PTT, and D-dimer when compared to the control group (P.value = 0.00 except in aPTT was 0.001). This is agreement with the previous studies performed by Alkandow, et al, 2017 in Sudan and also with study of (Doron and Elliot, 2002), (Abegunde et al., 2007;Cooper ,et al., 2001; Oldroyd et al.,2005) and also similar to the results reported by (Calee,2001) they founded

that the mean of PT, aPTT significantly lower in diabetes mellitus type 2 than those of control (p.value <0.05), and this result confirmed the hypothesis that diabetes present procoagulant state and on the other hand, elevation of procoagulant markers measured by D-dimer increase the risk of thrombosis specially cardiovascular disease and stroke among case group. But disagreed with Oalao, et al. in Northern Nigeria, 2009 that reported there was significant prolongation of PT and aPTT of diabetics when compared with the non–diabetic controls (P<0.005) and according to their explanation may be due to in-vitro interference of fibrin clot formation by inhibitors. When compared the means of diabetic patients type 2 in PT and D-dimer regarding to the gender Table 2 showed significance difference (P. value = 0.030 and 0.014) respectively; that mean females susceptible to risk of thrombosis (D-dimer 741.67 ng/ml) when compared with male D-dimer 364.29 ng/ml, and in our justification low

activity of Sudanese women that exclusive around their home and also due to assemblage and manners of Sudanese women like the obesity. This result disagreement with the study of Bararu, 2019 found that; this complication was associated with male rather than female [15]. While the aPTT parameter (with P.value = 0.663) showed no significance difference. When compared the diabetic patients with thrombosis, diabetic patient without thrombosis and control subjects; in diabetic patients without thrombosis (regard as early onset of occurring thrombosis) there were a highly significant low in PT (P. value = 0.000), while the FBG was high level with significant difference (P. value = 0.006). In our justification various mechanisms have been proposed for endothelial abnormality like persistence of high molecular weight of glucose outside tissue lead to tissue injure, that produced tissue thromboplastin and finally activate the extrinsic pathway in-vivo, so the PT was shortage, when this pathway active lead to occurring thrombosis that related specially with carduvascular disease, and the other parameters were no significance difference mean in aPTT and D-dimer (P. value = 0.895 and 0.082) respectively as shown in (Table 3).

5. CONCLUSION

In these study; Sudanese diabetic patients presented procoagulant state. We recommended that further case control studies with large sample size of diabetic patients with thrombosis are highly recommended to support the findings of this study. By this result give the diabetic patient specially type 2 antithrombotic drugs like at least in short term as prevention to avoid the thrombus formation specially cardiovascular events.

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the research ethical committee (REC) of The Faculty of Medical Laboratory Sciences in University of Gezira of Gezira University and ministry of health- Gezira state. Also, before collection samples, written consent were obtained from all participants.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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