

## Evaluation of Mean Platelet Volume in Diabetes Mellitus and Its Role in Microvascular Complications

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### ABSTRACT

**Background:** Diabetes mellitus (DM) is a metabolic disorder characterised by hyperglycaemia. The hyperglycemia results in altered platelet function as reflected in the platelet indices (mean platelet volume-MPV, platelet distribution width and plateletcrit). Altered platelet function has also been implicated in the occurrence of diabetic vascular complications. Evaluation of platelet indices may serve to provide an insight into the pathogenesis of DM as well as possibly evaluate the risk of progression of the disease. The aim of the current study was to evaluate the MPV in patients with DM and compare it with a non-diabetic control group. We also attempted to determine the association between MPV and microvascular complications within the diabetic cohort.

**Methods:** The study was carried out on patients with diabetes mellitus, attending the medicine out-patient department. Relevant history was taken and fasting blood glucose and hematological parameters (platelet indices and complete blood counts) were assessed as a part of the routine investigations requested by the physician itself. A total of 320 diabetics were screened for the study. After applying exclusion criteria, 52 diabetics were included in the study. We also included 62 non-diabetic, age and sex matched controls in the study. Statistical analysis was performed.

**Results and Conclusion:** MPV levels were significantly higher in diabetic patients when compared to non-diabetic controls. Also, within the diabetic group, MPV values were significantly higher in diabetics with microvascular complications (24 patients) as opposed to the ones without.

MPV is a simple, convenient and cost-effective routine hematological investigation which plays a significant role in the pathogenesis of diabetes mellitus and may serve as a useful prognostic marker to herald the onset of microvascular complications in the diabetic population.

**Keywords:** Diabetes Mellitus, Mean Platelet Volume, Microvascular Complications, Platelets, Fasting Blood Glucose.

### Introduction

Diabetes mellitus (DM) is a metabolic disorder which has attained the proportions of a global pandemic. [1] It has proved to be a cause of great concern, especially in a developing country like India due to its high degree of morbidity and ubiquitous prevalence. It is estimated that by 2030, there would be 79.4 million individuals afflicted with diabetes in India. [2] The fact that this condition requires close monitoring and continuous follow-up adds to its status as being one of the leading worldwide health issues. DM is characterized by chronic levels of hyperglycemia resulting in complications affecting almost all the organs in the body. [1] These complications further enhance the morbidity and mortality associated with DM.

Extensive research is being done on establishing a relationship between diabetes mellitus and platelet indices (mean platelet volume- MPV, plateletcrit- PCT, and platelet distribution width- PDW). Altered platelet morphology and function have been reported in patients with diabetes mellitus (DM) and MPV was found to be significantly higher in them, [3,4] thereby playing a crucial

role in the development of microvascular complications (diabetic nephropathy, neuropathy, and retinopathy) and macrovascular complications (coronary artery disease, transient ischemic attacks, peripheral arterial disease, and stroke). [4] A few studies have also noted that the mean MPV is higher in diabetics with poor glycemic control and in those with vascular complications as opposed to those without the same. [5]

Mean platelet volume (MPV) reflects the average size of platelets present in a person's blood sample. [6] It is a marker indicating subclinical platelet activation and its elevated level is an independent risk factor for various vascular episodes. [7] Automated cell counters have made platelet indices like MPV routinely available in most clinical laboratories. Hence, there is scope to make better use of the platelet parameters generated [6] by employing MPV as an important, simple, effortless, and cost-effective tool to understand the pathogenesis of the disease. It can probably also serve as an independent predictor of impending acute events and to necessitate prophylactic therapy in the form of anti-platelet agents. [8]

The objectives of the current study are;  
 1. To evaluate the MPV in patients with DM and compare it with a non-diabetic control group.  
 2. To determine the association between MPV and microvascular complications within the diabetic cohort.

### Material & 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.

History was elicited from them to acquire information about the status of hypertension and intake of any antiplatelet medication. 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). Data thus obtained was recorded methodically. Hematological parameters (platelet indices and complete blood counts-CBC) and fasting blood glucose (FBG) were assessed as part of the routine investigations requested by the physician himself.

A total of 320 diabetics were screened for the study. From this group, patients with anaemia (hemoglobin <12g/dl in males & 11g/dl in females), hypertension, infection (as reflected by leukocytosis), thrombocytopenia, thrombocytosis, malignancy and pregnancy were excluded. Patients with history of intake of any anti-platelet medication (aspirin and clopidogrel) were also excluded from the study. After exclusion, 52 patients were included in the study group. We also included 62 non diabetic controls (after application of the exclusion criteria) for the study.

Venous blood samples were collected in EDTA and biochemistry tubes, and tested within 1 hour of collection

to minimize variations due to sample aging. Samples were maintained at room temperature. 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 analyser).

The MPV values in the diabetic group were compared with that of the control group. The diabetics were divided into two groups based on the presence or absence of microvascular complications and the MPV 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 32 yrs to 76 yrs with a mean age of 52.21 yrs. Within the control group, the age of the patients ranged from 19 yrs to 78 yrs with a mean age of 41.02 yrs.

The mean FBG and MPV in the diabetic group were 219.04 mg/dl and 10.31±0.82 fl and that in the non-diabetic control group were 102.42 mg/dl and 9.76±0.71 fl respectively. The mean MPV was significantly higher in the diabetic group as opposed to the non-diabetic group (*P* value=0.000289) (Table 1).

Of the 52 diabetic cases, 24 had microvascular complications. The mean MPV of patients with microvascular complications was 10.68±0.77 fl and those without complications was 9.99±0.73 fl. MPV was significantly elevated in the diabetic group with microvascular complications (*P* value=0.002321) (Table 1).

**Table 1: Mean values of Age, MPV (mean platelet volume) and fasting blood glucose (FBG) according to subgroups: non-diabetics, diabetics without vascular complications and diabetics with vascular complications.**

	Non – Diabetic Control Group	Diabetics	Diabetics without vascular complications	Diabetics with vascular complications
Mean Age (yrs)	41.02	52.21	52.79	51.54
Mean MPV (fL)	9.76	10.31	9.99	10.68
Mean FBG (mg/dL)	102.42	219.04	216.07	222.5

## Discussion

Diabetes mellitus, is characterized by varying levels of hyperglycemia. [9] Several lines of evidence indicate that hyperglycemia induces the production of larger platelets. [10] This can be quantified as MPV by clinical hematology analyzers, which generally varies between 7.5 to 10.5 fl. [11] MPV may be affected by various factors such as anemia, leukocytosis, thrombocytosis, thrombocytopenia, infections, hypertension, dyslipidemia, pregnancy, malignancy, and intake of antiplatelet medication. [10]

It has been demonstrated that alterations in platelet and endothelial function that favor thrombosis occur early in the diabetic state and may contribute to microvascular disease. Based on this postulate, there are several ongoing studies on antiplatelet agents, that maybe employed in the preventive treatment of diabetic vascular disease. [12]

The current study shows that the MPV values were significantly increased in diabetic patients when compared to non-diabetic controls (mean MPV in diabetics -  $10.4 \pm 0.73$  fl, mean MPV in non-diabetics -  $9.74 \pm 0.72$  fl,  $P$  value=0.0002) which coincides with the results of other researchers. [1, 3, 4, 8, 13, 14, 15, 16, 17, 18]

Higher MPV in DM could be explained based on few of the following hypotheses. Firstly, plasma glucose is a major source of energy for platelets. [11] Under basal conditions, 40% to 50% absorbed glucose is used for glycogen production. [11] Due to chronic hyperglycaemia, platelets are overwhelmed with glucose and are subjected to synthesis of glycogen and glycosylation of certain proteins. The increased glycogen content in turn contributes to small percent of increase in the MPV. [19] Therefore, MPV reflects the hyperglycemic status of a diabetic individual. Another theory, to support increased MPV in hyperglycaemic patients, is osmotic swelling of platelets due to raised levels of some glucose metabolites. [20] The third theory, states that there is higher platelet turnover in DM, resulting in younger platelets which are both larger and more metabolically active. [20]

The increased reactivity and activation of platelets in diabetic patients may also be attributed to several biochemical factors such as hyperglycaemia, hyperlipidemia, insulin resistance, prolonged inflammatory and oxidant state and also, increased expression of glycoprotein receptors and growth factors. [1] Hyperglycaemia leads to increased platelet activity by increasing non-enzymatic glycation of proteins on the platelet surface, enhancing osmotic effects of glucose and activation of protein kinase C. [21-23] Insulin

also acts directly by controlling the platelet function via a functional Insulin Receptor and attenuates the platelet aggregation effect of agonists in healthy non-obese individuals. [21-23] Overall, a prolonged hyperglycaemic state leads to various microvascular and macrovascular complications and the platelets add up these effects. [20, 23]

Research is also being carried out in the diabetic population to find a correlation between increased MPV and the presence of microvascular complications with many studies suggesting a strong association between the two. [12, 24] The current study is in corroboration with the same and is in agreement with the results of other researchers, [3, 18, 25, 26] wherein there is a significantly higher MPV among the diabetic patients with microvascular complications when compared to those without the same (mean MPV in diabetics with microvascular complications -  $10.66 \pm 0.69$  fl, mean MPV in diabetics without microvascular complications -  $10.09 \pm 0.69$  fl,  $P$  value=0.024). This finding indicates that chronic hyperglycaemia and increased MPV may have a crucial role to play in the pathogenesis of microvascular complications associated with DM. The basic mechanism behind this could be the presence of larger platelets which are younger, more reactive, aggregable, contain denser granules and they also secrete more serotonin,  $\beta$ -thromboglobulin, and thromboxane A<sub>2</sub> than smaller platelets. [20, 26, 27, 28, 29] All these can produce a procoagulant effect and cause thrombotic vascular complications. This suggests a strong relationship between MPV and diabetic vascular complications.

## Conclusion

MPV is a simple, convenient and cost-effective routine hematological investigation which plays a significant role in the pathogenesis of diabetes mellitus and may serve as a useful prognostic marker to herald the onset of microvascular complications in the diabetic population. High risk candidates can be identified and started on prophylactic therapy in the form of anti-platelet agents to avoid any acute events leading to lifelong debilitating consequences and even fatality. However, further studies with larger sample size need to be carried out, to emphatically establish the role of MPV in the pathogenesis of diabetes mellitus and its associated vascular complications.

## Abbreviations and Symbols:

DM-diabetes mellitus, MPV-Mean platelet volume, FBG-fasting blood glucose, CBC-complete blood counts.

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## Declarations

This article has not been published/ or is being considered for publication anywhere else.

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