Section: General Medicine

Original Research Article

STUDY OF PLATELET INDICES AND THEIR ASSOCIATION WITH MICROVASCULAR COMPLICATIONS OF TYPE II DIABETES MELLITUS

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ABSTRACT

Background: Type II diabetes mellitus patients are known to be at a higher risk of micro and macrovaslcular complication that increase the cost of treatment and decreases the quality of life. Platelet indices are routine laboratory investigation that could be used to assess endothelial dysfunction and detect the microvascular complications. Hence, this study was done to evaluate the association between platelet indices and microvascular complications among type II diabetes patients. **Materials and Methods:** A cross-sectional study was conducted among 75 T2DM patients (50 with microvascular complications, 25 without) and 25 non-diabetic controls. A detailed clinical history was obtained, including duration of diabetes, presence of microvascular complications i.e. retinopathy, nephropathy, neuropathy. Independent t-test was used to assess the mean difference in the platelet indices across the group with a p-value less than 0.05 considered statistically significant. **Results:** Mean age and sex distribution was similar among the cases and controls. Among the platelet indices, MPV, PDW, PCT and P-LCR were found to higher among the diabetic group than control group which was statistically significant ($p<0.05$). Of 75 diabetic patients, 50 (66.7%) had at least one microvascular complication. Neuropathy was most common (40%), followed by retinopathy (24%) and nephropathy (16%). On comparing the platelet indices among patients with and without microvascular complication, it was seen that MPV and PDW was significantly more among those with complication while P-LCR was not. **Conclusion:** MPV and PDW were significantly elevated in diabetic patients, particularly those with microvascular complications, and correlated with poor glycemic control. These findings supports the use of platelet indices as accessible, cost-effective biomarkers for complication risk stratification in T2DM. However, variability in PCT and P-LCR associations and methodological challenges highlight the need for further research.

INTRODUCTION

Type 2 diabetes mellitus (T2DM), a chronic metabolic disorder, represents one of the most pressing global health challenges of the 21st century. According to the International Diabetes Federation’s 11th edition of the Diabetes Atlas, 537 million adults were living with diabetes in 2023, a figure projected to escalate to 783 million by 2045.[1] T2DM imposes a significant burden through its macrovascular complications (e.g., coronary artery disease, stroke) and microvascular complications (e.g., retinopathy, nephropathy, neuropathy), which collectively reduce life expectancy, impair quality of life, and strain healthcare systems worldwide.[2]

In India, over 50% of diabetic individuals remain undiagnosed, and those diagnosed often face delays in complication detection, exacerbating morbidity and mortality.[3] The high cost of treatment, coupled with low health insurance coverage, further complicates management, underscoring the urgent need for cost-effective strategies to prevent and manage diabetic complications.[4] Recent advances in screening technologies, including artificial intelligence-based retinal imaging, have improved the scalability and accuracy of retinopathy detection, offering promise for low-resource settings.[5]

However, the pathogenesis of microvascular complications remains incompletely understood. Chronic hyperglycemia is the primary driver, causing endothelial dysfunction, oxidative stress, and inflammation that disrupt microvascular structure and function.[6] Yet, emerging research highlights additional mechanisms, including platelet dysfunction, which may play a critical role in the development and progression of diabetic complications.[7]

Platelets, traditionally recognized for their role in hemostasis, are increasingly implicated in the pathophysiology of T2DM complications. Platelet volume indices (PVIs), such as mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT), are inexpensive, routinely measured parameters derived from complete blood counts.[8] In T2DM, studies consistently report higher PVI values compared to non-diabetic controls, attributed to chronic hyperglycemia and insulin resistance.[9] However, the association between PVIs and diabetic microvascular complications remains underexplored.

This study was planned to address these gaps by evaluating key platelet indices—total platelet count, MPV, and PDW—in T2DM patients compared to non-diabetic controls. It further investigates the association between these indices and microvascular complications, focusing on retinopathy, nephropathy, and neuropathy. By elucidating the role of PVIs, this research aims to contribute to the development of accessible, cost-effective tools for early detection and risk stratification in T2DM, ultimately improving patient outcomes in high-burden settings like India.

MATERIALS AND METHODS

Study Design and Setting: This cross-sectional observational study was conducted in the Outpatient Department (OPD) of General Medicine at Mahatma Gandhi Mission (MGM) Medical College and Hospital, Kamothe, Navi Mumbai, Maharashtra between March 2023 and May 2024, spanning 15 months.

Sample Size Calculation: The sample size was calculated based on an estimated prevalence of microvascular complications in T2DM patients of 10%, derived from prior literature.[10] Using the formula for sample size in prevalence studies: $n = (Z^2 \times P \times Q) / E^2$, where: Z = 1.96 (standard normal variate for a 95% confidence interval), P = 10% (prevalence of microvascular complications),Q = 100% – P = 90% and E = 6% (margin of error). The calculated sample size was: $n = (1.96^2 \times 0.10 \times 0.90) / 0.06^2 \approx 96$. To account for potential dropouts and ensure robust statistical power, a final sample size of 100 participants was selected, comprising 75 T2DM patients (50 with microvascular complications, 25 without) and 25 non-diabetic controls.

Sampling Method: Consecutive sampling was employed, enrolling all eligible patients attending the General Medicine and Diabetes Specialty OPD during the study period who met the inclusion and exclusion criteria. This method ensured a representative sample while minimizing selection bias. The detailed methodology is given in figure 1.

Study Population: Patients diagnosed with T2DM attending the OPD at MGM Medical College and Hospital. Non-diabetic controls were recruited from the same OPD, matched for age and sex to ensure comparability.

Inclusion Criteria

1. Patients aged 35–70 years, male or female, diagnosed with T2DM according to American Diabetes Association criteria.[11]
2. Patients able to read and write in Hindi, Marathi or English and willing to provide informed written consent.

Exclusion Criteria

1. Patients with diabetes types other than T2DM, including type 1 diabetes, latent autoimmune diabetes in adults (LADA), or maturity-onset diabetes of the young (MODY).
2. Pregnant or lactating women.
3. Patients with acute illnesses (e.g., recent myocardial infarction, COVID-19) or chronic conditions (e.g., HIV, rheumatoid arthritis, tuberculosis, chronic kidney disease, chronic liver disease, stroke, or other disabling conditions) that could affect platelet indices.
4. Patients with a history of blood transfusion within the past 14 days.
5. Patients with bleeding tendencies or significant blood loss.
6. Patients with known anemia, myeloproliferative disorders, or malignancies.
7. Patients with a history of bone marrow suppression (e.g., due to chemotherapy or medications).
8. Patients with active urinary tract infections.
9. Patients consuming high-protein diets or protein supplements, which may influence hematological parameters.
10. Patients unwilling to provide informed consent.

Data Collection: Eligible patients were identified during routine OPD visits and invited to participate after providing informed written consent. The study protocol was approved by the Institutional Ethics Committee of MGM Medical College and Hospital, ensuring compliance with ethical standards.

1. **Clinical Assessment**
   - A detailed clinical history was obtained, including duration of diabetes, presence of microvascular complications (retinopathy, nephropathy, neuropathy), smoking status, alcohol consumption, and medication use.
   - General physical examination included measurements of height, weight, waist circumference, and hip circumference to calculate body mass index (BMI) and waist-to-hip ratio (WHR). Systemic examination was assessed for microvascular complication.

2. **Blood Sample Collection:**
   - Venous blood (2 mL) was collected from the antecubital vein in a sitting position using an ethylene diamine tetraacetic acid (EDTA) vacutainer to measure platelet indices.
   - Samples were analyzed within 2 hours of collection using an automated hematology analyzer (Sysmex XP-300, Transasia, Mumbai, India) to determine platelet count ($\times 10^3/\mu L$), MPV (fL), PDW (%), PCT (%), and P-LCR (%).
   - An additional 2 mL of blood was collected for fasting blood sugar (FBS), postprandial blood sugar (PPBS), and glycated hemoglobin (HbA1c) levels, analyzed using standard biochemical methods.
   - Routine hematological investigations (e.g., hemoglobin, total leukocyte count) were performed to exclude confounding conditions (e.g., anemia, infection).
3. **Microvascular Complication Assessment**:
   - Retinopathy was diagnosed by fundoscopic examination by an ophthalmologist, classified per the Early Treatment Diabetic Retinopathy Study (ETDRS) criteria.[12]
   - Nephropathy was confirmed by elevated urinary albumin-to-creatinine ratio (>30 mg/g) or estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m², per Kidney Disease: Improving Global Outcomes (KDIGO) guidelines.[13]
   - Neuropathy was assessed using clinical symptoms (e.g., numbness, tingling) and tests (e.g., vibration perception threshold, monofilament testing)

Quality Control: Blood samples were handled per standard operating procedures to minimize pre-analytical errors (e.g., hemolysis, clotting). The hematology analyzer was calibrated daily, and quality control checks were performed using commercial controls to ensure accuracy. All laboratory personnel were trained to follow standardized protocols, reducing inter-operator variability.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables (e.g., platelet indices, FBS, HbA1c) were expressed as mean ± standard deviation (SD) and compared using independent t-tests for group differences. Categorical variables (e.g., sex, smoking status) were expressed as percentages and compared using chi-square tests. A p-value <0.05 was considered statistically significant.

Ethical Considerations: The study adhered to the Declaration of Helsinki principles. Informed written consent was obtained in the participant's preferred language (Hindi, Urdu, or English). Participants were informed of their right to withdraw at any time without affecting their medical care. Data were anonymized using unique identifiers to ensure confidentiality.

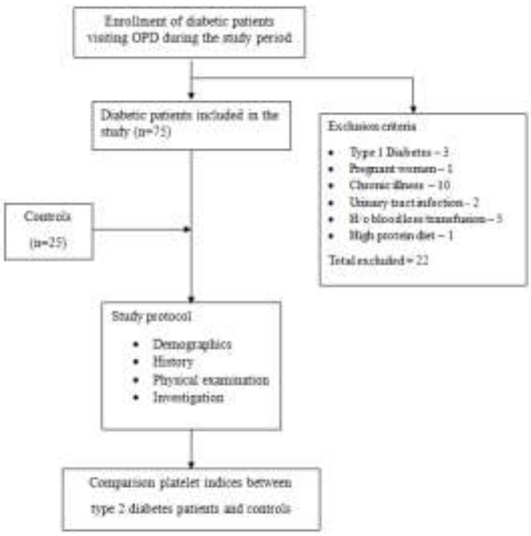

Figure 1: Flowchart for study methodology

RESULTS

Most of study participants belonged to the age group of 45 to 65 years of age with 65% being males. The baseline characteristics of cases and controls were similar with no significant difference in age, sex, BMI, WHR and addiction pattern. Majority of the patients i.e.44% with diabetes had it for a duration of 5 to 10 years. [Table 1]

Table 1: Baseline socio-demographic details of cases and controls (N=100)

Variable	Cases (n=75)	Controls (n=25)	p-value
Age (mean ± SD, years)	50.6 ± 8.7	49.1 ± 9.4	0.980
Sex			
Male	48 (64.0%)	17 (68.0%)	0.716
Female	27 (36.0%)	8 (32.0%)	
BMI (Kg/m^2)	24.6 ± 4.5	23.9 ± 3.8	0.955
Waist: Hip ratio (mean ± SD)	0.84 ± 0.12	0.80 ± 0.23	0.264
Smoking	26 (34.6%)	6 (24.0%)	0.322
Alcohol	14 (18.6%)	4 (16.0%)	0.763
FBS (Mean ± SD)	142.6 ± 25.1	97.02 ± 6.3	0.000*
PPBS (Mean ± SD)	187.5 ± 26.1	149.3 ± 7.1	0.000*
Duration of Diabetes	6.82 ± 3.20 years	-	-

Statistically significant

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The mean platelet indices were compared between the cases and controls. All platelet indices were found to be higher among the cases than control which was statistically significant ($p<0.05$) except platelet count. [Table 2]

Table 2: Comparison of Platelet Indices among cases and controls (N=75)

Platelet indices	Cases (n=75)	Controls (n=25)	p-value
Platelet count (x 103 /mcL)	261.7 ± 80.13	275.74 ± 85.9	0.457
MPV (fl)	12.34 ± 1.0	8.43 ± 0.9	0.000*
PDW (%)	16.6 ± 2.4	12.1 ± 4.1	0.000*
PCT (%)	0.26 ± 0.01	0.22 ± 0.02	0.000*
P-LCR	44.9 ± 9.5	35.2 ± 10.4	0.000*

Of the total 75 diabetic patients, 25 patients had at least one diabetic microvascular complication. Diabetic neuropathy (14 out of 25 patients) was the most common microvascular complication documented followed by retinopathy (10 out of 25) and nephropathy (7 out of 25). [Figure 2]

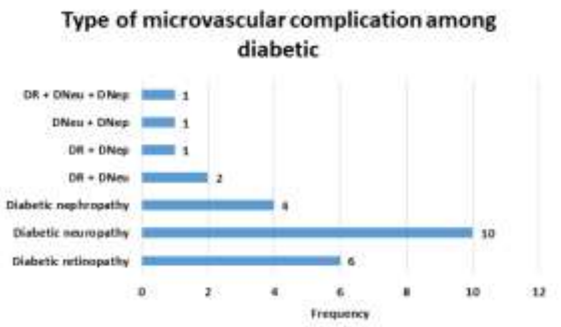

Figure 2: Type of microvascular complication among the study participants (n=25)

DR-Diabetic retinopathy, DNeu-Diabetic neuropathy, DNep- Diabetic neuropathy

On comparing the mean platelet indices among the diabetics with and without microvascular complication, the mean MPV, PDW and PCT were significantly high among those with complication than those without ($p<0.05$). The mean platelet count and PCT values were higher among those with microvascular complication but the difference was not statistically significant. [Table 3]

Table 3: Comparison of platelet indices between diabetics with and without microvascular complication (n=75)

	Diabetic cases (n=75)		p-value
	With complication (n=25)	Without complication (n=50)	
Platelet count (x 10^3 /mcL)	263.1 ± 65.1	261.5 ± 72.3	0.925
MPV (fl)	13.2 ± 1.4	11.6 ± 0.8	0.000*
PDW (%)	17.3 ± 1.8	14.6 ± 2.1	0.000*
PCT (%)	0.27 ± 0.03	0.26 ± 0.02	0.090
P-LCR	46.1 ± 7.3	42.8 ± 6.1	0.042*

The HbA1c level were categorized into three groups less than 7.5%, 7.5-10% and >10% and the mean platelet indices were compared. There was significant different in the MPV, PDW and P-LCR values across the HbA1c groups but not for platelet count and PCT. [Table 4]

Table 4: Comparison of platelet indices with HbA1c Levels (n=75)

Variable	HbA1c Levels			ANOVA-test p value
	<7.5%	7.5-10%	>10%	
Platelet count	265.1 ± 55.4	262.4 ± 67.2	261.1 ± 73.8	0.018 (0.98)
MPV (fl)	9.9 ± 1.5	11.5 ± 1.2	13.2 ± 2.3	17.4 (0.000*)
PDW (fl)	15.7 ± 2.1	17.4 ± 1.7	18.8 ± 2.0	14.4 (0.000*)
PCT (%)	0.25 ± 0.0	0.27 ± 0.1	0.26 ± 0.0	0.657 (0.52)
P-LCR	42.8 ± 8.7	46.5 ± 7.4	48.2 ± 8.8	12.24 (0.000*)

Statistically significant $p<0.05$

DISCUSSION

The findings of this study contribute to the growing body of evidence on platelet indices as potential biomarkers for diabetic complications, particularly in resource-limited settings like India, where T2DM prevalence is escalating.[1] The baseline characteristics of the cases and control were similar making them comparable.The mean platelet count was similar between T2DM patients (261.7 ± 80.1 ×10^3/μL) and controls (275.7 ± 85.9 ×10^3/μL; $p=0.45$), consistent with most studies (128, 130, 135, 136).[14,15,19] Rajas et al,[14] and Prabhat et al,[15] found higher platelet counts in T2DM but without statistical significance, while Zaccardi et al,[16] reported a significant increase (265 $\times 10^3/\mu L$ vs. 231 $\times 10^3/\mu L$; $p<0.001$). The lack of difference in our study suggests platelet count is not a reliable marker for T2DM-related changes, likely due to compensatory mechanisms maintaining platelet homeostasis despite hyperglycemia.[7]

In contrast, MPV was significantly higher in T2DM patients (12.3 ± 1.0 fL) than controls (8.4 ± 0.9 fL; $p<0.001$), corroborating findings from multiple studies (MPV range: 11.3–12.1 fL in T2DM vs. 8.2–11.4 fL in controls; $p<0.001$).[14,15] Elevated MPV reflects larger, more reactive platelets, which produce more prothrombotic factors and exhibit increased aggregability, contributing to vascular pathology.[8]

Similarly, PDW was significantly higher in T2DM (16.6 ± 2.4%) than controls (12.1 ± 4.1%; $p<0.001$), consistent with ranges reported by Jindal et al. (15.6–17.3% vs. 10.8–15.3%; $p<0.001$) .[14,15] PDW indicates platelet size heterogeneity, a marker of activation linked to hyperglycemia-induced stress.[18]

PCT was significantly higher in T2DM (0.26 ± 0.01%) than controls (0.22 ± 0.02%; $p<0.001$), aligning with studies reporting PCT ranges of 0.21–0.25% in T2DM vs. 0.19–0.22% in controls.[14,15,19] However, some studies found no correlation between PCT and HbA1c, questioning its utility.[9] P-LCR was also elevated in T2DM (44.9 ± 9.5% vs. 35.2 ± 10.4%; $p<0.001$), consistent with ranges of 35.0–44.1% in T2DM vs. 23.0–36.9% in controls.[20,21,22] These findings suggest that MPV, PDW, and P-LCR are more sensitive markers of platelet dysfunction in T2DM than platelet count or PCT.

Of 75 T2DM patients, 50 (66.7%) had at least one microvascular complication, with neuropathy (40%), retinopathy (24%), and nephropathy (16%) being the most common. This distribution aligns with Rajas et al,[14] who reported neuropathy as the most prevalent, but contrasts with Buch et al.,[23] where retinopathy predominated. Tanima et al. [24] found nephropathy associated with the highest platelet indices, suggesting complication-specific platelet responses. The mean diabetes duration (6.8 years) in our study is slightly longer than in these studies (4.3–5.6 years), potentially explaining the higher complication prevalence due to prolonged hyperglycemia.[25]

MPV was significantly higher in T2DM patients with complications (13.2 ± 1.4 fL) than without (11.6 ± 0.8 fL; $p<0.001$), consistent with Rajas et al,[14] Prabhat et al.,[15] and Taderegew et al.[26] PDW was also elevated in those with complications (17.3 ± 1.8% vs. 14.6 ± 2.1%; $p<0.001$), aligning with these studies. However, PCT (0.27 ± 0.03% vs. 0.26 ± 0.02%; $p=0.09$) and P-LCR (46.1 ± 7.3% vs. 42.8 ± 6.1%; $p=0.09$) showed no significant differences, contrasting with Kamilli et al,[19] who found PCT significantly elevated in complicated T2DM. Shilpi et al,[27] and Ravindra et al,[28] reported no association between any platelet indices and complications, highlighting variability in the literature.

Buch et al,[23] found MPV significantly associated with retinopathy and neuropathy ($p<0.05$), and PDW with retinopathy and nephropathy ($p<0.05$), but no association for P-LCR. Taderegew et al,[26] reported MPV and PDW linked to retinopathy and nephropathy, and P-LCR to retinopathy and neuropathy, but not PCT. Our findings suggest MPV and PDW are more consistently associated with microvascular complications, while PCT and P-LCR are less reliable, possibly due to their sensitivity to pre-analytical variables.[29]

Patients with higher HbA1c levels (>10%) exhibited significantly elevated MPV, PDW, and P-LCR ($p<0.001$), but not platelet count or PCT ($p>0.05$). This aligns with Rajas et al. [14] Shilpi et al,[27] and Tanima et al.,[24] who reported similar associations. Kamilli et al. [19] uniquely found PCT elevated with higher HbA1c, while Ravindra et al,[28] found no correlations, possibly due to differences in patient populations or assay techniques. Hyperglycemia induces platelet dysfunction by increasing oxidative stress and reducing platelet survival, leading to the release of larger, more active platelets from the bone marrow.[30] These platelets express higher levels of surface markers (e.g., GPIb-IX, GPIIb/IIIa), enhancing thromboxane synthesis and aggregation, which may contribute to microvascular damage.[31]

Hyperglycemia-driven vascular damage in T2DM promotes platelet hyperaggregability and activation, reducing platelet lifespan and increasing immature platelet release.[32] These platelets are functionally more active, with elevated surface markers and prothrombotic proteins, contributing to microvascular and macrovascular complications.[33] Our findings of elevated MPV and PDW in T2DM, particularly in those with complications, support this mechanism. MPV's consistent association across studies suggests it reflects platelet activation more reliably than other indices.[34] Haile et al,[35] demonstrated MPV's predictive value for T2DM comorbidities, with a sensitivity of 69.6% and specificity of 67.9% at a cutoff of ≥9.65 fL (AUC=0.747), reinforcing its potential as a biomarker.

However, the variability in P-LCR and PCT associations may reflect their susceptibility to pre-analytical factors, such as blood collection methods (stasis vs. non-stasis), anticoagulants (EDTA vs. citrate), storage temperature, and analysis timing.[36] Analyzer calibration and measurement techniques (optical vs. impedance) also influence results, as noted by studies.[37,38] These factors may explain discrepancies, such as Shilpi et al. [27] and Ravindra et al. [28] finding no associations with complications.

Compared to other biomarkers (e.g., C-reactive protein, microalbuminuria), platelet indices are more readily available and less invasive, offering a practical tool for early complication detection.[39] However, their predictive value for specific complications (e.g., retinopathy vs. nephropathy) remains inconsistent, necessitating standardized protocols for measurement and interpretation.[40] Our

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study's findings align with the literature suggesting MPV as the most robust marker, but prospective cohort studies are needed to establish temporal associations and cutoff values for clinical use.

CONCLUSION

This study demonstrates that MPV and PDW are significantly elevated in T2DM patients, particularly those with microvascular complications, and correlate with poor glycemic control. These findings align with the literature, positioning platelet indices as accessible, cost-effective biomarkers for complication risk stratification in T2DM. However, variability in PCT and P-LCR associations and methodological challenges highlight the need for further research. In India's high-burden context, leveraging routine blood counts for screening could enhance early detection and management of diabetic complications, improving patient outcomes.

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