Association of Mean Platelet Volume and Platelet Distribution Width with Hba1c

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Abstract

Diabetes mellitus type 2 (DMT2) is a metabolic disorder, and its prevalence is rising worldwide. The objective of the study was to investigate association of mean platelet volume (MPV) and platelet distribution width (PDW) with glycemic control marker HbA1c. So that MPV, PDW could be used as a prognosticators of deterioration of glucoregulation in diabetes mellitus type 2 instead of HbA1c value. This study included 87 DMT2 patients, which divided into two groups, A (n=41, presence in diabetics ≤ 6.5 – 6.9%) and B (n=46, target in diabetes ≥ 7.0%), according to HbA1c values. Spearsman correlation co-efficients were calculated to evaluate the relationship between MPV, PDW and HbA1c value. Binominal logistic regression analysis was performed to estimate the relationship between glycemic control, as dichotomous outcome of MPV and PDW as the main prognosticator. MPV and PDW were significantly higher in the group B compared to the group A. Significant positive correlations of MPV with Random Blood Sugar (RBS) and HbA1c value were found in the total sample. MPV and PDW correlate with glycemic control markers in DMT2 patients. In conclusion, MPV and PDW could be used as simple and cost effective prognosticators of deterioration of glucoregulation.

Introduction

Diabetic mellitus type 2 (DMT2), a metabolic disease, is the most challenging public health problem in todays world [1]. It is a complex disease characterized by insulin hormone resistance, relative lack of insulin, and high blood sugar[2,3]. According to international diabetes federation (IDF) an estimated 415 million people had diabetes worldwide in 2015 with type 2 diabetes mellitus making up about 90% of the cases [4,5]. Africa and Asia continental are living few ethnic & races predispose people to a greater risk of developing country [5]. According to Indian continental studies indicated a threefold rise in the diabetic prevalence in rural as well as urban areas [6].

Large platelet contain dense granules are metabolically and enzymatic ally more active than smaller ones and have higher thrombotic potential. Hence, increased MPV and PDW might be linked with increased thrombotic potential [7]. Platelets are a central element of the athero-thrombotic process due to their prothrombotic and proinflamatory function[8,9,10]. The association of increased MPV, PDW and decreased platelet count with disease related to endothelial dysfunction such as metabolic syndrome diabetes, coronary artery disease (CAD) and malignancy which has been shown in many studies [11-15]. Diabetes particularly DMT2 patients are exposed to the increased platelet reactivity due to multi factorial causes such as metabolic (e.g hyperglycemia, hypertriglyceridemia) and systemic abnormalities (eg. Oxidative stress, inflammation) and insulin resistance [16-19]. In diabetic thrombocytopathy, many biomarkers have been considered for the implementation in clinical practice [20]. Most parameter of platelet activity measurement is time consuming, expensive & required high sample volume [21]. Otherwise MPV & PDW are easy to measure of platelet size, enzymatic activity and prothrombotic potential. It can be determined by routine automated hemograms at a relatively low cost [22]. An increased of MPV is one of the risk factors for micro vascular and macro vascular complications, including cardiovascular disease (CVD), retinopathy, nephropathy occur due to chronic un control hyperglycemia in diabetics also myocardial infarction, ischemic stroke and venous thromboembolism [23-29].

HbA1c is a good marker for DMT2 patients should be kept below 6.5% in order to reduce the risk of micro & macro vascular complications [30.] Improve glycemic control decrease mean platelet volume [31]. It can be suggested that reduce platelet activity by proper glycemic control may prevent or delay vascular complications in these patients.

The aim of this study was to investigate association of MPV, PDW and platelet count with short term and long term glycemic control markers. So that MPV, PDW and platelet count could be used as a predictor of diabetes patients.

Material & Methods

Patients and Study Design

The study was conducted in Lab science Diagnostics, (153/1, Green Road, Dhanmondi, Dhaka-1205, Bangladesh). The study included 87 diabetic patients at least 5 - 6 months duration of diabetes from 02 April 2017 to 14 July 2015. In order to reduce the impact of the confounding factors, hematological disorders, pregnancy and malignancy were factors for exclusion from the study. According to HbA1c value patients were divided into two groups: Group A (n=41 HbA1c ≤ 6.5 – 6.9) and group (n=46 HbA1c ≥ 7.0). Demographic clinical and laboratory data including age, gender, complete blood cell count MPV, PDW, platelet count , fasting blood glucose (FBG), Random Blood Sugar (RBS), HbA1c and lipid profile (cholesterol, HDL, LDL and Triglycerides) in both groups were obtained.

Methods

Blood cell count and HbA1c and other parameters were measured. Blood samples were taken in tubes with EDTA anticoagulant. The tubes without anticoagulant were used for collecting blood for glucose and lipid profile measurement. Complete blood cell count was measured by sysmex XN-L series 350(6 part). HbA1c value was measured by fine care ID chips. Lipid profile, glucose, and other biochemistry profile were measured by ERBA Mannheim XL 200 Fasting blood glucose was measured using a hexokinase method. Standardization, calibration of instrument and processing of samples were done according to manufacturer instructions. All Data reserve into MYSOFT LTD in Lab science Diagnostics. The study approval was taken from the ethics committee of Lab Science Diagnostics.

Statistical Analysis

Statistical analysis was performed by statistical packages for the social sciences (IBM SPSS Statistics) version 20 (Chicago, IL). IBM SPSS was used to find the significant difference of Fasting Blood Sugar (FBS), RBS ,HbA1c, MPV, and PDW. Spearman's correlation coefficients were calculated to evaluate the relationship between MPV, PDW with HbA1c. Binominal logistic regression analysis was performed to assess independent relationship between MPV, PDW as the main prognosticator. The cut off value of MPV and PDW was determined for optimum sensitivity and specificity ratio of the diagnostic test. Positive and negative predictive values were calculated using recommended cut off value. Data were expressed as mean ± standard deviation. P value was considered statistically significant.

Result

According to the result of sample population are detailed in (Table 1). A total of 87 patients fulfilling the selection criteria included 37 (out of 87, 42.52%) females and 50 (out of 87, 57.47%) males. The average age of both patients was 25 to 80. The total number of study participants who were divided into two groups according to their diabetics status, 46 (out of 87, 52.87%) DMT2 patients were in the group B (target in diabetics, HbA1c value ≥7.00), 41 (out of 87, 41.13%) in the group A (presence in diabetics, HbA1c value≥ 7.00) . Statistically significant differences were observed between those groups for various parameters. We found significant differences among the groups for all examined demographic and biochemical characteristics. Median value of age, FBS, RBS, HbA1c, MPV, PDW, cholesterol, LDL, Creatinine were significantly higher in the group B compared to the group A. Except HDL, Triglycerides, Platelet count. A significantly higher MPV & PDW value in the group B compared to group A was found (P,0.191, 0.012).

Table 1: Characteristics and differences of the study participants				
Characteristics/ Parameter	DMT2	Group A(n=41)	Group B(n-46)	P=significance
Age (Years)	50±12.60	48(25-75)	55(35-80)	0.265
Female/Male, n (%)	37/50	16/25	21/25	0.011
FBG (mmol/L)	10.8(6.1-18.9)	6.9(6.1-6.85)	11.65(6.8-18.9)	0.255
RBS (mmol/L)	17.7(6.8-29.8)	7.25(1.20-14.20)	17.7(6.8-29.8)	0.955
HbA1c(%)	7.05 (6.514.90)	6.60 (6.5 -6.9)	9.1 (7- 14.90)	0.824
MPV (fL)	11.7 (8.20-16.80)	10.6(8.2-14.00)	12.75(10.5-16.8)	0.191
PDW (fL)	13.8(7.9-23.8)	12.5(7.9-20.8)	15.7(12.2-23.8)	0.012
Platelet count (/ccm)	274(10-559)x10³	268(150-559) x10³	277(10-554) x10³	0.190
Cholesterol (mg/dl)	195(140-310)	185(140-250)	206(143-310)	0.140
HDL (mg/dl)	40(25-63)	41.5(32-55)	38.5(25-235)	0.418
LDL (mg/dl)	106.5(50-170)	102(50-150)	108(56-170)	0.655
Triglycerides (mg/dl)	209(11.5-1845)	200(90-1180)	198(11.5-1845)	0.847
Creatinine (mg/dl)	1.15(0.75-6.15)	1.10(0.75-2.50)	1.15(0.9-6.15)	0.985

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Further analysis showed significant positive correlations between MPV (fL) and RBS (mmol/L) and MPV (fL) with HbA1c in figure 1, PDW (fL) with HbA1c (%) in figure 3 in the total sample. There were no correlations individually of MPV with RBS and HbA1c or PDW with HbA1c in the group A or group B (Figure 1,2,3).
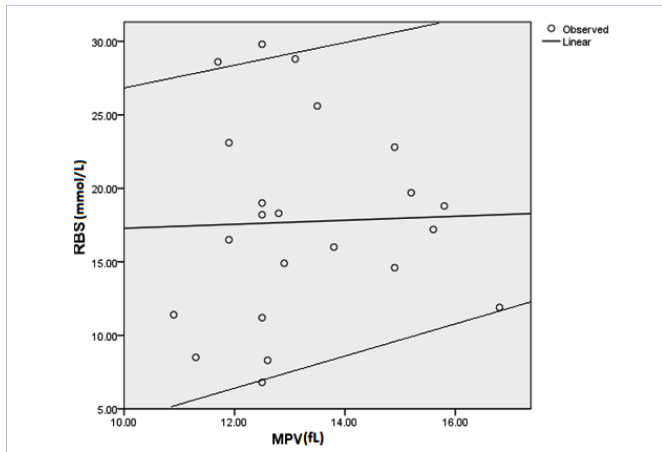

Figure 1: Correlation analysis between mean platelet volume (MPV) and Random blood sugar (RBS) levels in the total sample
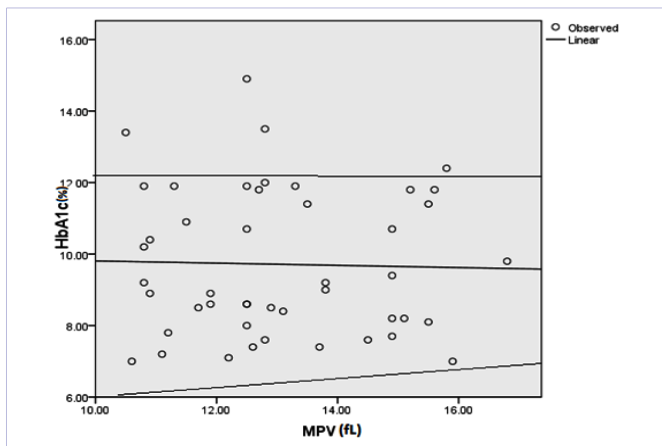

Figure 2: Correlation analysis between mean platelet volume (MPV) and glycated hemoglobin (HbA1c) levels in the total sample
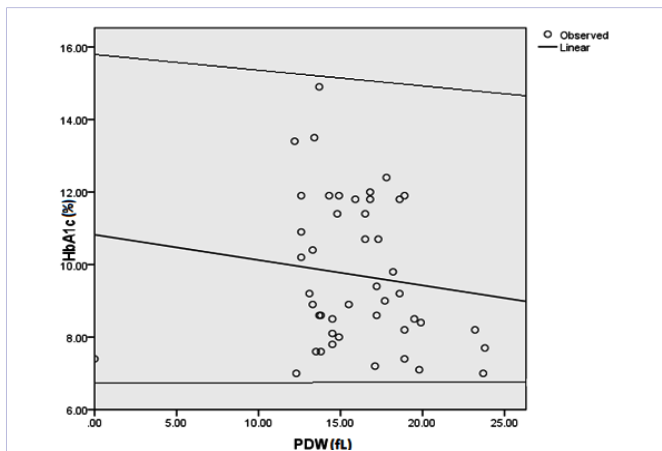

Figure 3: Correlation analysis between platelet distribution width (PDW) and glycated hemoglobin (HbA1c) levels in the total sample

Binominal logistic regression analysis model with MPV and PDW as a predictor of deterioration of glucoregulation was statically significant, (p 0.191, 0.012), Indicating that MPV distinguishes patients with good (HbA1c≤ 6.5-6.9) and poor (HbA1c≥ 7%) glucoregulation (Table 2). This model showed that the significant value of MPV and PDW were positively associated with the risk of inadequate glycemic control.

Table 2: Optimal cut-off, area under curve (AUC), sensivity, specificity, Positive predicting value (PPV) and Negative predicting value (NPV) of mean platelet volume (MPV) in prognostication of glucoregulation				
Variable	**Sensitivity (%)**	**Specificity (%)**	**PPV (%)**	**NPV (%)**
MPV (fL) (cutoff-9.55)	85.19	30.30	58.23	12.50
PDW (fL) (cutoff- 14.55)	45.77	67.86	75	37.25

Discussion

Diabetic is a growing health problem associated with increased risk of micro and macro vascular complications [32]. Some parameters can easily be detected by various blood tests such as platelet count, MPV, PDW that can be used as biomarker for early detection of diabetic complication.

Several researches found platelet count was decreased in diabetic patients as compared with non diabetic patients [33]. Platelet hypersensivity is a well-known factor to the prothrombotic state in diabetics, causing increased coagulation, impaired fibrinolysis and endothelial dysfunction. Hyperactive platelet plays a critical role in the pathophysiology of the thrombotic events leading to diabetic complications [16]. MPV is a parameter used to assess platelet size and it is a potential biomarker of platelet reactivity. Already it has been shown that longer platelet is more reactive than smaller ones [22, 34]. Several researches indicate positive correlation of RBS and HbA1c with MPV, PDW [31, 35]. However some studies have not shown any relation of RBS and HbA1c with Mean platelet volume [36, 37].

It was proposed that increase in MPV could be because of raised blood sugar effect to osmotic swelling and shorter life span of platelets in diabetic patients. Alternatively this may suggest that platelet activation is related to glycemic control [38,37]. Hyperglycemia occur non enzymatic glycation of proteins on the surface of the platelets, which decrease membrane fluidity and increase its reactivity [39]. Higher MPV responsible for increased production of young platelet due to a higher platelet turnover rate [40]. The relation between MPV and DMT2 was first reported by Sharpe and Trinick who founded a significant increase of MPV in diabetic compared with non diabetic patients [41]. This research was followed by numerous studies and with largest study conducted on 13,021 diabetic patients[14, 31, 42-44]. Similarly, Our study results had shown significantly higher MPV in the group B compared to the group A. Those findings

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are mainly consistent with previous finding Besides Ozder et al. found that MPV was significantly higher in patients with HbA1c levels ≤ 7.0% than in patients with HbA1c levels ≤ 6.9. [31,45,46] this was in consonance with the result of other studies [43, 45].

All of the studies listed above investigated the association of MPV and PDW with diabetic patients. [47 Obtained values indicate the possibility of using MPV, PDW as a hematological biomarker for prediction of the diabetics disease burden in terms of vascular complications. However, Data of MPV, PDW could be used as a predictor of deterioration of glucoregulation and a marker for distinguishing those patients.

Our study indicates that it might be used as a simple, effortless and cost effective prognicator of deterioration of glucoregulation. Considering that odds of inadequate glycemic control are 2 times increased per femto-liter greater MPV. Its use especially in the Lab science diagnostics could improve the screening of high risk individuals for vascular complications. Early diagnosis and appropriate treatment could thereby delay their onset or progression. Mean platelet volume can be used as a moderate quality indicator of deterioration of glucoregulation at best cut off value 9.55 fL with sensitivity of 85.19% and specificity of 30.30%. Similarly, Platelet distribution width can be used as a moderate quality indicator of glucoregulation at best cut off value 14.55 fL with sensitivity of 45.77% and specificity of 67.86%. Finally it can be concluded that MPV & PDW are not substitute for HbA1c but it can be replace it in the circumstances of limited testing availability or limited financial resources. Due to small sample size and few in number of patient in a same area like Dhaka are considered as two limitation of this study. This study supports gluco metabolic state, poor glycemic control and platelet activity as measured by MPV and PDW. So, the study suggests that MPV, PDW and platelet count could be used as a cost effective tool to monitor diabetic mellitus.

Conclusion

We all are aware of the risk factors for diabetic complications such as duration, glycemic control and dyslipidemia. We found increase in MPV, PDW and decrease platelet count in diabetic patients whose HbA1c value was 7 or more. This implies that raised MPV and PDW can be considered as biomarkers for early detection of impending complication instead of HbA1c value. Also we found that this platelet parameter were more significant in micro vascular complications as compared to macro vascular complications.

Acknowledgements

Conflicts of Interest

There are no conflicts of interest

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