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Platelet Activity in Patients with Type 2 Diabetes in Eastern Nigeria

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Abstract: Platelet dysfunction is one of the major mechanisms underpinning cardiovascular diseases in diabetes mellitus. The researchers hypothesize that a significant proportion of Nigerian diabetic patients have altered platelet activation and adhesiveness which could predispose to thrombotic disorders. To evaluate platelet adhesiveness in type 2 diabetic Nigerians as a measure of platelet dysfunction. A total 50 patients (30 males and 20 females) aged 30-70 years with established diagnosis of type 2 diabetes on their first visit to diabetes clinic of Abia State University Teaching Hospital, Aba in Eastern Nigeria and 30 apparently healthy age-matched controls (15 males and 15 females) were recruited into this study. Blood samples were collected from the diabetic patients and controls after an overnight fast for determination of platelet counts and platelet adhesiveness and results compared. The mean platelet count of the patients, 234 +/- 77×10^9 L^{-1} was not significantly different from that of the controls, 238 +/- 77×10^9 L^{-1} ($p>0.05$). The mean platelet adhesiveness of the patients 65.2 +/- 15.6% was however significantly higher than the mean value of the controls, 44.1 +/- 8.8% ($p<0.05$). There was a positive linear correlation between the fasting plasma glucose levels and platelet adhesiveness indices.

Key words: Cardiovascular, type 2 diabetes mellitus, platelet activation, thrombotic disorders, patient, Nigeria

INTRODUCTION

Platelet abnormalities have been implicated in the etiology of cardiovascular events among patients with diabetes and the burden of Cardiovascular Disease (CVD) among these patients is substantial. Individuals with diabetes are at increased risk of cardiovascular events compared with age and sex-matched individuals without diabetes (CDCP-NDFS, 2008). Platelets play a major role in the processes that keep blood in a fluidy state within the vascular space. They quickly plug any breach in the walls of the blood vessels and activate the intrinsic coagulation cascade. Platelets do this by adhering to sub-endothelial surfaces, undergoing changes in their shape, secretion of cellular organelle contents and aggregation to form a thrombus (Natarajan *et al*., 2008). This normal protective mechanism may become disordered in some pathological states such as diabetes mellitus.

A number of mechanisms for the increased cardiovascular risk in diabetes have been proposed including increased tendency towards intracoronary thrombus formation, increased platelet reactivity and worsened endothelial dysfunction (Reusch, 2003; Natarajan *et al*., 2008; Zachary and Bloomgarden, 2011). Chronic hyperglycemia, characteristic of diabetes, affects many physiological functions related to haemostasis (Santilli *et al*., 2010). There is increased platelet turnover, ultimately leading to enhanced platelet adhesion and aggregation, increased expression of platelet surface adhesion molecules and receptors as well as disturbances

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in platelet calcium homeostasis (McDonagh *et al*., 2003; Watala *et al*., 1998). There is also increased release of proaggregatory prostanoids such as thromboxane A_2 from arachidonic acid (Halushka *et al*., 1981). On the other hand, the synthesis and secretion of the anti-aggregatory agents such as prostacylin and nitric oxide are reduced (Martina *et al*., 1998; Amedeo *et al*., 1991). Thus, platelet dysfunction contributes significantly to the development of thrombotic disorders and the vascular complications of diabetes mellitus (Natarajan *et al*., 2008).

Prior to this study, there was a dearth of information on platelet activities in type 2 diabetic Nigerians. Hence, this study was designed as a preliminary step to investigate platelet changes in type 2 diabetic subjects living in Eastern part of Nigeria.

MATERIALS AND METHODS

Patients: A total 50 adults with established diagnosis of type 2 diabetes mellitus (30 males and 20 females) aged 30-70 years and a mean of 54 (SD±16) years were investigated and compared with 30 apparently healthy age-matched controls who were not on any medication and with Fasting Plasma Glucose (FPG) levels <6 mmols L^{-1}. All the participants were non-smokers. The study subjects were all living in Aba city and environs, all of which are in Eastern Nigeria. They were chosen randomly from among the patients on their first visit to diabetes clinic of Abia State University Teaching Hospital, Aba. Exclusion criteria included patients on hypoglycemic agents and existence of other illnesses requiring administration of other drugs.

Methods: About 6 mL of venous blood were obtained in the morning following an overnight fast by venipuncture. About 2 mL were collected into fluoride oxalate tubes for the estimation of Fasting Plasma Glucose (FPG) levels by the glucose/oxidase method and the rest was for estimation of platelet counts and adhesiveness. Platelet counts were determined using a manual technique while platelet adhesiveness indices were estimated using a modified method of Salzman (1963). All assays were performed in triplicates. The study had the approval of Abia State University, Teaching Hospital, Ethics Committee.

Statistical analysis: The data collected were analysed using the Statistical Package for the Social Sciences, Version 11 (SPSS -11). Continuous data were expressed as mean±Standard Deviation (SD) and compared using the Student t-test. Pearson's correlation analysis was used to determine the relationships between variables. $p<0.05$ was considered statistically significant.

RESULTS AND DISCUSSION

The results of this study are shown in Table 1 and Fig. 1 and 2. The mean platelet counts in the patients and controls were 234±53 and 238±77 ×10 L^{-1}, respectively. These were not statistically significantly from each other ($p>0.05$). Platelet adhesiveness indices were however significantly higher in the patients than in the controls with the patients having a mean value of 65.2±15.6% and the controls 44.1±8.8% ($p<0.05$). Figure 1 shows a positive linear correlation between FPG concentrations and platelet adhesiveness indices in type 2 diabetic patients ($R = 0.467$; $p<0.05$) while Fig. 2 shows the distribution of platelet adhesiveness indices in both patients and controls.

The major findings of this study are that while platelet counts are largely unaltered in type 2 diabetic

Table 1: Fasting Plasma Glucose (FPG), platelet count and platelet adhesiveness indices in type 2 diabetic patients and controls

Variables	Patients	Controls	p-value
Fasting Plasma Glucose (FPG) (mmol L^{-1})	13.0±2.90	4.6±0.60	<0.05
Platelet count (×10^9 L^{-1})	238.0±77.0	235.0±53.0	>0.05
Platelet Adhesiveness index (%)	65.2±15.6	44.1±8.80	<0.05

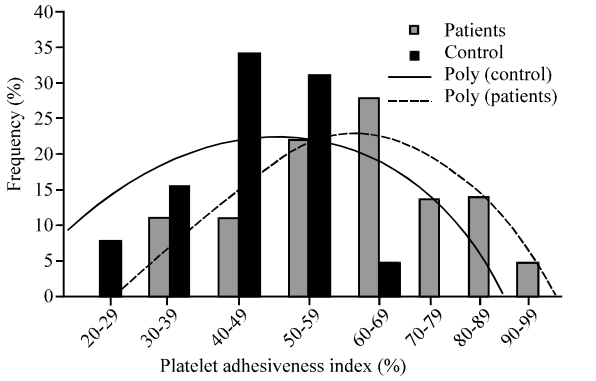

Fig. 1: Platelet counts and platelet adhesiveness indices in type 2 diabetic patients and controls

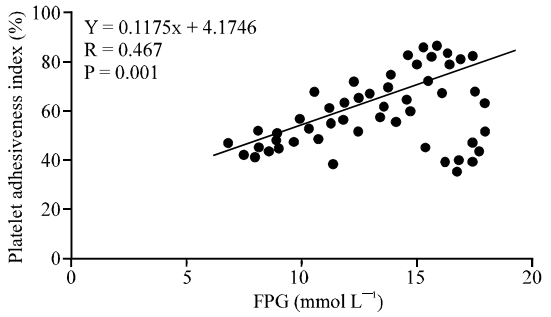

Fig. 2: Correlation graph between Fasting Plasma Glucose (FGP) and platelet adhesiveness indices in type 2 diabetic patients

Nigerians, their platelets show increased activation, demonstrated by higher platelet adhesiveness. Similar findings have been reported by other researchers (Santilli *et al*., 2010). Sustained hyperglycemia is associated with alterations in endothelial and platelet function (Zachary and Bloomgarden, 2011; Natarajan *et al*., 2008) and this is supported by the positive correlation between FPG concentrations and platelet adhesiveness indices in type 2 diabetic patients as shown in this study.

Several mechanisms have been proposed to explain the greater activation of platelets in diabetes with important physiological implications. It has been suggested that platelets from diabetic patients show reduced membrane fluidity as a result of increased mobilization of intracellular calcium ions with accompanying decrease in intracellular magnesium ion concentrations (Watala *et al*., 1998; Gawaz *et al*., 1994).

Platelets from diabetic patients produce less Nitric Oxide (NO) and prostacyclin (Martina *et al*., 1998; Amedeo *et al*., 1991). These normally inhibit platelet interaction with the vascular endothelium. Antioxidant levels such as vitamin E are also reduced in platelets from diabetic patients and this has been associated with increased aggregability (Nweke *et al*., 2009; Vinik *et al*., 2001). Again, platelets from diabetic patients show increased expression of activation-dependent molecules such as p-selectin, GP 1 and GP IIb/IIIa due to non-enzymatic glycation of the receptor proteins. GPIb mediates binding to von Willbrand factor and GP IIb/IIIa binds fibrinogen which are all important steps in thrombogenesis (Natarajan *et al*., 2008). There is also the possibility of platelet communication with leucocytes, thus increasing aggregability (Tschoepe *et al*., 1997). It is therefore possible that platelets play a role in the inflammatory tissue damage in the vasculature that occurs in diabetes.

Additionally, there is increased glycation of circulating Low Density Lipoproteins (LDL), rendering platelets hypersensitive. They may interact with these glycosylated LDL and immune complexes thereby increasing platelet adhesiveness, aggregabilityand propensity to form thrombus (Zachary and Bloomgarden, 2011). Finally, decreased platelet insulin receptor number and affinity has been reported which suggests that reduced insulin sensitivity may account for platelet hyperactivity in this condition (Vinik *et al*., 2001). Since altered platelet activity contributes significantly to microvascular and macrovascular complications in diabetes, these findings indicate that these patients may be at increased risk of atherothrombotic events.

CONCLUSION

The findings indicate that many Nigerian type 2 diabetic patients have high platelet activation and this could have cardiovascular consequences.

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REFERENCES

Amedeo, M.P., A. Fortini, G.F. Genisini, D. Vanni, D. Prisco and R. Abbate, 1991. Human prostacyclin platelet receptors in diabetes mellitus. Thromb. Res., 63: 541-548.

CDCP-NDFS, 2008. General information and national estimates on diabetes in the united states 2007. Atlanta GA, U.S.

Gawaz, M., I. Ott, A.J. Reininger and F.J. Newman, 1994. Effects of magnesium on platelet aggregation and adhesion. Magnesium modulates surface expression of glycoproteins on platelets *in vitro* and *ex vivo*. Thromb. Haemost., 72: 912-918.

Halushka, P.V., R.C. Rogers, C.B. Loadholt and J.A. Colwell, 1981. Increased platelet thromboxane synthesis in diabetes mellitus. J. Lab. Clin. Med., 97: 87-96.

Martina, V., G.A. Bruno, F. Trucco, E. Zumpano, M. Tagliabue and C. Di Bisceglie, 1998. Platelet $_cNO_3$ activity is reduced in patients with IDDM and NIDDM. Thromb. Haemost., 79: 520-522.

McDonagh, P.F., J.Y. Hokama, S.C. Gale, J.J. Logan, G. Davis-Gorman, S. Goldman and J.G. Copeland, 2003. Chronic expression of platelet adhesion proteins associated with severe ischemic heart disease in type 2 diabetic patients: chronic platelet activation in diabetic heart patients. J. Diabetes Complications, 17: 269-278.

Natarajan, A., A.G. Zaman and S.M. Marshal, 2008. Platelet hyperactivity in type 2 diabetes: Role of antiplatelet agents. Diabetes Vasc. Dis. Res., 5: 138-144.

Reusch, J.E.B., 2003. Diabetes, microvascular complications and cardiovascular complications: What is it about glucose? J. Clin. Invest., 112: 986-988.

Salzman, E.W., 1963. Measurement of platelet adhesiveness; a simple invitro technique demonstrating an abnormality in Von Willebrand's disease. J. Lab. Clin. Med., 62: 724-735.

Santilli, F., G. Formoso, P. Sbraccia, M. Averna and R. Miccoli *et al*., 2010. Postprandial hyperglycemia is a determinant of platelet activation in early type 2 diabetes mellitus. J. Thromb. Haemost., 8: 828-837.

Tschoepe, D., U. Rauch and B. Schwippert, 1997. Platelet-leukocyte-cross-talk in diabetes mellitus. J. Horm. Metab. Res., 29: 631-635.

Vinik, A.I., T. Erbas, T.S. Park, N. Roger and G.L. Pittenger, 2001. Platelet dysfunction in type 2 diabetes. Diabetes Care, 24: 1476-1485.

Watala, C., M. Boncer, J. Golanski, W. Koziolkiewcz and B. Trojanowiak, 1998. Platelet membrane lipid fluidity and intra-platelet calcium mobilization in type 2 diabetes. Eur. J. Haematol., 61: 319-326.

Zachary, T. and M.D. Bloomgarden, 2011. Diabetes and cardiovascular disease. Diabetes Care, 34: 24-30.