Thrombocytic Trends: Investigating Mean Platelet Volume in Type 2 Diabetes Mellitus.

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Abstract

Introduction: Platelet activity is a crucial factor in the pathogenesis of vascular complications in diabetes. Mean platelet volume (MPV) has been proposed as a marker of platelet reactivity and is associated with various vascular risk factors. This study aimed to investigate the association between MPV and glycemic control as indicated by HbA1c levels and the role of MPV as a predictor of vascular complications in diabetic patients.

Methods: A cross-sectional analysis was conducted on 100 diabetic patients and 100 non-diabetic controls. Diabetic patients were stratified into two groups: HbA1c <6.5% and HbA1c ≥6.5%. MPV and platelet count was measured for all participants using an automated blood cell counter. Statistical analysis was performed by using SPSS using Student's t test and Pearson correlation test.

Results: MPV was significantly higher in diabetics than non-diabetics (13.41±0.44 fl vs 12.29±0.0.53 fl: p=0.0001) as well as in diabetics with HbA1c ≥6.5% than those with HbA1c <6.5% (13.65±0.44 fl vs 12.93±1.79fl; p<0.0068). However, the mean platelet count did not show a statistically significant difference between diabetics and non- diabetics as well as the two HbA1c groups. Diabetics with vascular complications exhibited significantly higher MPV (13.6±0.47 fl) compared to those without vascular complications (13.21±0.32 fl; p<0.0001) .

Conclusion: Our study suggests a significant association between glycemic control, MPV and vascular complications in diabetic patients. These findings underscore the importance of maintaining glycemic control to mitigate platelet hyperactivity as well as the role of MPV as a predictor of diabetes-related vascular complications.

Keywords: Diabetes, Mean Platelet Volume, Glycemic Control, Vascular Complications, HbA1c

Introduction

Diabetes Mellitus (DM) is a widespread metabolic disorder characterized by chronic hyperglycemia due to insulin secretion or action defects [1]. It affects an estimated 422 million people globally, with Type 2 Diabetes Mellitus accounting for nearly 80% of all cases [2, 3]. In 2016, diabetes directly caused 1.6 million deaths and indirectly contributed to 2.2 million more.4 The World Health Organization predicts that diabetes will be the leading cause of death by 2030. India had approximately 72 million cases in 2017, earning it the title of "Diabetic capital" of the world [4].

Platelets, small discoid blood cells involved in hemostasis, play a crucial role in the development of advanced atherosclerosis [5]. Diabetic patients face an increased risk of microvascular and macrovascular complications due to accelerated atherosclerosis [6]. This risk is independent of and additive to other factors such as hypertension, albuminuria, obesity, cigarette smoking, and dyslipidemia. Platelet activity in diabetes contributes significantly to the development of vascular complications [7, 8].

Mean platelet volume (MPV), a marker of platelet function and activation, is higher in diabetic patients and is associated with increased secretion of pro-coagulant substances, leading to thrombotic vascular complications [9-12]. High MPV is an emerging risk factor for vascular complications in diabetes, particularly in atherosclerosis-related conditions. Therefore, platelet count and MPV are simple, effective, and cost-efficient tests that can predict angiopathy in Type 2 DM [10-12].

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Our study aims to investigate the activation of platelets by measuring MPV in diabetic patients with vascular complications, compare MPV between diabetic patients with and without vascular complications, assess the correlation of MPV with FBS, PPBS, HbA1c, BMI, and duration of diabetes, and compare MPV between diabetics with HbA1c <6.5% and those with HbA1c ≥ 6.5%.

Materials and Method

The study was conducted at the Department of Pathology, Assam Medical College and Hospital, over a one-year period from June 1, 2018, to May 31, 2019. It was a hospital-based comparative cross-sectional study aiming to collect data from 100 type 2 diabetic patients attending the Diabetic clinic and 100 non-diabetic controls attending different OPDs of Assam Medical College and Hospital. The sample size was determined based on a previous study. The selection criteria for cases included diabetes mellitus patients attending the Diabetic clinic, and all consenting non-diabetic adults attending different OPDs in the hospital. Exclusion criteria for controls included specific medical conditions and medication use, while exclusion criteria for cases included certain hemoglobin levels.

Data collected was presented as percentages and mean ± SD. Statistical significance was tested using t-test, chi-square, and Fisher's exact test, with p-values and r values calculated. Diagrams were used to represent the data. All analyses were performed using SPSS (statistical package for social sciences), version 16.0. A p-value of <0.05 was considered statistically significant.

Laboratory analysis involved measuring hemoglobin, platelet count, and mean platelet volume (MPV) using the Sysmex–XN–550, a six-part auto analyzer. The principle of working of the autoanalyzer was based on electronic impedance, flow cytometry method, and SLS-hemoglobin method.

Platelet count (PLT) and Plateletcrit (Pct) were measured within standard ranges. MPV was calculated using the equation MPV (fl) = Pct (%) X 100 / PLT (X104/ µL), with a standard range of 6.8-10 femtolitre (fl). Flow cytometry method using a semiconductor laser was used to analyse cells and other biological particles as they pass through extremely small flow cells, providing information on blood cell size, interior, and labelling.

Results and Observation

The study comprised 100 type 2 diabetes mellitus patients and 100 non-diabetic controls meeting the inclusion criteria. The mean age of the diabetic patients was 50.66±11 years, while that of the controls was 45±21.54 years. There was a male predominance in both groups, with 67 males and 33 females in the diabetic population and 58 males and 42 females in the non-diabetic population. The difference in BMI between the cases (24.18±4.19 kg/m2) and controls (23.65±2.82 kg/m2) was not statistically significant (p=0.265). The mean duration of diabetes was 4.63±3.26 years.

Systolic blood pressure was significantly higher in the diabetic group (133.04±17.20 mmHg) compared to the non-diabetic group (124.10±8.85 mmHg; p=0.0001). Similarly, there was a statistically significant difference in diastolic blood pressure between the diabetics (83.90±10.07 mmHg) and the non-diabetics (78.42±5.41 mmHg; p=0.0001).

The mean platelet count in the diabetic group (2.18±0.50×10^9/L) was slightly lower than in the non-diabetic group (2.20±0.53×10^9/L), but the difference was not statistically significant (p=0.823). However, the mean platelet volume in the diabetic group was significantly higher (13.41±0.44 fl) than in the non-diabetic group (12.29±0.53 fl), with a p-value of 0.0001.

The study also revealed significant differences in mean FBS levels between the diabetics and non-diabetics (166.03±54.32 mg/dl and 86.33±7.36 mg/dl, respectively, p=0.0001). Similarly, the mean PPBS levels were significantly different between the cases and controls (287.78±88.72 mg/dl and 110.46±20.14 mg/dl, respectively, p=0.0001). The difference in mean HbA1c levels between the two groups was also significant (6.95±1.88% and 5.05±0.50%, p=0.0001) Table 1.

Among the diabetic cases, a positive statistical Pearson correlation was seen between MPV and duration of diabetes (r=0.583; p=0.0001), BMI (r=0.240; p=0.016), HbA1c levels (r=0.649; p=0.0001), FBS levels (r=0.438; p=0.0001) and PPBS levels (r=0.488; p=0.0001).

In this study, a cohort of 100 patients with diabetes mellitus (DM) was stratified based on their HbA1c levels into two groups: Group A (HbA1c<6.%) and Group B (HbA1c≥ 6.5%). Group A consisted of 49 patients with a mean HbA1c of 5.55±0.80%, while Group B comprised 51 patients with a mean HbA1c of 8.33±1.76%.

The mean body mass index (BMI) in Group A was 23.55±5.25 kg/m2, slightly lower than that of Group B at 24.44±3.84 kg/m2, although this difference was not found to be statistically significant (p=0.3347). However, the mean fasting blood sugar (FBS) level in Group A was 138.74±23.80 mg/dl, significantly lower than the mean FBS level in Group B, which was 192.71±64.88 mg/dl (p<0.0001). Similarly, the postprandial blood sugar (PPBS) levels in Group A (245.99±47.92 mg/dl) were significantly lower than those in Group B (328.06±105.23 mg/dl) (p<0.0001).

The mean platelet count in Group A was 2.17±0.57 ×109/L, slightly higher than that in Group B at 2.16±0.48×109/L, but this difference was not statistically significant. However, the mean platelet volume (MPV) level in Group A (12.93±1.79 fl) was significantly lower than that in Group B (13.65±0.44 fl; p<0.0068) Table 2.

In individuals with diabetes, the mean platelet count in those with vascular complications (2.13±0.42 ×10^9 / L) was observed to be slightly lower than that of individuals without vascular complications (2.24±0.57×10^9 / L), although this disparity did not reach statistical significance (p=0.2746). Conversely, the mean platelet volume (MPV) in subjects with vascular complications (13.6±0.47 fl) was found to be significantly higher than that of subjects without vascular complications (13.21±0.32 fl) (p=0.0001) Table 3.

Table1. *Parameters in Diabetic and Non-diabetic subjects.*

Characteristic	Diabetics	Non-diabetics	p-value
Mean age (years)	50.66±11	45±21.54	-
Male (%)	67	58	-
Female (%)	33	42	-
Mean duration of diabetes (years)	4.6 ± 3.26	-	-
Systolic BP (mm Hg)	133.04±17.20	124.10± 8.85	0.0001
Diastolic BP (mm Hg)	83.90± 10.07	78.42± 5.41	0.0001
Body mass index (kg/m2)	24.18±4.19	23.65±2.82	0.265
FBS (mg/dl)	166.03±54.32	86.33±7.36	0.0001
PPBS (mg/dl)	287.78±88.72	110.46±20.14	0.0001
HbA1c (%)	6.95±1.88	5.05±0.50	0.0001
Platelets (×109/L)	2.18±0.50	2.20±0.53	0.823
MPV(fl)	13.41±0.44	12.29±0.53	0.0001

Table 2. *Comparison of diabetic study population between Group A and Group B.*

	Group A (HbA1c <6.5%)	Group B (HbA1c ≥6.5)	p-value
BMI (kg/m2)	23.55±5.25	24.44±3.84	0.3347
FBS (mg/dl)	138.74±23.80	192.71±64.88	<0.0001
PPBS (mg/dl)	245.99±47.92	328.06±105.23	<0.0001
HbA1c (%)	5.55±0.80	8.33±1.76	<0.0001
Platelet Count (X10^9/ L)	2.17±0.57	2.16±0.48	0.88
MPV(fl)	12.93±1.79	13.65±0.44	<0.0068

Table 3. *MPV and platelet count in diabetics with and without vascular complications.*

	Diabetics with vascular complications	Diabetics without vascular complications	p-value
MPV Mean±SD (fl)	13.6±0.47	13.21±0.32	0.0001
PC Mean±SD (X 109/L)	2.13±0.42	2.24±0.57	0.2746

Furthermore, among individuals with diabetic vascular complications, those with diabetic nephropathy and hypertension exhibited higher MPV levels (13.96±0.45fl and 13.78±0.45fl) compared to individuals with retinopathy, and peripheral vascular disease (PVD)(13.71±0.54fl and 13.56±0.43fl).

Discussion

The present study is a comparative cross-sectional analysis conducted at the Assam Medical College and Hospital, encompassing 100 type 2 diabetes patients attending the diabetic outpatient department (OPD) and 100 non-diabetic controls visiting various other OPDs from June 1st, 2018 to May 31st, 2019. All participants met the specified inclusion and exclusion criteria.

The primary objective of this study was to investigate platelet activation in diabetic patients and those with diabetic vascular complications by assessing mean platelet volume (MPV). Additionally, the study aimed to discern differences in MPV among diabetic patients with and without vascular complications, establish correlations between MPV and fasting blood sugar (FBS), postprandial blood sugar (PPBS), glycosylated hemoglobin (HbA1c), body mass index (BMI), and duration of diabetes in diabetic patients, and compare the MPV of diabetics with HbA1c <6.5% to that of diabetics with HbA1c ≥6.5%.

Regarding the age and sex distribution, the mean age of diabetic patients was 50.66±11 years, while that of the controls was 45±21.54 years. The majority of cases and controls fell within the 41-50 years age group. This aligns with previous studies, which also observed a higher prevalence of diabetes in individuals over 40 years of age, likely due to delayed symptom recognition and reluctance to seek medical assistance. In our study, 67% of diabetic patients were male, consistent with the higher male ratio observed in other investigations.

In terms of mean platelet count, our study found a mean platelet count of 2.18±0.50 ×10^9/L in the diabetic group, slightly lower than that in the non-diabetic group (2.20±0.53 ×10^9/L), although this difference was not statistically significant (p=0.823). These findings contrast with some previous studies, which reported significantly lower platelet counts in diabetic individuals compared to non-diabetic controls, while others reported higher platelet counts in diabetic groups. These discrepancies may be attributed to variations in platelet survival, production rate, and turnover rate in diabetes mellitus Table 4.

In our study, the mean platelet volume (MPV) in diabetic individuals was found to be 13.41±0.44fl, which was significantly higher than that of non-diabetic individuals at 12.29±0.44fl (p=0.0001). Similar findings of elevated MPV in diabetics were reported in studies by [10]. (10.62±1.71fl and 9.15±0.86fl) and [18]. (9.34fl and 8.63fl). Conversely [19] reported significantly lower MPV in diabetics compared to non-diabetics (8.29±0.735fl and 7.47±0.76fl; p<0.001). [20] Found lower MPV in diabetics compared to non-diabetics, although not statistically significant (8.69±0.67fl and

Table 4. *Mean platelet count in Diabetic and Non- Diabetic Groups.*

Studies	Mean Platelet count (diabetics) (x 103/µL)	Mean Platelet Count (non diabetics)	p- value
Hekimsoy et al[10]	260.38± 68.65	292.33±79.19	P=0.001
Yenigün et al[13]	2490.729±73.479	279.466±73.294	P=0.10
Jindal Set al[14]	229.33 ±70.27	229.52±65.80	P=0.99
Kshirsagar et al[15]	293±100	305±76	P=0.469
Walinjkar et al[16]	268.92±92.22	271.73±92.58	P=0.81
Ramasundari IM[17]	260 ±0.85	277 ±0.97	P=0.207
Zuberi et al[18]	230.42	210.04	-
Kodiatte et al[19]	277.46±81.13	269.79±70	P=0.256
Akinbami A et al[20]	235.29 ±76.81	211.32±66.44	-
Our study	218 ±50	220±53	P=0.823

8.91±0.80fl; p=0.593), potentially influenced by antiplatelet medication use in the majority of their diabetic cohort.

Our study also revealed higher MPV levels in both diabetic and non-diabetic individuals compared to findings in other populations, as observed in a study of the north-east Indian population. The variations in MPV values across studies may be attributed to factors beyond platelet reactivity alone, necessitating further investigation to elucidate potential underlying mechanisms.

Regarding mean platelet count in diabetes with and without vascular complications, our study found that the mean platelet count in diabetics with vascular complications (2.13±0.42 ×10^9/L) was slightly lower than that of diabetics without vascular complications (2.24±0.57 ×10^9/L), although this difference was not statistically significant (p=0.2746). Similar non-significant differences were reported by [17] and [15], while [21]. observed a statistically significant difference in platelet count between diabetics with and without vascular complications.

In the context of mean platelet volume in diabetes with and without vascular complications, our study revealed significantly higher MPV in diabetics with vascular complications (13.6±0.47fl) compared to those without complications (13.21±0.32fl; p=0.0001). This trend was also observed in studies by [22, 23, 16] and [17], among others. The increased platelet size observed in diabetics with vascular complications may contribute to the heightened risk of atherosclerosis associated with diabetes and its vascular complications.

The observed discrepancies in MPV values across studies may be attributed to the rapid consumption of activated platelets in diabetics with complications, suggesting the need for further exploration of the underlying pathophysiological mechanisms.

In our study, diabetics with HbA1c <6.5% had a mean platelet count of 2.17±0.57 ×109/L, slightly higher than those with HbA1c≥6.5% at 2.16±0.48 ×109/L, but the difference was not statistically significant (p=0.8800). Similar non-significant differences were observed by [19]. Conversely, diabetics with HbA1c≥6.5% had a higher mean platelet count than those with HbA1c <6.5% in studies by [24] and [25], but these differences were also not statistically significant. The variation in results across studies may be attributed to the influence of multiple vascular risk factors in diabetes, in addition to platelet count, affected by the degree of glycemic control.

Regarding mean platelet volume (MPV), our study found that diabetics with HbA1c ≥ 6.5% had a significantly higher MPV (13.65±0.44 fl) compared to those with HbA1c <6.5% (12.93±1.79 fl; p<0.0068). Similar findings were reported by [26, 19, 27, 28, 24] indicating a consistent trend. Hyperglycemia is implicated in increasing platelet reactivity through non-enzymatic glycation of proteins and activation of protein kinase C. While our data suggests that glycemic control may mitigate platelet hyperactivity and potentially delay diabetes-related vascular complications, further validation in larger studies is warranted. The higher prevalence of diabetics with HbA1c ≥6.5% in our study may be attributed to inadequate dietary practices and insufficient awareness of recommended diet and exercise regimens for diabetic management.

Limitations of the Study and Future Prospects

While our study sheds light on the association between mean platelet volume (MPV) and various parameters in diabetes, it is important to acknowledge its limitations. Diabetes mellitus is a complex, multifactorial disease, and while platelet activity is a significant factor in the development of vascular complications, other influential factors exist. Additionally, MPV can be influenced by variables such as stress and menstruation, which were not accounted for in our study. Furthermore, qualitative platelet disorders were not assessed, and factors leading to falsely low or high platelet counts, such as pseudo-thrombocytopenia and EDTA-induced platelet clumping, were not thoroughly investigated.

Moreover, our study was hospital-based and focused on a specific region, potentially introducing selection bias and limiting the generalizability of our findings to the broader population. To address these limitations, future studies should aim to conduct more comprehensive and analytical investigations involving the general population. These studies could provide a more nuanced understanding of the relationship between MPV and diabetes, considering a wider array of influential factors and incorporating a more diverse participant pool. Additionally, future research should strive to explore the impact of qualitative platelet disorders and account for potential confounding variables to yield more robust and widely applicable findings.

Conclusion

Our study revealed that diabetics with HbA1c levels ≥6.5% exhibited significantly higher mean platelet volume (MPV) compared to those with HbA1c <6.5%, suggesting a potential

link between glycemic control and platelet hyperactivity. MPV was also significantly higher in diabetics with vascular complications compared to diabetics without vascular complications, signifying its importance as a predictor of vascular complications. These findings align with similar observations in other studies, indicating the influence of hyperglycemia on platelet reactivity. While our data suggests that maintaining glycemic control may help mitigate platelet hyperactivity and potentially delay diabetes-related vascular complications, it also emphasises on the role of MPV as a predictor of vascular complications. But further validation in larger studies is necessary. Additionally, the higher prevalence of diabetics with HbA1c≥6.5% in our study underscores the importance of addressing inadequate dietary practices and promoting awareness of recommended diet and exercise regimens for effective diabetic management.

Source of Support

Nil

Conflict of Interest

Nil

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