

Association of Mean Platelet Volume in Diabetics and Non Diabetic Individuals in Khandwa**Harshul Patidar¹, Uditkumar Agrawal², Sadhna Sodani³, Shikha Agrawal^{4*}, Ranjana Hawaldar⁵**¹*Assistant Professor, Department of Pathology, GMC, Khandwa & Consultant Pathologist (Sampurna Sodani Diagnostic Clinic, Khandwa Branch), India*²*Associate Professor, Department of Biochemistry, GMC, Khandwa, India*³*Associate Professor, Department of Microbiology, MGMMC, Indore Hon. Director, Sampurna Sodani Diagnostic Clinic, Indore, Madhya Pradesh, India*⁴*Assistant Professor, Department of Anesthesia, GMC, Khandwa, India*⁵*Head Pathologist, Sampurna Sodani Diagnostic Clinic, Indore, Madhya Pradesh, India*

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Abstract

Background: Type 2 diabetes mellitus (T2DM) patients have a higher risk of developing complications, which lead to decrease in the quality of life and increase in morbidity. Platelet indices have been available in the laboratory routine using blood cell counters for several years. Platelets (PLT) are directly or indirectly involve in the processes of chronic complications in T2DM. Beside serving as a marker of platelet activation, mean platelet volume (MPV) is also considered as an inflammatory indice. Increased activity has been noted in Platelets with increased volume when compared to smaller ones, thus highlighting the utility of Mean platelet volume as a marker of platelet activity. **Aim:** To evaluate MPV in patients with type II DM in comparison with a healthy control group. **Materials and Methods:** In total, 50 diabetic patients along with age and sex matched non-diabetic controls were studied. A detailed history was taken regarding duration of diabetes, medication, past history of stroke and hypertension. Platelet indices, fasting blood glucose, Post prandial blood glucose and HbA1c were obtained from venous blood samples. All parameters were then subjected to statistical analysis using SPSS 20.0. Data was expressed as mean +/- standard deviation. A p-value <0.05 was considered statistically significant. **Results:** Platelet indices, namely MPV, PCT were significantly higher in diabetic individuals. Platelet dysfunction also showed a positive association with HbA1c. **Conclusion:** Changes in platelet indices were found to be statistically associated with diabetes.

Keywords: Type 2 diabetes mellitus, Mean platelet volume, HbA1c.

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Introduction

Diabetes mellitus (DM) is a major global health problem. [1,2] According to estimates of the World Health Organisation, there were 346 million people suffering from diabetes worldwide in 2011.[3] DM related deaths occurring due to the increased risk of developing atherosclerosis and the various disturbances at the cellular as well as metabolic levels. [1,2] Platelet volume, a marker of the platelet function and activation, is measured as mean platelet volume (MPV) by hematology analyzers. Platelets express procoagulant proteins such as P-selectin and glycoprotein IIIa on their surfaces.[4] Large platelets contain denser granules that are metabolically and enzymatically more active than smaller ones thus having higher thrombotic potential. This might be the basis of the link between increased MPV and increased thrombotic potential. [5] Diabetic patients have an increased risk of developing micro- and macrovascular disease, and platelets may be involved as a causative agent with respect to altered platelet morphology and function.[6,7] The aim of the present study was to evaluate MPV in patients with type II DM in comparison with the nondiabetics. Also to determine the correlation

of MPV with fasting blood glucose (FBS), postprandial plasma glucose (PPBS), glycosylated hemoglobin (HbA1c) and body-mass index (BMI) in the diabetic patients respectively.

Materials and Methods

This study was done in Sodani Diagnostic Laboratory, Khandwa Branch during the period from July 2019 to Dec 2019. This study was carried out in 50 patients who were already diagnosed to have Type 2 DM and 50 nondiabetic subjects without known coronary artery disease after taking their informed consent and was found to be within ethical standards as the Helsinki Declaration was followed. All the diabetic and nondiabetic subjects underwent a complete clinical evaluation with specific reference to any associated macro- or microvascular complications as well as any drugs taken. Height and weight of all the subjects were recorded. We measured the MPV and platelet counts in the above target groups who had a complete blood count done using a Nihon Kohden 3part Hematology analyzer. Venous blood samples were collected in dipotassium EDTA and tested within 1 hour of collection to minimize variations due to sample aging. Samples for plasma glucose estimation and HbA1c were collected in sodium fluoride and dipotassium EDTA, respectively. The estimation of plasma glucose levels (fasting plasma glucose and postprandial plasma glucose) was carried out by the glucose oxidase method in the semi auto analyzer and that of HbA1c by the Cobas C11-Roche-Biochemistry Analyzer.

Exclusion Criteria: Male patients with hemoglobin below 13 gm% and female patients below 12 gm% were excluded from the study.

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Diabetics on antiplatelet drugs such as aspirin and clopidogrel were also excluded. Subjects with any diagnosed malignancy were also excluded. After baseline evaluation, diabetic patients were divided into two groups according to their HbA1c levels: group A consisted of patients with HbA1c levels < 6.5% and group B consisted of patients with HbA1c levels \geq 6.5%. Statistical evaluation was performed by statistical package for the social sciences (SPSS) version 20. Data were expressed as mean \pm standard deviation. A *P* value < 0.05 was considered statistically significant.

Results

Among the 50 diabetic subjects in the study. There were 64% male diabetics and 36% female diabetics in the study. There were 57% nondiabetic males and 43% nondiabetic females in the study. The mean age of the diabetic population was 54 \pm 11.02 years, whereas that of nondiabetic population was 50.4 \pm 10.6 years. The mean

duration of diabetes was 5.1 \pm 4.23 years. The mean BMI in the diabetic group was 24 \pm 3.81 kg/m² whereas it was 23.61 \pm 4.1 kg/m² in the nondiabetic group (*P*=0.30). The mean FBS level in the diabetic population was 151.6 \pm 72.5 mg/dL while that of the nondiabetic group was 77.6 \pm 12.11 mg/dL (*P* < 0.005). The mean PPBS level in the diabetic population was 251.7 \pm 93.65 mg/dL while that of the nondiabetic group was 132.1 \pm 54.69 mg/dL (*P* < 0.004). The mean HbA1c level in the diabetic group was 9.11 \pm 2.41% as compared to 5.89 \pm 0.612% of the nondiabetic group (*P* < 0.001). The mean platelet count in the diabetic group was 275.46 \pm 80.12 \times 10⁹/L as compared to 270.71 \pm 70.1 \times 10⁹/L of the nondiabetic group (*P*=0.26). In the diabetic subjects, MPV was significantly higher (8.19 \pm 0.645 fl) as compared to the non-diabetic group (7.37 \pm 0.73 fl; *P* < 0.001)[Table 1].

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

Characteristic	Diabetics	Non- diabetics	<i>P</i> value
Number	50	50	—
Age (years)	54 \pm 11.02	50.4 \pm 10.6	—
Mean duration of diabetes (years)	5.1 \pm 4.23	—	—
Height (cm)	161.6 \pm 8.14	161.2 \pm 8.7	—
Body mass index (kg/m ²)	24 \pm 3.81	23.61 \pm 4.1	0.30
Weight (Kg)	65.13 \pm 11.1	64.1 \pm 11.9	—
Fasting blood sugar (mg/dL)	151.6 \pm 72.5	77.6 \pm 12.11	< 0.005
Post prandial blood sugar (mg/dL)	251.7 \pm 93.65	132.1 \pm 54.69	<0.004
HbA1c (%)	9.11 \pm 2.41	5.89 \pm 0.612	< 0.001
Hemoglobin (gm%)	14.6 \pm 1.44	14.7 \pm 4.9	0.07
Platelets (X 10 ⁹ /L)	275.46 \pm 80.12	270.71 \pm 70.1	0.26
Mean platelet volume (fl)	8.19 \pm 0.645	7.37 \pm 0.73	< 0.001

Among the diabetic subjects, a positive statistical correlation was seen between MPV and HbA1c levels (*P* < 0.001), FBS levels (*P* < 0.001) and PPBS levels (*P* = 0.002). However, no statistical correlation was seen between MPV and the duration of DM & BMI [Table 2].

Table 2: Correlation of MPV to the various parameters studied

Characteristic		Pvalue
MPV	Duration of DM	0.591
MPV	BMI	0.414
MPV	HbA1c	< 0.003
MPV	FBS	< 0.002
MPV	PPBS	0.005

We also divided the diabetic group based on the HbA1c levels into group A (HbA1c < 6.5%) and group B (HbA1c \geq 6.5%). Out of 50 DM patients, there were 7 patients in group A (mean HbA1c = 5.88 \pm 0.41%) and 43 patients in group B (mean HbA1c = 9.13 \pm 3.1%). The mean BMI in group A (23.1 \pm 2.89 kg/m²) was significantly lower than that of group B (25.19 \pm 4.2 kg/m²; *P* =

0.026). The mean FBS level in group A was 83.13 \pm 18.16 mg/dL while that of group B was 161.7 \pm 72.31 mg/dL (*P* < 0.005). The mean platelet count in group A (290.11 \pm 66 \times 10⁹/L) was higher than that of group B (276.1 \pm 84 \times 10⁹/L) but was not statistically significant. The mean MPV in group A (7.89 \pm 0.69 fl) was significantly lower than that of group B (8.15 \pm 0.73 fl; *P* = 0.005).

Table 3: Comparison of diabetic study population between group A and group B

Characteristics	Diabetic Population		<i>P</i> value
	Group A (HbA1c<6.5%)	Group B(HbA1c>6.5%)	
Total patients	7	43	—
MPV(fl)	7.89 \pm 0.69	8.15 \pm 0.73	0.005
BMI (kg/m ²)	23.1 \pm 2.89	25.19 \pm 4.2	0.026
Platelets (X10 ⁹ /L)	290.11 \pm 66	276.1 \pm 84	0.41
HbA1c	6.58 \pm 0.41	9.13 \pm 3.1	—
FBS(mg/dl)	83.13 \pm 18.16	161.7 \pm 72.31	< 0.005
PPBS(mg/dl)	149.9 \pm 46.8	270.1 \pm 89.11	< 0.005

Discussion

Diabetes mellitus is a chronic disease that causes increased morbidity and mortality due to its vascular complications. Most published studies aimed to investigate the relationship between MPV and the prevalence and severity of diabetes, [8] and its complications.[9, 10] However, few study examined causal effect of MPV and incident risk of T2DM. In addition, most of the previous studies were

conducted in Europeans and the sample size was relatively small. Therefore, it still remains to elucidate whether MPV level is associated with incident diabetes risk, especially in other populations including the population of our region. There is increased risk of thrombosis and atherogenesis in diabetic patients. Development of complications in DM has been contributed by the changes in hemostatic balance. Many studies in diabetic patients have reported

increase in thrombotic adhesion, aggregation and secretion which focused on the role of platelets in maintaining haemostatic balance. [11,12] Formation of advanced glycation end products, activation of protein kinase C and disturbances in polyol pathways are the possible mechanisms by which increased glucose induces vascular abnormalities.[13] The prevalence of diabetic microvascular complications is higher in people with poor glycemic control, longer duration of DM, associated hypertension, and obesity.[14] Platelets, the second most abundant cell type in the circulation, play a classical role in thrombosis and homeostasis.[15] In recent decades, an increasing number of evidence showed that platelets were also related to inflammation. [16] Mean platelet volume (MPV) is the size of circulating thrombocytes measured by automated blood analyzers. It is considered as a marker of platelet activation and moreover, as an inflammatory indice. Higher MPV level indicates larger platelets, which are metabolically and enzymatically more active. [6] Cross-sectional, [6] and case-control studies with relative small sample size indicated that person with diabetes or study participants with impaired fasting glucose had higher levels of MPV compared to the healthy controls.[8] A meta-analysis enrolling 30 case-control and cross-sectional studies also indicated that MPV was significantly higher among study participants with established diabetes than the healthy controls.[17] The findings from the present study also strongly support the positive association between MPV levels and incident DM risk. The platelet count in diabetics was higher than in non diabetics in the study by Kodiatte et al., [18] which is as similar to our study. In contrast The mean platelet count in non diabetes was lower when compared to the diabetic group.[19] An inverse relation was identified between MPV and the platelet count in the study made by Giovanetti et al., [20] While in our study there is a direct relationship observed between MPV and platelet count. Walinjkar et al., [21] showed that the platelet indices, namely MPV was significantly higher in individuals with diabetes as compared to non-diabetic controls. Also, platelet dysfunction showed a positive association with HbA1C which is quite similar to our study findings. Hiroyuki Inoue et al., [22] and Thomas Alex Kodiatte et al., [23] in their studies found higher MPV in Type II DM as compared to non diabetic subjects. Also MPV showed a strong positive correlation with fasting blood glucose, postprandial glucose and HbA1C levels. Both the study findings are similar with our study findings. Potential mechanisms that underlying this positive association remains unclear. However, several mechanisms might involve in these associations. Firstly, activated platelets could express soluble CD40 ligand (CD40L) and CD40L and its receptor CD40 extensively involved in oxidative stress and inflammatory pathways, which may play a role in the development of diabetes. Secondly, higher MPV might partly be due to the regulation of some cytokines, such as IL-6, which could increase the incident diabetes risk by damaging the body's glucose stability and β -cell function. [24]

Limitations of the Study: Small study population is the important limitation of our study. The platelet indices are also affected by thyroid and rheumatic diseases which were not considered in this study. Further studies are needed to evaluate the utility of Mean Platelet Volume in diabetes mellitus. One of the limitation of our study was a relatively small sample size and the study was from a single institution thus can't be generalised to the entire population.

Conclusion

These findings suggest that increased MPV is positively associated with HbA1c levels in type 2 diabetes mellitus patients. The current findings indicate that MPV, a low-cost, widely available and noninvasive marker, might be a potential risk factor of diabetes in middle-aged and older population. Measuring MPV could be a beneficial marker for determining diabetes-induced macrovascular complications in patients with type 2 diabetes mellitus. These findings need to be verified in other population with long follow-up period.

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References

1. Deferenzo RA, Abdul-Ghani M. Assessment and treatment of cardiovascular risk in prediabetes: Impaired glucose tolerance and impaired fasting glucose. *Am J Cardiol* 2011;108:3B-24B.
2. Lee M, Saver JL, Hong KS, Song S, Chang KH, Ovbiagele B. Effect of prediabetes on future risk of stroke: meta-analysis. *BMJ*. 2012;344:e3564.
3. World Health Organization August 2011. Available from: <http://www.who.int/mediacentre/factsheets/fs312/en/> [Last accessed on 2011 Nov 17]
4. Mathur A, Robinson MS, Cotton J, Martin JF, Erusalimsky JD. Platelet reactivity in acute coronary syndromes: evidence for differences in platelet behaviour between unstable angina and myocardial infarction. *Thromb Haemost*. 2001;85:989-94.
5. Endler G, Klimesch A, Sunder-Plassmann H, Schillinger M, Exner M, Mannhalter C, Jordanova N, Christ G, Thalhammer R, Huber K, Sunder-Plassmann R. Mean platelet volume is an independent risk factor for myocardial infarction but not for coronary artery disease. *Br J Haematol*. 2002;117: 399-404.
6. Hekimsoy Z, Payzinb B, Ornek T, Kandogan G. Mean platelet volume in Type 2 diabetic patients. *J Diabetes Complications* 2004;18:173-6.
7. Zuberi BF, Akhtar N, Afsar S. Comparison of mean platelet volume in patients with diabetes mellitus, impaired fasting glucose and non-diabetic subjects. *Singapore Med J* 2008;49:114-6.
8. Shah B, Sha D, Xie D, Mohler ER 3rd, Berger JS. The relationship between diabetes, metabolic syndrome, and platelet activity as measured by mean platelet volume: the National Health And Nutrition Examination Survey, 1999-2004. *Diabetes Care*. 2012;35:1074-8.
9. Kim ES, Mo EY, Moon SD, Han JH. Mean platelet volume is closely associated with serum glucose level but not with arterial stiffness and carotid atherosclerosis in patients with type 2 diabetes. *J Clin Endocrinol Metab*. 2015;100:3502-8.
10. Hudzik B, Szkodziniski J, Lekston A, Gierlotka M, Poloński L, Gąsior M. Mean platelet volume-to-lymphocyte ratio: a novel marker of poor short- and long-term prognosis in patients with diabetes mellitus and acute myocardial infarction. *J Diabetes Complicat*. 2016;30:1097-102.
11. Jindal S, Gupta S, Gupta R, Kakkar A, Singh HV, Gupta K, Singh S. Platelet indices in diabetes mellitus: indicators of diabetic microvascular complications. *Hematology*. 2011;16:86-89.
12. Unbul M, Ayhan M, Güney E. The relationship between mean platelet volume with microalbuminuria and glycemic control in patients with type II diabetes mellitus. *Platelets*. 2012 ;23(6):475-80.
13. Maitra A. The Endocrine System. In: Kumar V, Abbas AK, Fausto N, Aster JC, editors. *Robbins and Cotran Pathologic Basis of Disease*. 8th ed. New Delhi: Elsevier; 2010. pp. 1097-164
14. Zuberi BF, Aktar N, Afsar S. Comparison of mean platelet volume in patients with diabetes mellitus, impaired glucose and non diabetic subjects. *Singapore Med J*. 2008;49:114-16
15. Vermylen J, Verstraete M, Fuster V. Role of platelet activation and fibrin formation in thrombogenesis. *J Am Coll Cardiol*. 1986;8:2b-9b.
16. McFadyen JD, Kaplan ZS. Platelets are not just for clots. *Transfus Med Rev*. 2015;29:110-9.

17. Zaccardi F, Rocca B, Pitocco D, Tanese L, Rizzi A, Ghirlanda G. Platelet mean volume, distribution width, and count in type 2 diabetes, impaired fasting glucose, and metabolic syndrome: a meta-analysis. *Diabetes Metab Res Rev*. 2015;31:402–10.
18. Kodiatte TA, Manikyam UK, Rao SB, Jagadish TM, Reddy M, Lingaiah HK. Mean platelet volume in Type 2 diabetes mellitus. *Journal of laboratory physicians*. 2012;4(1):5.
19. Zubair H, Seema H, Iyshwarya U, Nirmala MJ, Parshwanath HA. Assessment of Mean Platelet Volume in Type 2 Diabetes Mellitus and Prediabetes. *National Journal of Laboratory Medicine*. 2016;5(3): 54-57.
20. Giovanetti TV, Nascimento AJ, Paula JP. Platelet indices: Laboratory and Clinical applications. *Revistabrasileira de hematologia e hemoterapia*. 2011;33(2):164-65.
21. Walinjkar RS, Khadse S, Kumar S, Bawankule S, Acharya S. Platelet indices as predictor of microvascular complications in type 2 diabetes. *Indian J Endocr Metab* 2019;23:206-10.
22. Hiroyuki I, Mayumi S, Kumiko K, Shun-ichiro A, Fumihiko N, Yoshiaki K. Association between mean platelet volume in the pathogenesis of type 2 diabetes mellitus and diabetic macrovascular complications in Japanese patients. *J Diabetes Investig* 2020; 11: 938–945.
23. Thomas AK, Udaya KM, Suraksha BR, Thej MJ, Madhavi R, Harendra KML, Venkataswamy L. Mean Platelet Volume in Type 2 Diabetes Mellitus. *Journal of Laboratory Physici - ans*. 2012; 4(1):5-9.
24. Zhaoyang Li, Jing Wang, Xu Han, Jing Yuan, Huan Guo, Xiaomin Zhang, Dan Zheng, Yuhan Tang, Handong Yang and Meian He. Association of mean platelet volume with incident type 2 diabetes mellitus risk: the Dongfeng–Tongji cohort study. *Diabetol Metab Syndr* 2018;10:29.

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