

Haemostatic Profile of Patients with Type 2 Diabetes Mellitus in Northern Nigeria

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Citation

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Abstract

Diabetes Mellitus is a major health problem that results in significant morbidity and mortality from diverse complications. Thrombo-haemorrhagic complications are well recognized among diabetic populations. Many of the previous haemostatic studies in diabetic Nigerians focused on patients from the west and south eastern parts with scanty information from northern Nigeria. A total of 50 diabetic subjects aged between 30 – 80 years attending the diabetic clinic of the Jos University Teaching Hospital were selected for the study. 50 aged and sex matched non – diabetic persons in the family medicine outpatient clinic of the same hospital were recruited as controls. Prothrombin Time (PT), Activated Partial Thromboplastin Time (APTT), Thrombin Time (TT) and fibrinogen weight were estimated using standard methods. There was significant prolongation of PT, APTT, TT of diabetics when compared with the non – diabetic controls ($P < 0.005$). Also the mean fibrinogen weight was significantly higher in the diabetic patients than the controls ($P < 0.05$). These findings suggest that despite the popular notion of a prothrombotic tendency in diabetes, diabetics may also be prone to developing haemorrhagic complications. It is helpful to bear this in mind, and to include incorporate PT, APTT, TT and fibrinogen assay as routine investigations for better management of these patients.

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder characterized by chronic hyperglycaemia due to disturbances of carbohydrate, fat, and protein metabolism that are associated with absolute or relative deficiencies in insulin secretion, insulin action or both (Charles FA, 1998. Albertis KG, 1998). Over 170 million people worldwide and about 1 – 7% of the Nigerian population are affected (Wokoma FS, 2002. Fabiyi et al, 2002).

A Nigerian national non-communicable disease survey estimated the prevalence to be 2.2% with over 90% being type 2 diabetes. (Akinkugbe OO, 1997). A prevalence of 3.1% has been reported in urban Jos (Puepet FH, 1996). The long term effects and complications of diabetes include progressive development of retinopathy, nephropathy, and neuropathy with microvascular and macrovascular diseases. Macrovascular disorders such as atherosclerosis are a recognized major cause of mortality in the diabetic population, and are implicated in the circulatory disturbances that are seen in diabetes. The circulatory disturbances are further compounded by alteration in platelet count and activity, coagulopathy, fibrinolytic aberration, haemorrhological factors, and changes endothelial

metabolism (McFarlane IA, 1997)

Many studies have shown that diabetes is a hypercoagulable state. Hypercoagulability results from enhanced vascular endothelial cell expression of tissue factor and Von Willebrand factor. Other factors include increased platelet adhesiveness, elevated level of procoagulant factor, and decreased fibrinolytic activity. (Alvin CP, 2001)

Many of the previous studies on haemostatic changes in diabetic Nigerians were conducted in the western and south eastern parts of Nigeria with dearth of reported data from northern Nigeria. For these reasons, it was important to study the haemostatic profile of diabetic patients resident in Jos, North central Nigeria.

MATERIALS AND METHODS

A total of 50 diabetic subjects (both males and females) aged between 30 – 80 years attending the diabetic clinic of the Jos University Teaching Hospital were selected for the study. Diabetes in this study was defined based on laboratory findings as a fasting plasma glucose levels greater than 7.0mmol/L on two or more occasions (WHO, 1999). Their medical history and personal data were obtained via a comprehensive questionnaire after due approval from the

ethnical committee of the hospital.

Fifty age and sex – matched non diabetic persons attending the family medicine out patient clinic of the hospital were used as controls in this study. Informed consent was obtained from all the participants.

Twenty milliliters (20mls) of venous blood was collected from each subject using aseptic procedure after a 12 – hour fast. Nine (9mls) of venous blood was dispensed into specimen bottles containing 1ml of trisodium citrate to make a ratio of one volume of anticoagulant to (nine) 9 volumes of venous blood for the determination of PT, APTT, TT and fibrinogen weight. Plasma was separated from the blood after centrifuging at 2000g/m for 10minutes in standard bench centrifuge to obtain platelet poor plasma required for these coagulation assays. Tests were performed within 3 hours of sample collection and in duplicates. Standard methods of Dacie and Lewis (1996) were employed for the determination of PT, APTT, TT and fibrinogen weight. For all participants, blood pressure, weight and height were measured, and body mass index (BMI) was calculated.

RESULTS

This study examined the haemostatic profile of diabetics resident in Jos, North Central Nigeria. The tests that were carried out include the determination of Prothrombin Time (PT), activated partial thromboplastin time (APTT), Thrombin Time (TT) and fibrinogen weight. Table 1 show the age and sex distribution of all participants. Participants were aged between 30 and 76 years. Females constituted 62% while males constituted 38%. There were 31 females and 19 males in each of the groups.

Table 2 shows the clinical parameters of all participants. There was no significant mean age difference between diabetic patients (51.8 ± 10.2 years) compared to non-diabetic controls (49.7 ± 8.7 years) [P > 0.05]. There was however significantly higher mean Systolic Blood Pressure in the diabetic patients (146.6 ± 19.4mmHg) than the controls (128.8 ± 22.0mm Hg) [P < 0.005]. There was also a significantly higher mean diastolic blood pressure in the diabetic patient (93.2 ± 12.0mm Hg) than the controls (83.8 ± 4.7 mmHg), P < 0.05. Diabetic patients had significantly higher mean Body Mass Index (BMI) (27.3 ± 4.4 kg/m²) than the non diabetic controls (25.3 ± 3.9 kg /m²), P < 0.005.

Table 3 shows the distribution of persons with diabetes according to the duration of disease. No patient had the disease for a period of less than one year. Fourteen persons

(28%) with DM had the disease for a period of 1 – 5 years while 42% had DM for 6 – 10 years. Seven (14%) and 8 (16%) persons had the disease for 10 – 15 years and above respectively. The haemostatic profile (PT, APTT, TT and fibrinogen weight) of diabetics and non – diabetic subjects is shown in table 4. There was significant prolongation of all the parameters in the diabetic group when compared with the control (P < 0.05) even though values were still within the normal limits.

Figure 1

Table 1: Age and Sex distribution of study population

Age (yrs)	Persons with DM No. (%)		Controls		Total
	M	F	M	F	
30 – 39	-	6(6)	1(1)	3(3)	10(10)
40 – 49	5(5)	8(8)	10(10)	14(14)	37(37)
50 – 59	4(4)	14(14)	6(6)	10(10)	34(34)
60 – 69	9(9)	2(2)	-	4(4)	15(15)
70 – 79	1(1)	1(1)	2(2)	-	4(4)
Total	19(19)	31(31)	19(19)	31(31)	100(100)

Figure 2

Table 2: The clinical parameters of study population

Parameter	Persons with DM Mean	Controls Mean	P value	Remark
Age (years)	51.8 ± 10.2	49.9 ± 8.7	0.20	NS
DBP (mmHg)	93.2 ± 12.0	83.8 ± 14.7	0.02	S
SBP (mmHg)	146.4 ± 19.4	128.8 ± 22.0	0.02	S
BMI (kg/m ²)	27.3 ± 3.9	25.3 ± 3.9	0.01	S

Key:

DBP – Diastolic Blood Pressure

SBP – Systolic Blood Pressure

BMI – Body Mass Index

S – Significant

NS – Not significant

Figure 3

Table 3: Distribution of persons with DM according to the duration of disease

Duration of disease (yrs)	No (%)
< 1	0(0)
1 – 5	14(28)
6 – 10	21(42)
11 – 15	7(14)
> 15	8(16)
Total	50(100)

Figure 4

Table 4: Haemostatic parameters of study population

Parameter	DM Mean (SD)	Control Mean (SD)	P-Value	Remark
PT (sec)	15.7 ± 2.1	14.9±2.3	0.01	S
APTT(sec)	27.3 ± 4.4	25.3±3.9	0.01	S
TT(sec)	18.9±2.5	17.1±2.9	0.01	S
Fibrinogen weight (g/l)	3.65±0.61	2.18 ±0.44	0.01	S

Key S- Statistical Significant

DISCUSSION

Diabetes mellitus is a syndrome characterized by presence of chronic hyperglycaemia due to defective insulin secretion, insulin action or both. It is estimated to afflict over 170 million people world wide (Wokoma FS, 2002). The circulatory disturbances in diabetes are characterized by alternation in platelet count and activity, coagulopathy, fibrinolytic aberration, haemorrhologic factors and changes in endothelial metabolism (.McFarlane IA, 1997)

It was observed in this study that the Prothrombin time (PT) of diabetic subjects (15.7 ± 2.1) was significantly prolonged compared to that of non diabetic controls (14.9 ± 2.3) even though the values were within normal limits. Partial thromboplastin time (APTT) in the diabetic subjects was significantly prolonged than that of controls ($P < 0.005$), although within normal limits. The mean Thrombin Time (TT) of diabetic subjects was also significantly prolonged compared to that of control subjects ($P < 0.05$). The mean fibrinogen weight of persons with diabetes in this study was significantly higher than the weight in the controls ($P < 0.05$). This higher fibrinogen weight found in the diabetic group agrees with Mark's report (2001) of elevated fibrinogen concentration as one of the risk factors for atherosclerosis among diabetics. This finding also agrees with Tekemoto et al., (1996) who also reported significant increases in fibrinogen concentration along with increased levels of TFPI, thrombin-antithrombin complex, PAI – 1 in diabetes mellitus. Bartoli (1994) also reported increased levels of fibrinogen, fibrinogen fragments 1 & 2, and D-dimers (DD) in plasma of non-insulin dependent DM. The fibrinogen levels in the control subjects in this study ranged between 1.5 and 3.1g/L while the Caucasians value is between 1.5 and 4.0g/L. This calls for the determination of reference fibrinogen level in our environment.

It is noteworthy that this study found the PT, APTT and TT to be significantly prolonged among diabetics when compared with the controls. While noting that values were

still within normal limits, the significant prolongations of these parameters raise a number of issues. First, it is known that the general notion about diabetes is that of a hypercoagulable tendency resulting from a shift of thrombo-haemorrhagic balance in favor of thrombosis and one would have expected a relative shortening of these parameters. Hence, the significantly prolonged PT, APTT and TT found in the diabetic group in this study may appear to be at variance with this submission. The exact patho-physiological reasons for these observations may not be immediately evident for now. Could there possibly be other in-vivo pathways that may occasionally tilt this thrombo-haemorrhagic balance in favor of haemorrhage in some diabetics? The prolongation of these parameters in the diabetic group may also be due to in-vitro interference of fibrin clot formation by inhibitors such as fibrinogen fragments 1 & 2 and D-Dimers as reported in several studies (Laffan MA, 1995). Whatever may be the plausible reasons, these findings suggest that haemorrhagic tendencies and complications should not be entirely ruled out among diabetics, and should be borne in mind during the management of these patients. It would also be helpful to incorporate coagulation screening as routine tests for better management of diabetic patients.

References

1. Akinkugbe OO. (1997) National expert committee on non-communicable diseases (NCD) in Nigeria. Final report of a national survey, Lagos: 64-90.
2. Albertis KG, Zimmet PZ. World Health Organization (WHO) (1998). Consultation definition, diagnosis and classification of DM and its complications, diabetes medicine.15:539-553
3. Alvin CP. (2001) Diabetes. In: principles of internal medicine, Braunwald E, Fauci AS, kasper DL, Havser SL,Longo DL,Jambon JL: harrinson (eds),15th edition,USA,New York,Mcgraw hill,:2109-2138
4. Bartoli L, Ettore F. (1994) fibrinogen plasma levels as markers of thrombin activation in Diabetes. Diabetes: 3:808-812
5. Charles FA, (1998) endocrinology, In: mayo internal medicine board review. Udaya B.S.P, millhouse O.E, Leann MS (eds), 3rd edition Raven, Lippincott: 187-278
6. Dacie JV, Lewis SM (1996).Tests for acute phase response. In:practical haematology, 8th edition New York, Churchill Livingstone.pp 559-563
7. Fabiyi AK, Kolawole BA,Adeshinto O, Ikem RT (2002).The impact of knowledge, attitude, practice and belief of type two Nigerian diabetes patients on drug compliance. Diabetes.Int.291:15-17
8. Laffan MA, Brandshow AE, (1995) Investigation of haemostasis.In: practical haematology, Dacie JV, Lewis SM (eds), 8th edition. Edinburgh, Churchill Livingstone: 297-310.
9. Mark BT.(2001) Atherosclerosis, thrombosis and coronary artery disease: In: Williams' haematology: Ernest B. Marshall AI,Barry SC,Thomas JK,Uri S (eds),6th edition New York, McGraw-Hill:1743-1761.

10. McFarlane IA (1997). Endocrine diseases and diabetes mellitus. In Williams JC, (Ed), Textbook of Diabetes (2nd Edition) Oxford: Blackwell, pp 640-660
11. Puepet FH (1996). Prevalence of diabetes mellitus and associated risk factors in adults in Jos, part two FMCP dissertation, internal medicine national postgraduate medical college of Nigeria.
12. Tekemoto T, Ken-ichi M.(1996) Mechanisms of disorders of coagulation and fibrinolysis in diabetes. Diabetes: 7:582-586
13. Wokoma FS (2002). Diabetes and hypertension in Africa, an overview. Diabetes Int.12 (12):36-40
14. World Health Organization (WHO) (1999). Diabetes Mellitus and its complications. Report of WHO consultation (part 1): Diagnosis and classification of diabetes mellitus. Bull.WHO, 99(2):1-58

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