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ORIGINAL RESEARCH

Mean Platelet Volume and Platelet Distribution Width as Markers of Vascular Thrombosis in Type 2 Diabetes Mellitus

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ABSTRACT

Aims: The objective of the study was to determine the mean platelet volume (MPV) and platelet distribution width (PDW) in subjects with type 2 diabetes mellitus (type 2 DM) compared to subjects without type 2 DM and their correlation with fasting blood glucose, glycosylated hemoglobin (HbA1c), and duration of type 2 DM respectively.

Materials and methods: A prospective analytical case–control study was conducted involving 50 subjects with type 2 DM and 50 subjects without type 2 DM. The mean and standard deviation were estimated for both the groups separately and independent Student's "t"-test was used for evaluating the significant difference. The statistical evaluation was carried out at 95% confidence level.

Results: Mean MPV and PDW in case group was significantly higher compared to control group ($p < 0.005$). Fasting blood glucose, HbA1c, and duration of type 2 DM did not significantly alter MPV or PDW.

Conclusion: The study concludes that MPV and PDW are significantly increased in patients with type 2 DM compared to patients without type 2 DM. Platelet volume indices are an important, simple, and cost-effective tool that should be used and explored extensively, especially in countries, such as India, for predicting the possibility of impending acute vascular events in patients with type 2 DM.

Clinical significance: This analytical method helps us to use MPV and PDW as early markers of vascular thrombosis.

Keywords: Case–control study, Mean platelet volume, Platelet distribution width, Type 2 diabetes mellitus, Vascular thrombosis.

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INTRODUCTION

Platelets play an important role in the integrity of normal homeostasis, and mean platelet volume (MPV) is the indication for its function.[1] The larger platelets contain more dense granules, produce more thromboxane A2, platelet factor A, and beta-thromboglobulin, and hence are more potent than the smaller platelets and more thrombogenic. Both the size and number of granules in platelets in circulation are under independent hormonal control and do not change during the lifespan of the platelet.[2-4]

Platelet volume indices are an important, simple, effortless, and cost-effective tool that should be used and explored extensively, for predicting the possibility of impending acute events in patients with type 2 diabetes mellitus (DM).[5] A large proportion of patients with type 2 DM suffer from preventable macrovascular complications, so there is a need to develop risk factor modification intervention to reduce the impact of these long-term complications.[6] It has been shown in previous studies that patients with type 2 DM have larger platelets which are more thrombogenic and can lead to macro- and microvascular complications. Moreover, patients with larger platelets can be easily identified during routine hematological analysis and could possibly benefit from preventive treatment and hence was the need for this study.[7]

Mean platelet volume is a determinant of platelet function and is a newly emerging risk factor for atherothrombosis. Many studies have shown that increased MPV is one of the risk factors for myocardial infarction, cerebral ischemia, and transient ischemic attacks. Elevated MPV is associated with a worse outcome for acute ischemic cerebrovascular events independent of other clinical parameter.[8-11] Altered platelet morphology and function have been reported in patients with type 2 DM. They are likely to be associated with the pathological processes and increased risk of vascular disease seen in these patients.[12]

MATERIALS AND METHODS

Study Design

This was a prospective analytical case–control study.

Inclusion Criteria

- Patients having fasting glucose level > 126 mg/dL were considered as cases.
- Patients having fasting glucose level < 110 mg/dL were considered as controls.

Exclusion Criteria

- Patients suffering from following diseases were excluded:
  - Idiopathic thrombocytopenic purpura
  - Acute post streptococcal glomerulonephritis
  - Renal failure
  - Myocardial infarction, ischemic heart disease, and cerebrovascular accident
  - Hypertension
- Patients on antiplatelet drugs

Source of Data

- Patients attending the outpatient medicine department
- Inpatients admitted to the medicine units.

Method of Collection of Data

Data for the purpose of this study was collected on a pre-tested proforma, meeting the requirements of this study. The 50 cases and 50 controls were selected on the basis of simple random sampling technique. The size of the sample was selected on the basis of the suitable formula of sampling. All the investigations were done in the clinical biochemistry and pathology laboratory in the hospital. The analyzer used to find out serum sodium levels was AVL 9180 electrolyte analyzer, made in USA, and the reagent used was SnapPack. Samples for platelet volume indices was collected using ethylenediaminetriacetic acid (EDTA) as anticoagulant and were processed on a Sysmex auto analyzer.

Statistical Analysis

All the statistical methods were carried out through the Statistical Package for the Social Sciences (SPSS) software for windows (version 16.0). The mean and standard deviation (SD) were estimated for both the groups separately, and independent Student's t-test was used for evaluating the significant difference. The statistical evaluation was carried out at 95% confidence level. In addition, the differences in factors, such as duration of type 2 DM, glycosylated hemoglobin (HbA1c), and fasting blood glucose (FBG) were also evaluated between the groups by product moment correlation.

RESULTS

The present study was conducted over a period of 2 years. During this study period, 100 patients were taken into the study, out of which 50 were controls and 50 were cases. Of the total 100 subjects, 72 were males and 28 were females. Gender distribution was similar in both the groups. Of these 100 cases, 30 (30%) cases were in the age group of 41 to 50 years. This group constitutes the maximum number of cases (Table 1).

Mean platelet volume in type 2 DM subjects was 9.372 (SD 0.677) fl, whereas in controls it was 8.634 (SD 0.778) fl. Mean PDW in our study in type 2 DM subjects was 12.19 (SD 1.19), whereas in controls it was 11.27 (SD 1.06) (Table 1). Mean platelet volume was significantly higher in type 2 DM compared to controls, p-value being 0.000 ($p < 0.005$) and 95% CI of –0.98 to –0.44. Platelet distribution width was significantly higher in cases compared to controls, p-value being 0.000 ($p < 0.005$) and 95% CI of –1.37 to –0.471 (Table 2).

As shown in Table 3, the mean platelet count in the case group was 2.81 lakh/mm^3 (SD 0.92), whereas in controls it was 2.59 (SD 0.71). There was no significant difference between platelet counts in type 2 DM subjects compared to controls, p-value being 0.143 ($p > 0.005$) (Table 4). Mean

Table 1: Comparison of MPV and PDW between cases and controls

	Groups	*n*	*Mean*	*Std. deviation*	*Std. error mean*
MPV	DM	50	9.3720	0.67794	0.09588
	Control	50	8.6340	0.77817	0.11005
PDW	DM	50	12.1920	1.19878	0.16953
	Control	50	11.2700	1.06986	0.15130

Table 2: Significance of MPV and PDW in cases and controls

	Groups	*n*	*Mean*	*Std. deviation*	*Std. error mean*
Platelet count	DM	50	2.8130	0.92429	0.13071
	Control	50	2.5694	0.71280	0.10080

Table 3: Platelet count in cases and controls

		t-test for equality of means			
		t	*df*	*Sig. (two-tailed)*	*Mean difference*
MPV	Equal variances assumed	5.056	98	0.000	0.7380
PDW	Equal variances assumed	4.058	98	0.000	0.9220

Table 4: Platelet count significance in cases and controls

		t-test for equality of means			
		t	*df*	*Sig. (two-tailed)*	*Mean difference*
Platelet count	Equal variances assumed	1.476	98	0.143	0.2436

Table 5: Comparison of MPV, PDW with the duration of type 2 DM, FBG, and HbA1c in cases and controls

		Duration of Diabetes	*MPV*	*PDW*	*HbA1C*	*FBG*
Duration of diabetes	Pearson correlation	1	0.086	0.183	0.005	0.073
	Significance	–	0.553	0.204	0.972	0.613
	n	50	50	50	50	50
MPV	Pearson correlation	0.086	1	0.655**	0.076	0.115
	Significance	0.553	–	0.000	0.598	0.427
	n	50	50	50	50	50
PDW	Pearson correlation	0.183	0.655**	1	0.202	0.309*
	Significance	0.204	0.000	–	0.160	0.029
	n	50	50	50	50	50
HbA1c	Pearson correlation	0.005	0.076	0.202	1	0.378**
	Significance	0.972	0.598	0.160	–	0.007
	n	50	50	50	50	50
FBG	Pearson correlation	0.073	0.115	0.309*	0.378**	1
	Significance	0.613	0.427	0.029	0.007	–
	n	50	50	50	50	50

*Correlation is significant at the 0.05 level (two-tailed); **Correlation is significant at the 0.01 level (two-tailed)

platelet volume was not linearly correlated with the duration of type 2 DM as the correlation coefficient was 0.086 and p-value being 0.553. Similarly, PDW was also not correlated with the duration of type 2 DM, coefficient being 0.183 and p-value 0.204 (Table 5).

DISCUSSION

Several studies indicate that high MPV levels and high platelet reactivity are associated with overall vascular mortality, including myocardial infarction.[13-16] Mean MPV in the case group was 9.372 (SD 0.677) fl, whereas in controls it was 8.634 (SD 0.778) fl. Mean platelet volume was significantly higher in type 2 DM subjects compared to controls, p-value being 0.000 ($p < 0.005$) and 95% CI of –0.98 to –0.44. In Papanas et al[12] study, MPV in case group was 14.1 (SD 2.1) fl, whereas in controls it was 7.1 (SD 1.2) fl, which was significant. In Demirtunc et al[17] study, MPV was significantly higher in patients with type 2 DM than in controls [8.7 (SD 0.8) fl *vs* 8.2 (SD 0.7) fl, $p = 0.002$]. In Hekimsoy et al[18] study, MPV was significantly higher and the mean platelet counts were significantly lower in case group compared to age and sex-matched healthy controls [10.62 (S.D 1.71) fl *vs* 9.15 (SD 0.86) fl ($p = 0.00$)].

Mean PDW in our study in case group was 12.19 (SD 1.19), whereas in controls it was 11.27 (SD 1.06). Platelet distribution width was significantly higher in cases compared to controls, p-value being 0.000 ($p < 0.005$) and 95% CI of –1.37 to –0.471. Most of the studies conducted previously have compared MPV in patients with and without type 2 DM, but in our study, we compared both MPV and PDW as a measure of platelet activity. The latter was also significantly higher in patients with type 2 DM which was in accordance with the study done by Jindal et al,[19] which concluded that PDW are different between cases and controls as well as between type 2 DM patients with and without microvascular complications. In this study, we have shown a significant increase in MPV between control and case groups, while there was no significant change in platelet counts. This was in agreement with other studies that have also reported the increase in MPV in type 2 DM patients in comparison to patients without type 2 DM.[20]

Comparison of Platelet Count in Cases and Controls

In this study, mean platelet count in cases was 2.81 lakh/mm^3 (SD 0.92), whereas in controls it was 2.59 lakh/mm^3 (SD 0.71). We found no significant difference between platelet counts in cases compared to controls, p-value being 0.143 ($p > 0.005$). This is in accordance with the study by Zuberi et al[21] in which also, no significant difference was found between platelet counts in patients with and without type 2 DM. Mean platelet counts were 2.3 and 2.1 in cases and controls respectively. But, Hekimsoy et al[18] in their study also concluded that mean platelet counts were significantly lower in type 2 DM patients compared to age and sex-matched healthy controls [260.38±68.65 × 10(9)/l *vs* 292.33±79.19 × 10(9)/l ($p = 0.001$)] respectively, which was in contrast to our study and Zuberi et al[21] study, which showed no significant difference in mean platelet counts between the groups.

Comparison of Duration of Type 2 DM, FBG, and HbA1c in Cases with Controls

Mean platelet volume was not linearly correlated with duration of type 2 DM, as the correlation coefficient was 0.086 and p-value was 0.553. Similarly, PDW was also not correlated with duration of type 2 DM, coefficient

being 0.183 and p-value 0.204. There was no correlation of HbA1c with MPV and PDW, as the correlation coefficient was 0.076 for MPV and 0.202 for PDW, and p-value was 0.598 and 0.160 respectively. Similarly, no correlation could be found between FBG with MPV and PDW. Correlation coefficient for MPV and PDW was 0.115 and 0.272; p-value was 0.272 and 0.052 respectively.

In our study, no correlation could be found between MPV and HbA1c which was in contrast to the study by Demirtunc et al,[17] in which there was a significant positive correlation between MPV and HbA1c levels ($r = 0.39$, $p = 0.001$). In this study, we have shown a significant increase in MPV from the control group to case group, while there was no significant change in platelet counts in the same samples of blood. This was in agreement with other studies that have also reported the increase in MPV in type 2 DM patients in comparison with healthy controls.[22,23] It has been shown that the platelets in type 2 DM patients are hyperactive.[24]

The issue is still unresolved as to whether it is the primary hyperactivity of platelets or secondary hyperactivity of platelets due to the continuous low-grade exposure to the damaged microvascular bed. Platelet hyperactivity results in increase in MPV, and vice versa.[4,25] Increase in MPV is now emerging as an independent risk factor for thromboembolism, stroke, and myocardial infarction.[5,8,9,26] Type 2 DM patients are known to have higher incidence of stroke and myocardial infarction.[27] Presence of high MPV in these patients was an important finding that could increase the risk of thrombotic complications. It has also been shown that among type 2 DM patients, those with retinopathy and other complications have higher MPV values than those who do not have this complication.[12] Increased MPV has also been documented in gestational DM,[28] congestive cardiac failure,[29] and coronary artery ectasia.[30] Thereby, we conclude that MPV and PDW are significantly increased in patients with type 2 DM and hence can be used as a diagnostic tool.

CONCLUSION

The study concludes that MPV and PDW are significantly increased in patients with type 2 DM compared to controls. However, no association was found between MPV or PDW and duration of type 2 DM, HbA1c, and FBG. This suggests that platelets may play a role in the micro- and macrovascular complications of type 2 DM patients.

CLINICAL SIGNIFICANCE

Elevated MPV and PDW can be used as markers of an impending vascular thrombosis in patients with type 2 DM. These tests can be done easily and are the most economical; hence it can be a boon in developing countries. However, further larger studies are needed to clarify cut offs of MPV and PDW, which reliably and strongly predicts possible vascular thrombosis, so that the most appropriate, timely, and necessary measures can be initiated at the earliest.

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