

Coagulation Profile in Type2 Diabetes Mellitus Sudanese Patients

Saadia Salaheldin Rabei¹*

¹ Medical Laboratory Sciences/Department of Immunology, Sudan Academy of Sciences, Khartoum, Sudan

Email Address

sosohilal1989@gmail.com (Saadia Salaheldin Rabei)

*Correspondence: sosohilal1989@gmail.com

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Abstract:

The incidence of type 2 diabetes mellitus (T2DM) is rapidly rising worldwide during the recent decade. Diabetes Mellitus is associated with a high prevalence of vascular diseases. These alterations result from the interaction between hyperglycemia, insulin resistance, inflammation and oxidative stress. This study was conducted to investigate the coagulation profile in type 2 diabetic patients in order to find out the extent of their exposure to thrombotic risk. A total of 60 consented patients of T2DM were involved in the study, 56% were males and 44% were females, 30 non-diabetic participants were enrolled as controls. The coagulation profile (PT, INR and APTT) were measured by the Coagulometer analyzer and the results were interpreted in seconds. The results of coagulation tests revealed that the Prothrombin Time (PT), for T2DM patients was lower insignificantly than that of the control participants (p value was 0.102), while APTT and INR were significantly lower for T2DM patients in comparing to controls with P value of 0.006 and 0.007, respectively. The study concluded that type 2 diabetes mellitus patients are more hypercoagulable than non-diabetic subjects & in female patients more than males. Hence, Evaluation of coagulation profile should be evaluated regularly in T2DM patients. Further studies are needed to be conducted with inclusion of other coagulation profile tests like fibrinogen and von Willbrand factor (vWf).

Keywords:

Diabetes mellitus (D.M), T2DM, Coagulation, PT, INR, APTT

1. Introduction

Diabetes mellitus is a group of metabolic disorders sharing the common underlying feature of hyperglycemia. Hyperglycemia itself can impair pancreatic beta cells function and increase insulin resistance, causing a worsening metabolic state [1]. Diabetes is a risk factor for the development of atherothrombosis and venous thromboembolism (VTE). Several mechanisms contribute to the diabetic prothrombotic state, such as endothelial dysfunction, coagulative activation, and platelet hyper-reactivity [2]. In addition, the impairment balance in fibrinolysis which caused by increased level of PAI-1. Hyperglycemia and hyperinsulinemia increase PAI-1 levels in diabetic patients [3].

Prothrombin time (PT) and activated partial thromboplastin time (APTT) are hematological indices that give an idea about the coagulation status of patients [4]. Many studies have shown the hyper coagulation state and shortened APTT and PTT values in type2 diabetic patients(T2DM). In one study, the coagulation and fibrinolysis parameters were measured in 60 T2DM patients with and without diabetic microvascular complications, and in 30 nondiabetic healthy individuals. The study showed the shortened APTT and PT in diabetic patients comparing with non-diabetic [5]. Hypercoagulability in diabetes in some studies has been evidenced by increased fibrinogen level and PAI-1 levels that affect the fibrinolysis [6].

In Sudan, diabetes mellitus is currently emerging as an important health problem. Some of reasons that increase the seriousness of the situation, lack of efficient diabetes care centers in Sudan and most of patients do not follow a healthy diet, in addition to the wrong believes. Few studies on the coagulation problems in diabetics have been carried out in Sudan in spite of the growing number of diabetic patients, and these few studies show different results. Currently, hemostatic profile tests are not part of routinely tests done in the management of T2DM patients and usually requested in certain cases as in the tests that are performed before entering surgery. So this study was conducted to investigate the coagulation profile in T2DM in Sudan to assess their vulnerability to thrombosis.

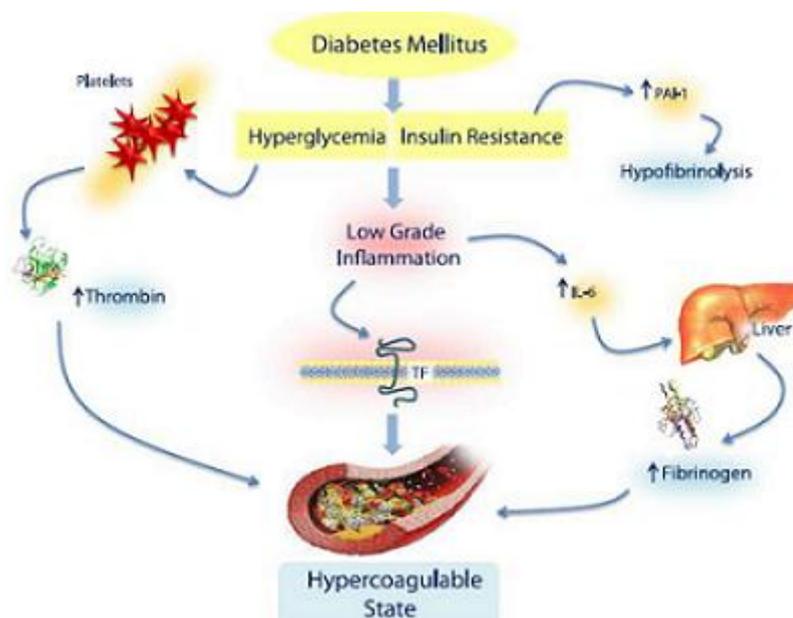


Figure 1. Prothrombotic mechanisms in Diabetes Mellitus [2].

2. Materials and Methods

This study was a cross sectional study that conducted at Diabetic and Endocrine Centre /Khartoum North province during November 2014 to January 2015. A total of 60 T2DM patients and 30 volunteers as non-diabetic control participated in the study. The age of participants ranged from 23 years to 80 years .The mean age was 47 years old.

2.1. Blood Sample Collection

Under all aseptic conditions, 1.8 ml of venous blood for PT and APTT was collected from each of the study participants in sodium citrate containers. Samples in

sodium citrate were centrifuged immediately at 1500g for 15 minutes. Plasma was then separated and transferred into siliconized glass tubes and stored at 40C in a fridge.

2.2. Sample Analysis

PT and APTT results were tested using the coagulometer analyzer (COAIRON M2). The reagents were incubated in 37 °C for at least 15 min.

2.2.1. Prothrombin Test

In clean small test cups, 50 π l from the PT reagent (thromboplastin+ calcium chloride) was added to each test cup. Then 25 μ l from the samples were added and the start key was pushed and then the coagulation time was calculated machinery.

The results of PT test and INR were interpreted in seconds.

2.2.2. Activated Partial Thromboplastin Test

The APTT test was done by the same steps, 25 π l from the APTT reagent (kaolin+ phospholipid) was added to test cups with 25 π l from the sample. Then 25 μ l from the calcium chloride reagent added and the clotting time was calculated. The results were interpreted in seconds.

2.3. Data Analysis

All data of the questionnaire and blood tests were analyzed using version11 of SPSS software(Statistical Package for Social Sciences). ANOVA Test was used for correlation between the results of tests with all recorded variables. T-test was performed to compare the different groups. Statistical significance of results was designed at ($P < 0.05$).

3. Results and Discussion

3.1. Coagulation Profile Results

The mean Prothrombin Time for T2DM patients was lower than that of the control participants with non-significant differences ($P = 0.102$).

The mean INR of the patients is lower significantly than that of the controls with P value= 0.007 .

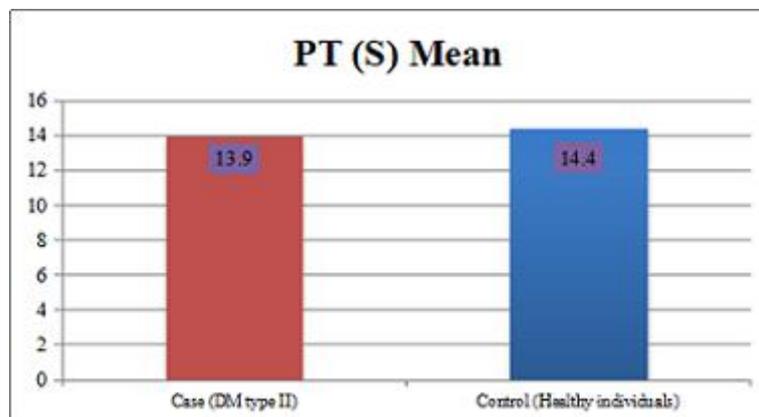


Figure 2. Comparison between the means of PT (S) among Case (T2DM) and Control (Healthy individuals)

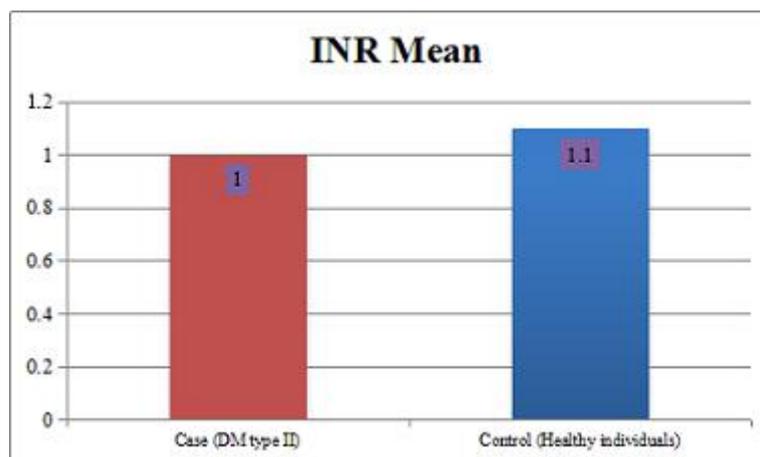


Figure 3. Comparison between the means of INR among Case (T2DM) and Control (Healthy individuals).

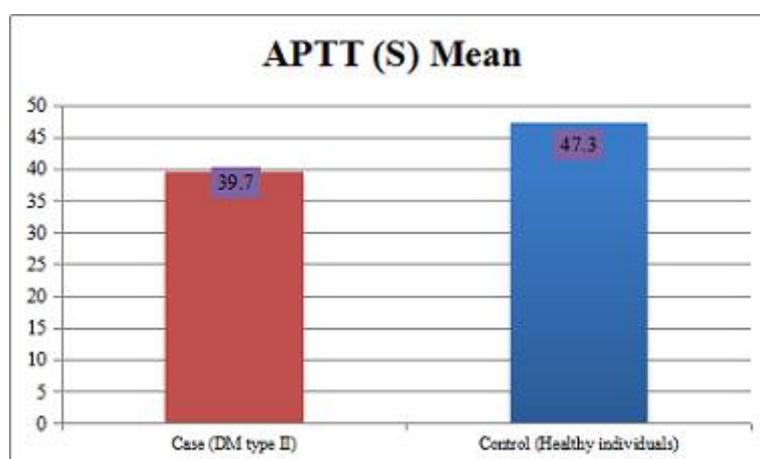


Figure 4. Comparison between the means of APTT (S) among Case (T2DM) and Control (Healthy individuals).

As shown in Table 1, the mean Activated Partial Thromboplastin Time for T2DM patients was significantly lower than control group ($P=0.006$).

Table 1. Comparison between the means of coagulation profiles among T2DM and Control.

Variables	DM type II (N=60) Mean (SD)	Control (N=30) Mean (SD)	p-value
PT (S)	13.9 (1.5)	14.4 (0.9)	0.102
INR	1.0 (0.1)	1.1 (0.2)	0.007
APTT (S)	39.7 (13.4)	47.38.6	0.006

3.2. Comparison of coagulation profile among diabetic patients according to the gender and age

Table 2 shows the comparison of mean PT between males and females of T2DM patients, there was a significant difference (P value= 0.032). In other hand the difference in the INR was insignificant with P value= 0.068 . There was insignificant difference also in APTT between males & females (P value was 0.838).

In the correlation between the coagulation profile and the age, there was a weak negative correlation which was significant in PT and INR, while it was insignificant in APTT.

The results of the current study agree with a study that reported insignificant shortened PT in T2DM patients as compared to control subjects [7]. The results are also consistent with another study suggests that hemostatic parameters have a lower predicting value for type2 diabetes mellitus. The findings demonstrate decreased APTT and PLT (platelets) levels in T2DM patients without complications compared with controls [8].

Table 2. Comparison between the means of coagulation profile among males and females of T2DM patients.

Variables	Male patients	Female patients	P value
PT	14.2	13.5	0.032
INR	1.0	1.0	0.068
APTT	39.4	40.1	0.838

Lippi *et al.*, [9] also found shortened PT and APTT in T2DM patients than in non-diabetic control subjects, but only the APTT results were significantly shorter [9].

Shortened APTTs may result from an accumulation of circulating activated coagulation factors in plasma caused by enhanced coagulation activation *in vivo*. There is supporting evidence that shortened APTT values in some cases may reflect a hypercoagulable state, which gives the possibility of increased thrombotic risk and adverse cardiovascular events in diabetic patients [10].

On other hand, the insignificant PT results support the hypothesis that the extrinsic pathway has less involvement in hypercoagulability state than intrinsic pathway. In a path analysis study, used to assess the interactions between coagulation factors in relation with pathogenic events in both diabetics and healthy subject. The results showed that FII, as the main cause for hypercoagulable state, is directly induced by FX and FVIII in normal individuals and by FX, FXI, FV and VWF co-factors in diabetic patients [11].

Unexpectedly, the results of the present study in contradiction with findings of a study had been conducted in Sudanese diabetic patients showed slight increase in both type1 & T2DM. INR also showed slightly increase when compared to the mean INR of normal controls in both type1 and T2DM [12]. The results of increased plasma levels of PT and APTT in T2DM were observed in another study which hypothesize the abnormal coagulation mechanisms may interpreted as a tendency for bleeding and cardiovascular disorders [13].

Changes that occur in the vascular system in older patients could be attributed with the hypercoagulable state. This may explain the significant correlation between the coagulation profile & patients ages.

The significant difference in PT results in the current study according to the gender, agree with a study that revealed sex was significantly associated with hypercoagulability. Type 2 diabetes mellitus female patients were 3.98 times more likely to be more hypercoagulable in male patients. Even after adjusting for confounders such as obesity, hypercholesterolemia and hypertension [14]. The results are also in concomitant with Soliman G. [15], who reported that female T2DM patients were more hypercoagulable than male patients by finding significantly higher fibrinogen levels in female T2DM patients than male patients.

Soltani *et al.*, [11] had reported shorter PT and APTT in T2DM patients than in control participants, there was no statistical difference in PT and APTT between male and female diabetic patients.

The finding of the present study supports the hypothesis which states that females are more hypercoagulable than males. According to some study, Differences caused by sex hormone levels do not explain the findings. In women higher estrogen levels are associated with lower PAI-1 levels while in healthy postmenopausal women not receiving estrogen replacement, PAI-1 levels are no higher than in men of the same age [16]. Further studies are needed to explain the relation between the gender and hypercoagulability.

4. Conclusions

According to the findings of this study, we conclude that T2DM patients are more hypercoagulable than non-diabetic individuals and hypercoagulability was more prevalent in female T2DM than in male T2DM . The study also revealed that there was a correlation between the coagulation profile & age.

5. Recommendations

Coagulation profile should be evaluated regularly in T2DM patients.

Further studies are needed to be conducted on large population of T2DM and other coagulation profile tests like fibrinogen and von Willbrand factor(vWf) should be included.

The use of Aspirin as protective dose in diabetes mellitus patients should be intensified.

Conflicts of Interest

The author declares that there is no conflict of interest regarding the publication of this article.

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