



PLATELET DISTRIBUTION WIDTH: ROLE IN DIABETES MELLITUS AND ITS MICROVASCULAR COMPLICATIONS

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ABSTRACT

Introduction: Diabetes mellitus (DM) is a global pandemic with high mortality and morbidity due to its long term microvascular and macrovascular complications. Altered platelet morphology and function play a key role in the pathogenesis of DM and its vascular complications. This is reflected as a change in various platelet indices such as Mean Platelet Volume, Platelet Distribution Width and Platelet Large Cell Ratio. The aim of study is to evaluate platelet distribution width (PDW) in diabetic patients and compare it with a non-diabetic control group. We also attempted to compare PDW within the diabetic cohort amongst those with and without microvascular complications. **Methodology:** The study was carried out on patients with DM, attending the medicine out-patient department. Relevant history, fasting blood glucose and hematological parameters (platelet indices and complete blood counts) were assessed as part of the routine investigations. A total of 320 diabetics were screened for the study. After applying exclusion criteria, 52 diabetics and also 62 non-diabetic controls were included in the study. Statistical analysis was done. **Results:** The PDW was significantly higher in diabetic patients when compared to the control group, ($p=0.000022$). Among the diabetics, PDW was significantly higher in those with microvascular complications as compared to those without ($p=0.00223$). **Conclusion:** Evaluation of PDW provides an insight into the pathogenesis of DM and also its microvascular complications. PDW is a simple, cost effective haematological investigation, which can possibly be used as a screening tool in DM patients and a prognosticator of diabetic microvascular complications.

KEYWORDS: Platelet Distribution Width, Diabetes Mellitus, Microvascular complications.

INTRODUCTION

Diabetes mellitus (DM) is a global health burden with increasing morbidity and mortality in recent decades, especially in low and middle income countries.^[1] It is a complex disease characterized by chronic hyperglycemia, metabolic abnormalities, and long term macrovascular and microvascular complications involving the blood vessels, eyes, kidneys and nerves. According to international diabetes federation (IDF) an estimated 415 million people had diabetes worldwide in 2015, with type 2 diabetes mellitus making upto 90% of cases.^[2]

Abnormal insulin activation in patients with DM increases platelet activation and precipitate microvascular complications (retinopathy, neuropathy, nephropathy). Altered platelet morphology and function has been observed in diabetes in the form of enhanced platelet activity which may contribute to a prothrombotic state, as reflected in various platelet parameters.^[3] Platelet parameters can be routinely measured in

hematology analyzer and include plateletcrit, mean platelet volume (MPV), platelet distribution width (PDW) and platelet large cell ratio (PLCR).^[4] Among these, increased MPV and PDW have been extensively studied as indicators of platelet activation in various thromboembolic states, inflammatory states and DM.^[5,6]

PDW directly measures variability in platelet size, changes with platelet activation, and reflects the heterogeneity in platelet morphology.^[7] Gender specific reference intervals for PDW vary from 9.8fL to 16fL in females and 9.3fL to 14.3fL in males.^[8,9] Increased PDW has been seen to be associated with conditions like metabolic syndrome, diabetes mellitus, coronary artery disease and malignancy.^[3,10]

MATERIALS AND METHODS

The current study was carried out on patients with diabetes mellitus, attending the medicine OPD at a tertiary care hospital. It also included age and sex matched controls. Ethical approval was obtained from

the Institutional Ethics Committee before the commencement of the study. Informed consent was procured from the participants at the time of recruitment into the study.

A total of 320 diabetics were screened for the study. In order to reduce the impact of confounding factors; cases with anemia (hemoglobin <12g/dl in males & <11g/dl in females), hypertension, infection (as reflected by leukocytosis), thrombocytopenia, thrombocytosis, malignancy, hematological disorders, pregnancy, and patients on antiplatelet drugs (such as aspirin and clopidogrel) were all excluded from the study. After exclusion, 52 patients were included in the study group. Also, 62 age and sex matched control subjects were selected as controls (after application of exclusion criteria).

Demographic, clinical and laboratory data including age, gender, PDW (platelet distribution width), FBG (fasting blood glucose), CBC (complete blood counts) and HbA1c in both groups were obtained. In addition, the presence of vascular complications was identified based on the history obtained/ clinical examination performed (for neuropathy) and the investigations carried out (fundoscopic examination for retinopathy, albuminuria for nephropathy).

Blood samples were taken under aseptic precautions from the ante-cubital vein by a clean puncture avoiding bubbles and froth. Samples were collected in EDTA and biochemistry tubes. The anticoagulated blood was analyzed in automated hematological analyzers (SYSMEX XT1800i) to obtain the platelet indices and CBC. FBG was measured by hexokinase enzymatic method (Roche Cobas C 501 chemistry analyzer).

The PDW values in the diabetic group were compared with that of the non-diabetic control group. The diabetics were divided into two groups based on the presence or absence of microvascular complications and the PDW values were further compared between them.

The data thus obtained was compiled and statistically evaluated. Statistical analysis was performed using SPSS statistics program version 16. A p value of less than 0.05 was considered statistically significant.

RESULTS

The current study included 52 diabetic patients (21 females and 31 males). The non-diabetic control group of 62 patients included 26 females and 36 male patients. The age of the patients within the diabetic group ranged from 32yrs to 76 yrs with a mean age of 52.21 yrs. Within the control group, the age of the patients ranged from 19yrs to 78 yrs with a mean age of 41.01 yrs.

Table 1: Mean values of Age, PDW (platelet distribution width) and fasting blood glucose (FBG).

	Non – Diabetic Control Group	Diabetics	Diabetics without vascular complications	Diabetics with vascular complications
Mean Age (yrs)	40.54	52.21	52.60	52.49
Mean PDW (fL)	11.05	12.38	12.29	12.42
Mean FBG (mg/dL)	102.38	219.04	219.96	218.43

The mean FBG and PDW in the diabetic group were 219.04 mg/dl and 12.38±1.71fL and that in the non-diabetic control group were 102.42 mg/dl and 11.05±1.46fL respectively. The mean PDW was significantly higher in the diabetic group as opposed to the non-diabetic group (P value=0.000022) (Table 1).

Of the 52 cases, 24 had vascular complications. The mean PDW of patients with vascular complications was 12.42±1.66fl and those without vascular complications was 12.29±1.50 fl. PDW was significantly elevated in the diabetic group with vascular complications (P value=0.002235)(Table 1).

DISCUSSION

Diabetes is a growing health problem associated with increased risk of microvascular and macrovascular complications.^[2,3] The chronic hyperglycemia along with other biochemical factors like insulin resistance, hyperlipidemia, prolonged inflammatory and oxidant

state, increased expression of growth factors and glycoprotein receptors contributes to a pro-thrombotic state. Also seen is, non-enzymatic glycation of proteins which enhances the osmotic effects of glucose leading to activation of protein kinase C thus increasing the platelet activity.^[11,12,13] This altered platelet activity is reflected as variations in the platelet indices which are easily measured in the hematology analyzers.

The current study shows that PDW was significantly elevated in the diabetic group when compared to the control group (P value=0.000022). These findings are in corroboration with other studies.^[14,15,16]

MPV and PDW are two widely studied platelet indices, as indicators of platelet activation. Platelet distribution width is an indicator of platelet volume variability and heterogeneity. During the process of platelet activation, to obtain larger surface area, the platelets change from a discoid to a spherical shape. This is reflected by an

increase in MPV. In addition to this, there is formation of platelet pseudopodia giving rise to anisocytosis which is reflected as an increase in PDW.^[17,18] Studies on platelet parameters in stored blood (which has decreased platelet activity) have also shown that though there is an increase platelet distention and swelling, there was a decrease in PDW (due to absence of pseudopodia formation). This further indicates that PDW is a more specific marker of platelet activation.^[19]

The study also shows that PDW is significantly higher in the group with microvascular diabetic complications as compared to that without complications (P value=0.002235). This is also in corroboration with other studies.^[14,20,21]

Thus, we can conclude that the chronic hyperglycemia in diabetes mellitus produces a procoagulant state, with activation of platelets which is reflected as a significant increase in PDW. This suggests a strong relationship of PDW with DM and also diabetic microvascular complications.

CONCLUSION

PDW is a simple, cost effective hematological investigation which can be used as a marker to reflect the pathogenesis and progression of DM. It can also be used as a screening tool and prognosticator of diabetic microvascular complications. This could help in identifying high risk candidates, who could possibly be started on prophylactic anti-platelet therapy to avoid lifelong debilitating consequences.

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