

Mean Platelet Volume In Diabetes Mellitus Type II

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ABSTRACT

Background: Diabetes Mellitus (DM) is a metabolic disorder and a major health problem because of its high prevalence and morbidity. Platelets have a key role in development of its thrombogenic complications. Platelet size is considered as a marker and determinant of platelet function with younger, larger platelets exhibiting more reactivity. This study was carried out to compare Mean Platelet Volume (MPV) in subjects with diabetes and non diabetic controls.

Method: Total 211 subjects, 105 diabetics and 106 nondiabetic controls were included. MPV, platelet count, blood glucose levels, lipid profile and HbA1c levels were measured and data analyzed by independent “t” test.

Result: Mean MPV was significantly higher in the diabetic group compared to the controls (9.94 ± 1.07 fl versus 9.36 ± 0.96 fl; $p=.00003$). Mean BMI, cholesterol and triglycerides were also significantly higher in the diabetic group. Within the diabetic group, mean MPV, cholesterol and triglycerides were significantly higher in subjects with HbA1c $\geq 6.5\%$ (10.30 ± 0.95 fl vs 9.82 ± 1.08 fl, $p=.03$; 206.28 ± 37.17 mg/dl vs 185.07 ± 41.91 mg/dl, $p=.026$; 176.96 ± 88.54 mg/dl vs 133.19 ± 46.30 mg/dl, $p=.002$ respectively).

Conclusion: High MPV in diabetics may indicate platelet hyperactivity, which may contribute to the vascular complications of type II DM. Thus MPV can be used as a simple, costeffective parameter to assess the probability of developing vascular complications in diabetes.

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Introduction

Diabetes mellitus (DM) is the most common endocrine disease characterized by metabolic abnormalities, hyperglycemia, and by long term complications. There are two major subgroups of DM, type I insulin dependent (IDDM) and type II (NIDDM).^[1] Thrombosis, atherosclerosis and other vascular diseases are common complications of diabetes mellitus.^[2]

Platelets play an important role in the normal hemostasis; the Mean Platelet Volume (MPV), an accurate measure of the platelet size is considered a marker and determinant of platelet function.^[3] Larger platelets with higher MPV are hemostatically more reactive and produce higher amounts of the prothrombotic factor Thromboxane A₂, increasing a propensity to thrombosis.^[3]

Platelets from subjects with DM, particularly from those with type 2 diabetes, exhibit increased reactivity. Factors that may contribute to this greater platelet reactivity are not completely elucidated and include metabolic abnormalities such as hyperglycemia, hyperlipidemia, insulin resistance, and conditions as oxidative stress, inflammation, and endothelial dysfunction.^[4] MPV, a determinant of platelet function, is a newly emerging risk factor for atherothrombosis. A large proportion of persons with type 2 DM suffer from preventable macrovascular complications. There is a need to develop risk factor modification interventions to reduce the impact of long-term complications.^[5]

MPV can be easily measured during routine haematological analysis by automated hematology analyzers. Thus, MPV can emerge as an important, simple, effortless, and cost-effective tool for monitoring and for early recognition of patients that could possibly benefit from preventive treatment.

Materials and Methods

This study was done in a tertiary care hospital of Ahmedabad, Gujarat, India over a period of 6 – 8 months after approval of the IEC. A total of 211 subjects were included in this study, 105 were type II diabetic patients, 106 were healthy individuals matched for age and gender. Height and weight of all subjects was recorded. Patients with anemia, hypertension, hypo-hyperthyroidism, congestive heart failure, leukocytosis, thrombocytopenia or history of stroke, antiplatelet medication were excluded as they may affect platelet size.

Venous blood samples were collected in EDTA & Plain vacuties. Blood samples were taken after an 8–12 hour period of fasting for estimation of glucose and lipid profile. Haemoglobin (Hb), MPV, platelet count was done by

automated hematology analyzer(KX- 21) & serum was analyzed for fasting (FBS) and post prandial blood sugar (PPBS), glycosylated haemoglobin (HbA1c) and lipid profile. Glucose level was measured by the oxidase method, HbA1c level was analyzed by immunoturbidimetric method, total cholesterol, triglyceride, low density lipoprotein (LDL) cholesterol and high density lipoprotein (HDL) cholesterol were measured by commercial enzymatic methods by fully automated biochemistry analyzer (XL- 640). All the investigations were carried out within one hour of collection of samples to avoid error due to sample ageing.

The statistical analysis of the results was performed by using the Statistical Package for Social Sciences (SPSS) for IBM version 20.0. Independent “t”-test was used for testing difference significance, *P* value < 0.05 considered statistically significant.

Result

A total of 211 subjects (105 patients with type 2 diabetes and 106 healthy controls) were included in the study. There were 55 males and 50 females in the diabetic group and 49 males and 47 females in the nondiabetic group. Mean age of diabetic patients was 53.5 ± 9.2 yrs whereas that of non-diabetic population was 47.9 ± 11.7 yrs.

Table 1 shows the comparison of laboratory data between the study and control groups. The mean FBS level in the diabetic group was 152.13 ± 57.7 mg/dl as compared to 95.34 ± 8.3 mg/dl in the non-diabetic group ($p = < .00001$). In the diabetic group the mean PPBS was 229.1 ± 90 mg/dl while it was 122.2 ± 15.5 mg/dl in the non-diabetic group ($p < .0001$). The mean HbA1c in the diabetic group was $8.61 \pm 2.43\%$ as compared to $5.87 \pm .39\%$ in the non-diabetic group ($p < .00001$). The mean MPV was significantly higher, 9.94 ± 1.07 fl, in the diabetic group as compared to 9.36 ± 0.96 fl in the non-diabetic group ($p = .00003$). Mean BMI, Cholesterol and triglycerides (TG) were also significantly higher in the diabetic group. Platelet count was lower in the diabetic group though not statistically significant. There was no significant difference in the value of HDL between the two groups.

Diabetic patients were further grouped according to the HbA1c level into two groups: HbA1c < 6.5% ($n=76$) and HbA1c \geq 6.5% ($n=29$) (Table 2). Individual variables were analyzed by independent student's “t” test. Mean MPV (10.29 ± 0.95 fl) in patients with HbA1c \geq 6.5% was significantly higher than that of HbA1c < 6.5% (9.82 ± 1.08 fl) ($p = .03$). Similarly the mean FBS and PPBS were also significantly higher in patients with HbA1c \geq 6.5% ($p < .0001$). There was no significant difference in the platelet count between the two groups.

Data was available in 100 patients for lipid profile. The mean cholesterol in patients with HbA1c $\geq 6.5\%$ (n=71) was 206.2 ± 37.17 mg/dl was significantly higher than that of patients with HbA1c $< 6.5\%$ (n=29) (185.07 ± 41.91 mg/dl) (p=.026). Similarly the mean triglyceride level was also significantly high in the patients with HbA1c

$\geq 6.5\%$ (176.96 ± 88.54 mg/dl vs 133.19 ± 46.30 mg/dl) (p=.002). However there was no significant difference in the BMI and HDL between the two groups. Within the diabetic group no significant pearsons correlation could be found between MPV and FBS, PPBS, HbA1c or BMI.

Table 1: Comparison of general characteristics and laboratory parameters between study group(Diabetic) and controls.

Parameters	Diabetic group			Controls			p-value
	n	mean	Std. Deviation	n	mean	Std. Deviation	
Age (years)	105	53.50	9.250	106	47.97	11.71	-
Males	55			49			-
Females	50			57			-
Height (cm.)	105	159.90	9.27	86	156.91	8.94	-
Weight (kg)	105	71.74	13.02	87	64.16	14.39	-
Body Mass Index (Kg/m ²)	105	28.22	4.82	42	25.22	4.81	0.0025
MeanPlateletVolume (fl)	105	9.94	1.07	106	9.36	0.96	0.00003
Platelet Count (x 10 ⁹ /L)	105	265.44	74.48	106	283.84	80.82	0.087
FastingBloodSugar (mg/dl)	105	152.13	57.74	106	95.34	8.29	<0.00001
PostParandialBloodSugar (mg/dl)	105	229.11	90.05	105	122.25	15.51	<0.0001
HbA1c (%)	105	8.61	2.43	102	5.87	0.39	<0.00001
Cholesterol (mg/dl)	100	199.39	39.34	105	186.90	35.68	0.018
Triglyceride (mg/dl)	100	164.29	80.33	105	128.06	85.45	0.004
High Density Lipoprotein (mg/dl)	100	48.47	13.60	105	49.20	8.57	0.65

Table 2: Comparison of individual variables in diabetic population according to HbA1c levels.

Parameters	HbA1c (%)	Total	N	Mean	Std. Deviation	p - value
Body Mass Index(Kg/m ²)	≥ 6.5	105	76	27.72	4.18	0.503
	< 6.5		29	28.38	4.21	
Platelet Count (x10 ⁹ /L)	≥ 6.5	105	76	265.23	71.21	0.938
	< 6.5		29	263.78	86.59	
MPV(fl)	≥ 6.5	105	76	9.82	1.08	0.038
	< 6.5		29	10.30	0.95	
FBS(mg/dl)	≥ 6.5	105	76	169.37	60.12	<0.0001
	< 6.5		29	107.00	10.98	
PPBS(mg/dl)	≥ 6.5	105	76	262.16	86.35	<0.0001
	< 6.5		29	144.48	15.59	
Cholesterol(mg/dl)	≥ 6.5	100	71	206.28	37.17	0.026
	< 6.5		29	185.07	41.91	
Triglycerides(mg/dl)	≥ 6.5	100	71	176.96	88.54	0.002
	< 6.5		29	133.19	46.30	
HDL(mg/dl)	≥ 6.5	100	71	49.03	15.22	0.683
	< 6.5		29	47.96	9.57	

Discussion

Diabetes mellitus (DM) is associated with macrovascular and microvascular complications (coronary artery disease, ischemic stroke, peripheral arterial disease, nephropathy, and retinopathy). Platelets have a “key role” in atherogenesis and its thrombotic complications in subjects with DM.^[6] Countries with the highest absolute number of diabetics are in India(19 million), China(16 million), and the United States(14 million).^[7]

MPV was found to be significantly higher in the diabetic group as compared to the non-diabetic group in the present study. This is in agreement with the studies done by Hekimsoy et al,^[8] Zuberi et al,^[9] Kodiatte et al,^[10] Ulutas et al.^[11] Larger platelets are more active hemostatically and enzymatically, and they contain more prothrombotic molecules, such as platelet factor 4, serotonin, and platelet-derived growth factor, and possess greater aggregability in response to ADP.^[12] Mean platelet volume (MPV), which is used to measure platelet size, can reflect platelet activity.^[13] Increased MPV may lead to a prothrombotic condition with increased thromboxane A2 (TXA2) and B2 and adhesion molecule expression, such as P-selectin and glycoprotein IIb/IIIa, and β -thromboglobulin release.^[12] Platelets of diabetic patients are characterized by dysregulation of several signaling pathways and have been suggested to be hyperreactive, showing increased adhesion, activation, and aggregation.^[14] Several mechanisms may account for the increased platelet activity in diabetes. The glycation of platelet surface proteins reduces membrane fluidity and increases platelet adhesion, causing incorporation of glycated proteins into the thrombi. An increase in calcium mobilization from intracellular storage pools, resulting in increased intracellular calcium levels, has been correlated with reduction in membrane fluidity.^[15]

MPV was found to be significantly increased in patients with HbA1c $\geq 6.5\%$ as in other studies.^[10,16] Hyperglycemia can increase platelet reactivity by inducing nonenzymatic glycation of proteins on the surface of the platelet, by the osmotic effect of glucose and activation of protein kinase C.^[10] Mean platelet volume was significantly decreased at the 3-month follow-up period, compared to baseline MPV, in diabetic patients who achieved improved glycemic control with intensive diet and pharmacotherapy.^[17] Significant positive correlation between the reduction in thrombus formation and the reduction in HbA1c has also been reported.^[18] These findings suggest that glycemic control may be helpful in decreasing the platelet reactivity and thus may prevent or delay possible vascular complications.

No positive pearsons correlation could be established between MPV and glycemic indices especially FBG and

HbA1c similar to studies done by Sharpe et al,^[19] Lutfullah Cakir et al,^[20] Unubol M et al,^[21] E.C.Yenigun et al.^[22] Kim JH found that MPV was only positively correlated with FPG in newly diagnosed diabetic women.^[23] This could explain why no significant correlation was found in this study as the patients selected were having diabetes for a longer duration and were also taking treatment for the same. If vascular damage was only due to increased number of large and reactive platelets, then the rate of damage would have been constant for the duration of disease independent of glycemic control. This clearly shows that platelet reactivity alone cannot explain the progression of vascular complications in DM since there are other vascular risk factors that may be influenced by the degree of control of diabetes.^[10] This is supported by the nonsignificant correlation between MPV and HbA1c.

Platelet count was lower in the diabetic patients similar to results of E.C.Yenigun et al^[22] and Tschöpe et al,^[24] this difference was not statistically meaningful. In the diabetic group a negative linear relationship between MPV and the number of platelets was seen ($p=0.018$). Decreased count could be the result of small platelets being consumed in order to maintain a constant platelet functional mass.^[25] Association of increased platelet volume and reduced platelet survival in diabetic patients has been reported by Jones et al.^[26]

Lipid abnormalities significantly contribute to the increased risk of cardiovascular disease and other morbidity in diabetics. In this study the level of total cholesterol, TG, were increased in diabetics as compared to controls and also significantly higher in diabetics with HbA1c $\geq 6.5\%$. Increased total cholesterol, TG and LDL in diabetics was reported by Farah Jabeen et al^[27] and Vijaya C et al.^[28] Kamilla R Alhadas^[29] found higher levels of Triglycerides only in diabetics as compared to controls. Within the diabetic group higher cholesterol was reported by Dindar et al^[16] while Kadic et al^[30] found significantly higher TG in diabetics with poor glycemic control(HbA1c $> 7\%$). These findings are in accordance with the present study. Diabetes mellitus is a complex disease where the carbohydrate, protein and fat metabolism are impaired.^[31] Insulin stimulates synthesis of fatty acid in liver, adipose tissue and in the intestine and synthesis of cholesterol.^[32] In diabetes mellitus abnormal increased levels of lipid, lipoprotein and lipid peroxides in plasma may be due to the abnormal lipid metabolism.^[33] Poor glycemic control associated with abnormal lipid profile can hasten the development of vascular complications.

Micro and macrovascular complications are often seen in DM and represent the main causes of morbidity and

mortality, which are closely associated with glycaemic control.^[34] Mean platelet volume is usually established to associate with macrovascular complications such as myocardial infarction and restenosis after percutaneous coronary intervention.^[25]

Many studies^[16,22] have shown association between higher MPV and vascular complications. This underlines the fact that MPV can be used as a parameter to assess platelet function and activity and can provide an indication to the development of complications. Considering that odds of inadequate glycemic control are 2 times increased per femtoliter greater MPV, its use, especially in the primary health care centers, could improve the screening of high-risk individuals for vascular complications. Early diagnosis and appropriate treatment could thereby delay their onset or progression.^[30] Several measurements of platelet activity have emerged as potential contributors to atherothrombosis. Many of the parameters are time-consuming, expensive, use a high sample volume, or require specialty training.^[35,36] MPV is an easily available, economical, clinical marker of platelet reactivity done by routine automated hemograms.

A small sample size and subjects were known diabetics on treatment may be the two limitations of this study. This study could not establish a causal relationship between MPV and vascular complications in diabetes but it supports a link between platelet activity, glucometabolic state and glycemic control.

Conclusion

This study shows significantly high MPV in diabetics as compared to controls thus establishing that MPV is strongly and independently associated with diabetes. Glycemic control plays a role in the reactivity of platelets and thus MPV can be used as a simple cost effective tool for monitoring diabetic patients.

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Competing Interests

None Declared

Reference

1. Bishop ML, Duben-Engelkrik JL, Fody EP. Clinical Chemistry: Principles, Procedures, Correlations. 4th edition. Lippincott Williams and Wilkins: Philadelphia, London, New York, Tokyo, Hong Kong, 2000; 220.
2. UK Prospective Diabetes Study Group (UKPDS): Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet*. 1998; 352:837–853.
3. Vizioli L, Muscari S, Muscari A: The relationship of mean platelet volume with the risk and prognosis of cardiovascular diseases. *Int J Clin Pract*. 2009; 63:1509–1515.
4. Tschoepe D, Roesen P, Schwippert B, Gries FA. "Platelets in diabetes: the role in the hemostatic regulation in atherosclerosis," *Seminars in Thrombosis and Hemostasis*. 1993; 19: 122–128.
5. Khuwaja AK, Rafique G, White F, Azam SI. Macrovascular complications and their associated factors among persons with type 2 diabetes in Karachi, Pakistan--a multi-center study. *J Pak Med Assoc*. 2004; 54:60-6.
6. Tufano A, Cimino E, Di Minno M.N.D, et al. "Diabetes Mellitus and Cardiovascular Prevention: The Role and the Limitations of Currently Available Antiplatelet Drugs." *International Journal of Vascular Medicine*. vol. 2011; Article ID 250518: 1-5.
7. King H, Aubert RE, Herma WH. Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. *Diabetes Care* 1998; 21:1414-31.
8. Hekimsoy Z, Payzin B, Ornek T, Kandoğan G. Mean platelet volume in Type 2 diabetic patients. *J Diabetes Complications* 2004; 18:173-6.
9. 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: 114-116
10. Kodiatte TA, Manikyam UK, Rao SB, Jagadish TM, Reddy M, Lingaiah HK and Lakshmaiah V. Mean platelet volume in Type 2 diabetes mellitus. *J Lab Physicians* 2012; 4: 5-9.
11. Ulutas KT, Dokuyucu R, Sefil F, Yengil E et al. Evaluation of mean platelet volume in patients with type 2 diabetes mellitus and blood glucose regulation: a marker for atherosclerosis?. *Int J Clin Exp Med* 2014;7(4):955-961
12. Gasparyan AY, Ayvazyan L, Mikhailidis DP, Kitas GD. Mean platelet volume: a link between thrombosis and inflammation? *Curr Pharm Des* 2011; 17:47-58.

13. Bath PM, Butterworth RJ. Platelet size: measurement, physiology and vascular disease. *Blood Coagul Fibrinolysis* 1996; 7:157-61.
14. Randriamboavonjy V, Fleming I. Platelet function and signaling in diabetes mellitus. *Curr Vasc Pharmacol* 2012; 10:532-8.
15. Jokl R, A. CJ. Arterial thrombosis and atherosclerosis in diabetes. *Diabetes Metab Rev* 1997; 5:1-15.
16. Dindar S, Cinemre H, Sengul E, Annakkaya AN. Mean Platelet volume is associated with glycemic control and retinopathy in patients with type 2 diabetes mellitus. *West Indian Med J* 2013; 62(6): 519-523.
17. Demirtunc R, Duman D, Basar M, Bilgi M, Teomete M, Garip T. The relationship between glycemic control and platelet activity in type 2 diabetes mellitus. *J Diabetes Complications* 2009; 23:89-94.
18. Ozder A, Eker HH. Investigation of mean platelet volume in patients with type 2 diabetes mellitus and in subjects with impaired fasting glucose: a cost-effective tool in primary health care? *Int J Clin Exp Med* 2014; 7:2292-7.
19. Sharpe PC, Trinick T. Mean platelet volume in diabetes mellitus. *Q J Med* 1993; 86: 739-42.
20. Cakir L, Aktas G, Enginyurt O, Cakir SA. Mean Platelet volume increases in type 2 diabetes mellitus independent of HbA1c level. *Acta Medica Mediterranea* 2014; 30: 425-428.
21. Unubol M, Ayhan M, Guney E. The relationship between mean platelet volume with microalbuminuria and glycemic control in patients with type II diabetes mellitus. *Platelets* 2012; 23: 475-80.
22. Yenigün EC, Okyay GU, Pirpir A, Hondur A, Yıldırım IS. Increased mean platelet volume in type 2 diabetes mellitus. *Dicle Medical Journal*. 2014; 41 (1): 17-22
23. Kim JH, Kang SB, Kang JI, Kim JW, Kim SY, Bae HY. The relationship between mean platelet volume and fasting plasma glucose differs with glucose tolerance status in a Korean general population: gender differences. *Platelets* 2013; 24: 469-73.
24. Tschöpe D, Langer E, Schauseil S. Increased platelet volume- sign of impaired thrombopoiesis in diabetes mellitus. *Klin Wochenschr* 1989; 67: 253-259.
25. Chu SG, Becker RC, Berger PB, et al. Mean platelet volume as a predictor of cardiovascular risk: a systematic review and meta-analysis. *J Thromb Haemost* 2010; 8: 148-156.
26. Jones R L, Paradise C, Peterson C M. Platelet survival in patients with diabetes mellitus. *Diabetes* 1981;30:486-489.
27. Jabeen F, Rizvi HA, Aziz F, Akhtar Y. Effect of Glycemic Control on Lipid Profile, Platelet Indices and Antioxidant Enzymes (Catalase and Superoxide dismutase) Activities in Type 2 Diabetics. *International Journal of Advanced Research* 2013; 1: 207-215.
28. Vijaya C, Shetty A, Parikshith. Comparative Study of Significance of Lipid Profile, Platelet Count and MPV- Diabetics and Non-Diabetics. *Sch. J. App. Med. Sci.* 2014; 2(5B):1584-1588
29. Alhadas KR, Santos SN, S. Freitas MM, Viana SMAA, Ribeiro LC, Mônica B. Costa MB. Are platelet indices useful in the evaluation of type 2 diabetic patients? *Bras Patol Med Lab*, April 2016 ;52(2): 96-102.
30. Kadić D, Hasić S, Spahić E. Mean platelet volume predicts the glycemic control deterioration in diabetes mellitus type 2 patients. *Medicinski Glasnik* 2016; 13(1): 1-7.
31. Altamer E, Vendemisle G, Chicco D; Increased lipid peroxidation in Type-II poorly control Diabetic patients. *Diabetes Etab.*, 1991; 18(4):264-671.
32. Jain AP, Gupta DP; Study of blood lipids in Diabetics without any manifest vascular complications. *J Dia Asso Ind.*, 1980; 20: 29-34.
33. Suckling KE., Brian J; Animal Models of Human lipid Metabolism. *Prog Lipid Res.*1993; 32(1): 124-124.
34. Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ* 2000; 321: 405-12.
35. Michelson AD; Methods for the measurement of platelet function. *Am J Cardiol.*, 2009;103(3Suppl.): 20A-26A.
36. Nicholson NS, Panzer-Knodle SG, Haas NF, Taite BB, Szalony JA, Page JD et al.; Assessment of platelet function assays. *Am Heart J.*, 1998;135(5 Pt 2 Su):S170-S178.