Pattern of Some Haemostatic Profile among Diabetes Mellitus Patients Attending Aminu Kano Teaching Hospital, Kano

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ABSTRACT
Diabetes mellitus is a heterogeneous disorder that affects cellular metabolism in many ways, and haemostatic profiles were reported to be adversely affected. This study was aimed to determine the pattern of some haemostatic profiles of subjects with Diabetes mellitus attending Aminu Kano Teaching Hospital, Kano. This cross-sectional study was carried out on eighty (80) participants comprising forty (40) diabetic patients along with forty (40) healthy controls. Five millilitres of venous blood was collected from each participant and placed in appropriate containers for prothrombin time (PT), activated partial thromboplastin time (APTT), and platelet count (PLC). The mean ± standard deviation of PLC and APTT of studied groups showed a statistically significant difference (p-value = 0.0373 and <0.0001 respectively) while PT of diabetic subjects and controls revealed no statistically significant difference (p-value=0.9128). We inferred that reduced APTT and increased PLC may contribute to a hypercoagulable state in subjects with Diabetes mellitus.

Keywords: Diabetes, Prothrombin Time, Activated Partial Thromboplastin Time, platelet count

INTRODUCTION

Diabetes Mellitus (DM), commonly referred to as diabetes, is a group of metabolic diseases in which there are high blood sugar levels over a prolonged period of time. Diabetes is due to either the pancreas not producing enough insulin or the cells of the body not responding to the insulin produced, which gives rise to Type 1 and Type 2 Diabetes mellitus respectively.[1] Another type of Diabetes is Gestational Diabetes mellitus which occurs when pregnant women without a previous history of Diabetes develop a high blood glucose level. Diabetes mellitus is an endocrine disease with multiple aetiologies and results in significant morbidity and mortality from diverse complications.[2] Thrombo-haemorrhagic complications are well recognized among Diabetes populations.[3] The haematological disturbances in Diabetes are characterized by alterations in platelet count and activity, coagulopathy, fibrinolytic aberration, haemorrheologic factors and changes in endothelial metabolism.[4]

Several articles have reported Diabetes mellitus related abnormalities in haemostasis.[5] Diabetes mellitus is associated with an increased risk of atherosclerosis, and coronary artery disease is a leading cause of death in patients with diabetes.[6] In Nigeria and the world at large, about 90% of Diabetic patients are non- insulin-dependent (type II) while about 10% are insulin-dependent (type I).[2] The global prevalence of Diabetes mellitus has been estimated at 347 million individuals and is rapidly increasing.[7] The mortality associated with Diabetes is due to thrombotic and cardiovascular complications in 80% and 75% of cases respectively, while other causes of death are from cerebrovascular events and peripheral vascular disease.[8] The vascular endothelium is the primary site of defence against thrombosis and it is functionally impaired in patients with Diabetes.[9]

Body of evidence suggests that certain haematological indices are altered in patients with Diabetes-glycation of haemoglobin and clotting factors such as prothrombin and fibrinogen, results from persistent hyperglycaemia.[10,11] The glycation results in the incomplete activation and function of both the intrinsic and extrinsic clotting cascades.[2,12] Prothrombin time (PT) and activated partial

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thromboplastin time (APTT) are important haemostatic parameters which give an insight into the coagulation status of patients.[13]

Most studies done on Nigerians with Diabetes were from the West and Southeastern part with the scarcity of information on subjects in our study area in Northern Nigeria. We evaluated some haemostatic profiles of patients with Diabetes mellitus attending Aminu Kano Teaching Hospital.

MATERIALS AND METHODS
Study design/area

This was a cross-sectional study carried out at Aminu Kano Teaching Hospital (AKTH), for the period of seven months (June through December 2017). The Hospital is located within Kano metropolis. Kano state is a state located in the North-western Nigeria.[14] It lies between latitude $11^0 30`N$ and longitude $8^0 30`E$. Kano state was created on May 27, 1967, from the then Northern Region. Kano state borders Katsina to the north-west, Jigawa State to the north-east, Bauchi State to the south-east and Kaduna state to the south-west.[15]

Study Population

A total of 80 subjects were recruited in this study, 40 were diabetic patients attending AKTH and 40 healthy individuals.

Inclusion Criteria

Diabetic patients attending AKTH and healthy individuals who fasted for 8-12 hours and consented to participate were recruited into the study.

Exclusion Criteria

Subjects with the following conditions were excluded: pregnant women, oncology patients, patients with thrombotic tendencies and those on anticoagulant therapy, due to the effect of this conditions on haemostatic profiles.

Ethical Clearance

Ethical clearance to conduct the research was obtained from the ethics committee of Aminu Kano Teaching Hospital. Permission to carry out the study in the selected departments was also obtained from the respective Head of Departments. Informed Consent was obtained from all the participants before sample collection

Sample Collection and Analysis

All specimens for APTT, PT, platelet count, and fasting blood sugar (FBS) estimation were obtained by venipuncture in the morning after fasting for at least 12 hours. Sterile 5ml syringe was used to withdraw 5ml of blood specimen from each subject and was divided into three aliquots (Two milliliter (2ml) into fluoride oxalate vial for FBS, 2ml into vial containing 0.2ml of 3.2% tri-sodium citrate and mixed properly for **PT and APTT and** the remaining 1.0ml was placed into EDTA tube (pediatric EDTA) for platelet count**. The FBS was estimated using glucose oxidase peroxidase method. Platelet-poor plasma was separated from citrated blood by centrifugation at 3000rpm for 15 minutes and stored at -80°C until required. APTT, PT and the platelet count were assayed manually.

Data Analysis

Data were analyzed using statistical package for social science (SPSS) software version 20. The mean and standard deviation were calculated and unpaired t-test was used for comparison of values of Diabetic patients and those of apparently healthy individuals. All statistical analyses were at 95% confidence interval i.e. $P \leq 0.05$ and considered statistically significant.

RESULTS

A total of eighty (80) participants were enrolled in this study. Forty (40) were diabetic patients while forty were (40) were healthy controls. Among the Diabetes subjects, eighteen 18(45%) were males while the remaining twenty-two 22(55%) were females. The mean age of subjects and controls were 39.1±12.3 years and 35.1±8.3 years, respectively.

In table 1, we present mean ± Standard Deviation (M±SD) of platelet count,

PT and APTT in Diabetic patients and controls. The mean FBS in Diabetic patients was 7.9±3.1mmol/L while in controls it was 4.3±0.7mmol/L. The mean PT in Diabetic patients was 14.2±2.0 seconds while in controls it was 14.2±2.2 seconds. The mean APTT in Diabetic patients was 21.6±4.0 seconds while in controls it was 27.9±4.2 seconds. The mean platelet count in Diabetic subjects was 289.6±19.2 x 10^9/L while in controls it was 280.2±20.9 x 10^9/L. There was statistically significant higher FBS among the Diabetic patients than in the controls (p-value = <0.0001). No statistically significant difference in PT was observed between Diabetic patients and controls (p-value = 0.9128). There was statistically significant lower APTT among the Diabetic patients than controls (p-value = <0.0001). There was also a

statistically significant higher platelet count among the diabetic patients than in controls (p-value = 0.0373).

Table 2: Indicated the PLC, PT and APTT in male and female Diabetic patients. The mean platelet count among males and females was 295.4±18.8 X 10^9/L and 284.9±18.7 X 10^9/L respectively, and no statistically significant difference was observed (p-value = 0.0866). The mean PT among males and females was 14.6±2.2 seconds and 13.8±1.8 seconds, respectively, and no statistically significant difference was observed (p-value = 0.1945). Also the mean APTT among males and females was 20.9±3.7 seconds and 22.2±4.3 seconds, respectively, and no statistically significant difference was observed (p-value = 0.3199).

Table 1: Biochemical, Haematological and Haemostatic parameters in subjects and controls

Test/Assay	Study Population		P- value
	Diabetic (N=40)	Controls (N=40)	
FBS (mmol/L)	7.9 ± 3.1	4.3± 0.7	<0.0001
PT (sec)	14.2 ± 2.0	14.3 ± 2.3	0.9128
APTT (sec)	21.6 ± 4.0	27.9 ± 4.2	<0.0001
PLC (x10?/L)	289.7 ± 19.2	280.2 ± 20.9	0.0373

KEY: PLC = Platelet count, PT= Prothrombin time, APTT=Activated partial thromboplastin time, N = Number of subjects, Sec = Seconds

Table 2: Haemostatic Parameters by gender in Diabetic patients

Parameters	Males (N=18)	Females (N=22)	p-value
PLC (x10^9/L)	295.4±18.8	284.9±18.7	0.0866
PT (seconds)	14.7±2.2	13.8±1.8	0.1945
APTT *(seconds)*	20.9±3.7	22.2 ± 4.3	0.3199

KEY: PLC = Platelet count, PT= Prothrombin time, APTT =Activated partial thromboplastin time, N = Number of subjects

DISCUSSION

In this study APTT in Diabetic patients was significantly lower than that of control. The result was consistent with Lippi *et al.,* who found reduced APTT in Diabetic patients than in controls.[12] Acang *et al.,* also found that there was a significantly lower APTT value, in Diabetic patients, especially

in patients with long-term Diabetes with chronic complications, which is also consistent with the results of this study.[16] However, this result was in contrast with the study carried out by Abdurrahman *et al.,* which reported that there was a significant elevation in APTT between untreated Diabetic patients and controls but no

significant elevation between treated patients with Diabetics and controls.[2] The result was also not in agreement with the study conducted by Hassan who reported significant elevation of APTT in Diabetic patients compared to control individuals.[17] Reduced APTT in Diabetes mellitus recorded in this study could be a risk factor for hypercoagulability in Diabetic patients following various studies that have demonstrated shortened APTT to be associated with an increased risk of thrombosis and hence hypercoagulability.[18-20] Reduced APTT may result from an accumulation of circulating activated coagulation factors in plasma caused by enhanced coagulation activation in vivo.[12,21] Reduced APTTs are generally considered to be laboratory artefacts arising from problematic venepunctures. However, there is mounting evidence that shortened APTT values in some cases may reflect a hypercoagulable state, which is potentially associated with increased thrombotic risk and adverse cardiovascular events.[12,21]

The result of this study has shown no statistically significant difference ($p>0.05$) for PT of Diabetic patients and control individuals, in contrast with the study conducted by Abdurrahman *et al*., that reported significant elevation of PT between Diabetic patients and controls.[2] It is also not in agreement with research conducted by Lippi *et al*., that reported shortened PT in diabetic patients compared to controls, however, it was in agreement with a study conducted by Abdallah *et al*., that reported no significance different in PT of Diabetic patients and controls.[12,20] The insignificant PT results support the hypothesis that there is less involvement of the extrinsic pathway in hypercoagulability state in Diabetic conditions because injury occurring to the vascular system in Diabetic patients does not involve tissue factor from outside the vascular system.[22] Boekel and Bartels reported that PT and APTT tests are standard screening tests for function of the coagulation system and their utility in monitoring therapeutic anticoagulation is widely accepted.[23]

In this study, it was shown that the mean platelet count was higher in the Diabetic group than in the control group, and the difference was statistically significant ($p< 0.05$). This was similar to other studies.[24,25,26] However, it is in contrast with the study conducted by Hekimsoy *et al*.,[27] that reported an increased platelet count in a group of non-diabetic patients compared with Diabetic patients.[27] This finding may be due to the presence of other factors that may have influenced the platelet count, such as the mean platelet survival, and the platelet production and turnover rate in Diabetes mellitus. This is because hyperglycaemia may lead to shortened red cell lifespan and decreased Erythrocyte deformability and finally results in thrombocythaemia (usually pseudo) during endocrine diseases. In our study there was no statistical difference for PT, APTT and platelet count of males compared to females with Diabetes mellitus, which is not in agreement with research conducted by Abdallah *et al*. that reported significant elevation of PT, APTT and PLC in females than in males diabetic patients.[20]

CONCLUSION

In conclusion, results obtained in this study indicate that patients with Diabetes mellitus were prone to develop a hypercoagulable state. Therefore, routine examinations of APTT and platelet count are necessary to assess coagulation abnormality in Diabetic patients to prevent diabetes-associated thrombosis**.**

RECOMMENDATIONS

1. Patient with Diabetes mellitus should access APTT and PLC during routine checkup.
2. Further research should be done to include bleeding time to determine the vascular integrity of these patients.
3. Diabetes mellitus patients need to be educated on the risk factors, complications and management to improve on glycaemic control to prevent complications.

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