

Relevance of platelet indices in predicting prothrombotic activity in type 2 diabetes mellitus in correlation with HbA1C

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Abstract

Context: Diabetes mellitus is a chronic metabolic syndrome. Recently, a prothrombotic state, characterized by abnormalities in platelet function has been recognized as a component of metabolic syndrome. The increased platelet activity may play a role in the development of vascular complications of this metabolic disorder. The mean platelet volume (MPV) is an indicator of the average size and activity of platelets.

Aims: To compare platelet indices between type 2 diabetic patients and control group, to analyse the correlations between MPV and FBG, PBG in diabetic patients, to evaluate MPV according to HbA1C levels in diabetic group.

Materials and Methods: Platelet counts and MPV were measured in 300 Type 2 diabetic patients and 300 nondiabetic subjects using an automated blood cell counter. The blood glucose levels and HbA1c levels were also measured. Statistical evaluation was performed by SPSS using Student's t test and Pearson correlation tests.

Results: the mean platelet counts and MPV were higher in diabetics compared to the nondiabetic subjects [277.46 ± 81 X 10⁹/l vs. 269.79 ± 78 X 10⁹/l (P= 0.256)], 8.29±0.735 fl versus 7.47±0.73 fl (P= 0.001), respectively. MPV showed a strong positive correlation with fasting blood glucose, and HbA1C levels (P=0.001).

Conclusions: This study showed that, Mean platelet volume is increased in diabetic patients than in healthy controls. MPV is positively correlated / associated with glycemic control (FBG, HbA1C). MPV significantly increased in diabetics with HbA1C more than 7% than those with less than 7%. In diabetes mellitus, MPV is increased and it is indicative of worsening glycemic control.

Date of Submission: 16-01-2019

Date of acceptance: 31-01-2019

I. Introduction

Diabetes mellitus is a global pandemic disease. It is a chronic metabolic syndrome principally characterized by persistent hyperglycemia⁽¹⁾. A majority of patients with type 2 DM have signs of the metabolic syndrome. Recently, a prothrombotic state, characterized by abnormalities in platelet function and elevated circulating levels of C- reactive protein, PAI-1 and fibrinogen has been recognized as a component of metabolic syndrome⁽²⁾.

Platelet function is of pathophysiological importance in atherothrombotic disease and there is a strong support for platelet dysfunction with platelet hyperreactivity in both type 1 and type 2 DM^(3,4). Platelets acting in concert with vascular endothelium, leucocytes and coagulation, play a key role in the development of diabetic angiopathy⁽²⁾.

Altered platelet morphology and function has been observed in the form of enhanced platelet activity⁽⁵⁾. Large platelets are younger, more reactive and aggregable. They contain denser granules and are metabolically, enzymatically more active than smaller ones and have higher thrombotic potential^(3,6-8). Platelet hyper-reactivity and increased baseline activation in patients with diabetics is multifactorial^(3,9-12). Hyperglycemia can increase platelet reactivity by inducing non-enzymatic glycation of proteins on the surface of the platelet, by the osmotic effect of glucose and activation of protein kinase C⁽⁹⁻¹¹⁾. Such glycation decreases membrane fluidity and increases the propensity of platelets to activate⁽⁹⁻¹¹⁾. Platelet function is directly regulated by insulin via a functional insulin receptor found on human platelets⁽⁹⁻¹¹⁾.

The platelet indices (platelet count, mean platelet volume-MPV, platelet distribution width-PDW and platelet large cell ration-PLCR) are the determinants of platelet functionality, among which increased mean

platelet volume and platelet distribution width were found to be attributed in the causation of thromboembolic complications^(13,14).

Fasting blood glucose (FBG), post prandial blood glucose (PBG) and hemoglobin A1C (HbA1C) are widely used to monitor glycometabolic control in patients with DM. Haemoglobin A1C is a more useful marker to determine mean blood glucose levels over a longtime period^(15,16).

The determination of HbA1C levels serve as a convenient and suitable test for evaluation of the adequacy of diabetic control in the prevention of various diabetic complications.

The newer hematological analysers give many platelet parameters which help in easy detection of changes in platelet structure. This may help in early detection of prothrombotic state of platelets, which can act as an alarm for diagnosing initiation/ progression of diabetic complications.

II. Aim of the study

1. To compare platelet indices between type 2 diabetic patients and control group.
2. To analyse the correlations between MPV and FBG, PBG in diabetic patients.
3. To evaluate MPV according to HbA1C levels in diabetic group.

III. Materials and methods

This is a cross-sectional study conducted in tertiary care hospital and research center in Andhra Pradesh. The study included 300 type 2 diabetic patients and 300 non-diabetic controls. All cases and controls were recruited from the outpatient department of medicine over a period of 6 months. Institutional Ethical committee clearance was obtained before the start of study. Informed and written consent of patients was taken.

Inclusion criteria: Already diagnosed type 2 diabetic patients between age group 35-60yrs. Control group is obtained from individuals without DM as obtained from the medical records.

Exclusion criteria: subjects having anemia (males Hb<13gm%, females Hb<12gm%), malignancy, chronic renal failure, cyanotic heart disease, inflammatory conditions, thrombocytopenia, hypo/hyper thyroidism, diabetic on anti-platelet drugs such as aspirin and clopidogrel.

We measured platelet indices in target groups using an automatic blood counter. Venous blood samples were collected in dipotassium EDTA and tested within one hour of collection to minimize variations due to sample aging. Samples were maintained at room temperature. Samples for plasma glucose estimation and HbA1C were collected in sodium fluoride and dipotassium EDTA respectively. The estimation of plasma glucose levels (FBG,PBG) was carried out by glucose oxidase method in autoanalyser and HbA1C by high performance liquid chromatography method.

Diagnosis of diabetic patient was established using 2014 ADA criteria⁽¹⁷⁾:

Fasting plasma glucose of >126mg/dl, considered as diabetics
HbA1C > 6.5%

Statistical analysis was performed by statistical package for the social sciences (SPSS) version 17. Student t-test was used to find the significant difference of FBS, HbA1C, MPV, PDW. Data expressed as mean \pm standard deviation. A p<0.05 was considered statistically significant.

IV. Results

The mean age of the diabetic population was 55 \pm 11.32 years, whereas that of nondiabetic population was 51.5 \pm 10.1 years.

Our study revealed that MPV values are higher in diabetic patients compared with healthy people. No significant difference observed in other indices like platelet count, PDW, P-LCR between two groups. (Table:1) A positive correlation was observed between MPV, FBG in diabetics. No significant association seen between MPV and PPBG.(Table:2)

Diabetic group was divided into two groups on the basis of HbA1C values:(Table:3) Group 1 – with HbA1C level less than 7%. Group 2 – with HbA1C level more than or equal to 7%. Out of 300 patients in diabetic group 79 showed HbA1C value to be less than 7% and 221 patients showed HbA1C to be more than 7%.

Fasting plasma glucose was significantly raised in group 2 with HbA1C more than 7%. FBG in group 1 and 2 were 140 \pm 3mg/dl and 175 \pm 15mg/dl, which was highly significant between the two groups with p-value 0.001.

Mean value of mean platelet volume was higher in diabetics with HbA1C more than 7% (mean MPV- 13.2 \pm 1) compared to those with HbA1C less than 7% (mean MPV- 11.8 \pm 1) and statistically significant (pvalue – 0.003)

Mean value of platelet count and platelet distribution width does not show much difference in the two groups, and statistically not significant.

The mean duration of diabetes in group with HbA1C <7% is 6.4±3 years and mean duration of diabetes in group with HbA1C ≥7% is 5.3±3 years. Mean MPV is significantly high in those with HbA1C≥7% irrespective of their duration of diabetes.

Table 1: Comparison of various parameters between the diabetic and nondiabetic subjects

C h a r a c t e r i s t i c	D i a b e t i c s	N o n d i a b e t i c s	P v a l u e
Fasting blood sugar (mg/dL)	150.5 ± 71.71	78.5 ± 13.15	< 0.001
Post prandial blood sugar (mg/dL)	252.9 ± 94.85	133.4 ± 56.75	—
H b A 1 c (%)	9.13 ± 2.5	5.95 ± 0.73	< 0.001
P l a t e l e t s (X 1 0 9 / L)	277.46 ± 81.13	269.79 ± 70	0.256
Mean platelet volume (fl)	8.29 ± 0.735	7.47 ± 0.73	< 0.001

Table 2. Correlation of MPV to the various parameters studied in DM group

C h a r a c t e r i s t i c			t v a l u e	p v a l u e	
M	P	V	Fasting Blood Glucose	5.67	0.000
M	P	V	Post prandial blood glucose	3.12	0.074

Table 3: Comparing the various parameters in two groups of diabetic patients with reference to HbA1c level.

P a r a m e t e r s	HbA1c less than 7(%)	HbA1c more than 7(%)	p-value	t-value	Statistical Significance
	7 9	2 2 1			
Mean FPG (mg/dl)	140 ± 3	175 ± 15	0.001	4.87	S
Mean platelet count (lacs/cumm)	244 ± 0.65	270 ± 0.79	0.3187	1.002	N S
Platelet distribution width (%)	17.2 ± 0.80	18.6 ± 10.35	0.0018	3.21	N S
Mean of mean platelet volume (fl)	13.2 ± 1	11.8 ± 1	0.003	2.17	S

V. Discussion

In our study, statistically significant increment in MPV and PDW were found in T2 diabetics patients than that in non-diabetic control group. Similar results were seen in studies done by – Li S et al, Demirtune R et al, Kodiatte TA et al, Gresesle et al, Farah Jabeen et al, Ozder A et al, Hekimsoy et al, Zuberi et al, Jndal et al, Papanas et al, Perkn BA et al, ArauzPacheco C et al.

several studies showed increased number of large circulating platelets in diabetics compared with controls⁽¹⁸⁻²³⁾. The reason might be related to the vascular complications in DM patients. There might be small vascular bleeds due to rupture of atherothrombotic plaques leading to bonemarrow stimulation to recruit larger hyperactive platelets^(1,24).

Among the diabetic individuals, increased platelet aggregability and adhesiveness may be due to reduced membrane fluidity, altered calcium and magnesium homeostasis, increased arachidonic acid metabolism leading to enhanced thromboxane A2 production, decreased NO production, decreased antioxidant levels and increased expression of activation dependent adhesion molecules^(3,25).

In our study, significantly positive correlation observed between MPV and FBG in diabetic patients. Similar results observed in studies done by Kodiatte TA et al, Gresesle et al, Farah Jabeen et al, Demirtune R et al, Shah B Sha D et al, Dalamaga M et al.

Increase in MPV could be because of raised blood sugar leading to osmotic swelling and shorter lifespan of platelets in diabetic patients. This may suggest that platelet activation is related to glycemictcontrol⁽¹³⁾.

Our study showed significantly higher MPV in diabetics with HbA1C more than 7% than diabetics with HbA1C less than 7%. PDW & platelet count doesnot show any significance between two groups. Similar results seen in Li S et al, Demirtune R et al, S Dindar et al, ArchanaBuch et al, IshanDubey et al.

Platelets in DM have dysregulated signalling pathways that lead to an increased activation and aggregation in response to a given stimulus^(10,11). It may be concluded that glycemict control improves platelet activity and function and may prevent or delay the possible diabetic vascular complications⁽²⁾.

If vascular damage was only due to increased numberof large and reactive platelets, then the rate of damagewould have been constant for the duration of disease(3,6). This clearly shows thatplatelet reactivity alone cannot explain the progression ofvascular complications in DM since there are other vascularrisk factors that may be influenced by the degree of controlof diabetes(3,6).This was supported by the nonsignificant statistical correlationbetween MPV and duration ofdiabetes in the study. A direct relation between plateletdysfunction and the development of diabetic complications has yet to be firmly established(6,26).

VI. Conclusion

This study showed that, Mean platelet volume is increased in diabetic patients than in healthy controls. MPV is positively correlated / associated with glycemic control (FBG, HbA1C). MPV significantly increased in diabetics with HbA1C more than 7% than those with less than 7%. In diabetes mellitus, MPV is increased and it is indicative of worsening glycemic control.

The increased platelet size may be one of the factors in the increased risk of atherosclerosis associated with diabetes mellitus and associated micro- and macro-vascular complications. Therefore, MPV and HbA1C can be a useful prognostic markers of vascular complications in diabetics. MPV can be used as a simple and cost-effective tool to monitor the progression and control of DM and thereby in preventing vascular events.

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Dr. Apuroopa M, Dr. Sruthi N, Dr. Naveen Chandra Rao D, Dr. Gayathri D, Dr. Prasanthi M, Dr. Ranga Rao D. Relevance of platelet indices in predicting prothrombotic activity in type 2 diabetes mellitus in correlation with HbA1C. "IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol.18, no. 1, 2019, pp 05-08.