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To assess the relationship of mean platelet volume (MPV) and platelet large cell ratio (PLCR) with diabetic retinopathy

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Abstract
Background: Diabetic retinopathy (DR) is a common microvascular complication of type 2 diabetes mellitus (T2DM), and early detection of DR is crucial for preventing vision loss.
Methods: A cross-sectional study was conducted with 130 T2DM patients attending the Ophthalmology outpatient department. Patients were classified into two groups: Group I (controls) consisting of T2DM patients without DR, and Group II (cases) consisting of T2DM patients with non-proliferative diabetic retinopathy (NPDR) or proliferative diabetic retinopathy (PDR). Comprehensive dilated fundus examination, along with routine blood tests (including CBC), were performed to assess Mean Platelet Volume (MPV) and Platelet-Large Cell Ratio (P-LCR).
Results: MPV was significantly higher in the DR group (12.27±2.04 fL) compared to the control group (9.32±0.77 fL) ($p< 0.01$). Both MPV and P-LCR increased progressively with the severity of DR, from mild NPDR to PDR, with p-values <0.01. The duration of diabetes was strongly correlated with DR severity ($p< 0.001$), and MPV and P-LCR both showed a clear rise with increasing disease duration. Additionally, patients on insulin therapy were more likely to have advanced DR ($p = 0.078$).
Conclusions: MPV and P-LCR are significantly associated with both the presence and severity of diabetic retinopathy in T2DM. As these indices are readily available from routine CBC tests, they provide a cost-effective, non-invasive tool for early detection and risk stratification of DR, especially in resource-limited settings. Incorporating MPV and P-LCR into routine diabetes care can facilitate earlier identification of at-risk individuals, enabling timely referral and intervention to prevent vision loss.

Keywords: Diabetic retinopathy, type 2 diabetes mellitus, mean platelet volume, platelet-large cell ratio, early detection, risk stratification

Introduction

Diabetic retinopathy (DR) is a significant microvascular complication of diabetes mellitus (DM), and it remains one of the leading causes of blindness worldwide. Hyperglycaemia induces a cascade of pathological changes in retinal microvasculature, including endothelial dysfunction, capillary leakage, and eventual neovascularisation in more advanced stages [1]. Identifying early biomarkers for DR is critical in preventing or slowing disease progression. Among the potential biomarkers, platelet indices such as Mean Platelet Volume (MPV) and Platelet Large Cell Ratio (PLCR) have been increasingly recognized for their role in assessing platelet activation, which may correlate with microvascular damage. MPV, which reflects the size of platelets, is believed to be an indicator of platelet reactivity and procoagulant activity [2]. Larger platelets are more biologically active and have a greater potential for thrombotic activity, which is pertinent to the pathogenesis of DR.

Several studies have reported elevated MPV in diabetic patients, with some evidence suggesting that MPV values correlate with the presence and severity of DR [3]. A study by Citirik *et al.* [2] found that MPV was significantly higher in diabetic patients with DR than in those without, suggesting a potential link between platelet size and microvascular damage in the retina. Similarly, PLCR, which measures the proportion of large platelets in the blood, has been associated with diabetes and its complications, though fewer studies have explored this relationship in DR specifically [4]. A study by Singh *et al.* [5] also noted that both MPV and PLCR were significantly elevated in diabetic patients with DR compared to those without.

The rationale for examining MPV and PLCR in DR lies in their role in thrombogenesis. In diabetes, chronic hyperglycaemia contributes to endothelial dysfunction and low-grade

inflammation, processes that activate platelets and promote their aggregation [1]. Since larger platelets are more thrombogenic, an increase in both MPV and PLCR may signify an elevated risk of microvascular injury, including in the retinal vessels. The connection between platelet activation and DR, however, remains a subject of ongoing investigation [4]. Therefore, understanding how MPV and PLCR are related to DR could provide valuable insights into early detection and prevention strategies.

Materials and Methods

This study was conducted in the Outpatient Department of Ophthalmology at the Government Medical College and Associated Group of Hospitals in Kota, Rajasthan, following approval from the Institutional Ethical Committee. The study was a cross-sectional observational design and was carried out until December 2024. The study included patients with Type 2 Diabetes Mellitus (T2DM) who attended the ophthalmology outpatient clinics. All participants underwent a detailed dilated fundus examination to detect and classify diabetic retinopathy (DR).

The total sample size consisted of 130 subjects, equally divided into two groups: cases and controls. Group I (controls) included age- and gender-matched T2DM patients without diabetic retinopathy, while Group II (cases) comprised T2DM patients diagnosed with either Non-Proliferative Diabetic Retinopathy (NPDR) or Proliferative Diabetic Retinopathy (PDR). The sample size was determined based on the prevalence of diabetes in India.

Exclusion criteria included patients with Type 1 Diabetes Mellitus, anemia, those on antiplatelet medications like aspirin or clopidogrel, individuals with hematological or platelet disorders, thyroid disease, pregnant women, or those with fever, cardiovascular diseases, or ocular conditions that could interfere with the diagnosis of diabetic retinopathy.

After obtaining written informed consent, participants' clinical history was recorded, including the duration and nature of diabetes, dietary habits, alcohol or tobacco consumption, and relevant family history. Additionally, information regarding previous anti-diabetic treatments, use of other medications, and any systemic illnesses influencing platelet indices was noted. Ocular history, including previous surgeries or treatments, was also recorded.

A general physical examination was performed, including the recording of vital signs such as pulse rate and blood pressure, assessment of peripheral pulses, and anthropometric measurements (height and weight). A systemic examination of the CNS, cardiovascular system, respiratory system, and abdomen was also conducted.

Visual acuity was assessed using Snellen's chart, and refractive status was documented. A slit-lamp biomicroscopy was used to examine the anterior segment of the eye, while diabetic retinopathy was assessed via dilated fundus examination and graded using the Early Treatment Diabetic Retinopathy Study (ETDRS) classification.

For laboratory investigations, 6 ml of venous blood was drawn under aseptic conditions. Three ml was transferred into an EDTA vial for glycated hemoglobin (HbA1c) and complete blood count (CBC), while the remaining 3 ml was transferred to a plain vial for fasting blood glucose (FBS) estimation. Additionally, a postprandial blood sample was collected 2 hours after a meal to measure postprandial blood sugar (PPBS) levels. Diagnosis of T2DM was confirmed using the WHO criteria, which include fasting plasma glucose $\geq$ 7.0 mmol/L, 2-hour postprandial plasma glucose $\geq$ 11.1 mmol/L, or HbA1c $\geq$ 6.5%.

Data were compiled and analyzed using Microsoft Excel and the Statistical Package for the Social Sciences (SPSS) version 29.0. Descriptive statistics were used to summarize qualitative variables, while quantitative data were presented as mean ± standard deviation (SD). Comparisons between groups were performed using the Student's independent two-tailed t-test, and a p-value of less than 0.05 was considered statistically significant.

Results

The age distribution was similar between the two groups, with most participants falling within the 61–70-year range. The mean age of the control group was 60.12±11.41 years compared with 58.95±10.16 years in the case group, showing no significant difference (p = 0.08). Gender distribution was also comparable, with males constituting 61.53% of controls and 60.00% of cases (p = 0.07). These findings confirm that neither age nor gender acted as confounders in the analysis.

A clear divergence emerged in disease chronicity. The mean duration of diabetes mellitus (DM) was significantly longer in the case group (10.65±7.18 years) than in the control group (4.88±2.99 years), with $p< 0.001$. Stratification of duration revealed a strong, graded association between longer diabetes duration and increasing severity of diabetic retinopathy (DR). Patients with <5 years of DM were predominantly controls, whereas those with >10 years increasingly exhibited moderate NPDR, severe NPDR, and PDR. This relationship was statistically significant ($p< 0.001$), reinforcing the established impact of disease duration on DR risk.

Glycemic control parameters showed marked differences between groups. Mean fasting blood sugar (FBS) was higher in the case group (183±27.13 mg/dL) compared with controls (162.58±18.65 mg/dL), with $p< 0.01$. Mean postprandial blood sugar (PPBS) was also significantly elevated among cases (271.92±47.85 mg/dL) compared with controls (221.61±5.93 mg/dL), $p< 0.01$. HbA1c levels demonstrated the clearest discrepancy, rising to 8.7±1.23% in cases versus 6.03±0.58% in controls ($p< 0.01$), confirming worsened long-term glycemic control among patients with DR.

Treatment patterns differed significantly. Insulin usage was higher among cases (16.92%) than controls (4.62%), p = 0.02. Conversely, oral hypoglycemic agents (OHA) were used by 95.38% of controls versus 83.07% of cases (p = 0.04). Within the case group, OHA users most commonly had mild NPDR (38.89%) and moderate NPDR (35.19%). Insulin users exhibited more advanced disease, with 63.64% showing moderate NPDR and 18.18% each having severe NPDR or PDR. Although this pattern was clinically meaningful, it did not reach statistical significance (p = 0.078).

Mean Platelet Volume (MPV) differed strikingly between groups. DR patients had significantly higher MPV (12.27±2.04 fL) compared with controls (9.32±0.77 fL), $p< 0.01$. MPV also demonstrated a progressive increase with DR severity: mild NPDR (10.05±1.06 fL), moderate NPDR (12.56±0.71 fL), severe NPDR (13.25±0.46 fL), and PDR (14.19±0.93 fL), with $p< 0.01$ for the trend. This relationship persisted across diabetes duration strata. Among patients with <5 years of DM, MPV rose from 10.16 fL in mild NPDR to 13.14 fL in severe NPDR. In those with >10 years, MPV values exceeded 14 fL in PDR, confirming that MPV correlates strongly with both disease duration and retinopathy severity.

Platelet-Large Cell Ratio (PLCR) followed a similar pattern.

Controls exhibited low and stable PLCR values (21.52–22.26%). In contrast, the case group showed significantly elevated PLCR (35.02±4.23%), $p< 0.01$. PLCR increased steadily with DR severity: mild NPDR (33.08±5.66), moderate NPDR (35.6±7.49), severe NPDR (37.2±8.05), and PDR (39.4±7.2). The overall trend across DR stages reached statistical significance ($p< 0.01$). Duration-wise analysis further strengthened this pattern. PLCR values rose markedly in advanced DR among patients with >10 years of DM, peaking at 47.49% in moderate NPDR and 42.34% in severe NPDR in those with >20 years of diabetes.

Severity analysis of DR cases revealed that moderate NPDR was the most common stage (40%), followed by mild NPDR (32.31%), severe NPDR (16.92%), and PDR (10.76%). Both MPV and PLCR showed clear, monotonic rises with increasing DR severity, identifying them as strong hematological markers associated with retinopathy progression.

Overall, MPV and PLCR demonstrated highly significant associations with the presence and severity of diabetic retinopathy, independent of age and gender, but strongly linked to duration of diabetes and glycemic control.

Table 1: Demographic and Clinical Characteristics of Control and Case Groups

Variable	Control Group (n=65)	Case Group (n=65)	P-Value
	Mean ± SD		
Age Years	60.12±11.41	58.95±10.16	0.04
Duration of DM Years	4.88±2.99	10.65±7.18	<0.01
Gender (Female) n,%	25 (38.46%)	26 (40.00%)	0.07
Gender (Male)	40 (61.53%)	39 (60.00%)	0.07
FBS (mg/dL)	162.58±18.65	183±27.13	<0.01
PPBS (mg/dL)	221.61±5.93	271.92±47.85	<0.01
HbA1c (%)	6.03±0.58	8.7±1.23	<0.01
DM means Diabetic Mellitus; FBS= Fasting Blood Sugar; PPBS= Post Prandial Blood Sugar; HbA1c= glycated hemoglobin; SD =Standard Deviation *P*< 0.05 is considered to be statistically significant			

Table 2: Platelet Indices in Control and Case Groups

Variable	Control Group (n=65)	Case Group (n=65)	P-Value
	Mean ± SD		
Platelet-Large Cell Ratio (%)	21.96±2.08	35.02±4.23	<0.01
Mean Platelet Volume (fL)	9.32±0.77	12.27±2.04	<0.01
SD =Standard Deviation *P*< 0.05 is considered to be statistically significant			

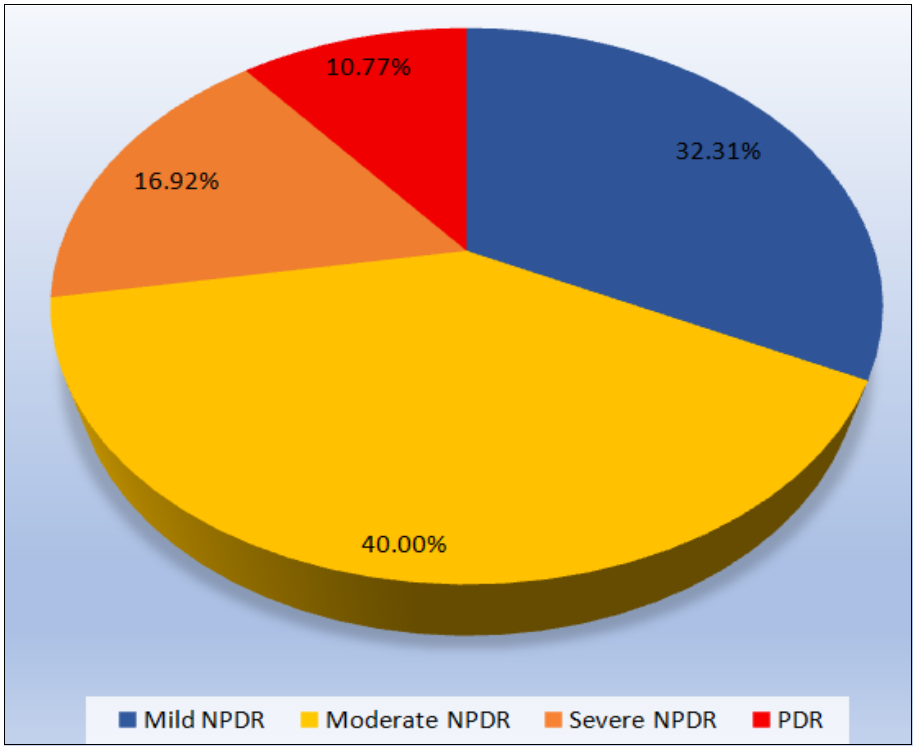

Fig 1: Graphical Distribution of Diabetic Retinopathy Stages in the Case Group

Table 3: Mean Platelet Volume (MPV) and Platelet Large Cell Ratio (PLCR) in Diabetic Retinopathy Patients

Diabetic Retinopathy Classification	Mean Platelet Volume (fL)	PLCR (%)	P-Value
	Mea n± SD		
Mild NPDR	10.05±1.06	33.08±5.66	<0.01
Moderate NPDR	12.56±0.71	35.6±7.49	<0.01
Severe NPDR	13.25±0.46	37.2±8.05	<0.01
PDR	14.19±0.93	39.4±7.2	<0.01
Total	12.27±2.04	35.11±7.42	<0.01

SD =Standard Deviation; Platelet Large Cell Ratio (PLCR); NPDR= Non Proliferative Diabetic Retinopathy
P< 0.05 is considered to be statistically significant

Discussion

This cross-sectional study evaluated whether Mean Platelet Volume (MPV) and Platelet-Large Cell Ratio (P-LCR) are associated with the presence and severity of diabetic retinopathy (DR) in adults with type 2 diabetes mellitus. A total of 130 patients were enrolled, evenly divided into controls (T2DM without DR) and cases (T2DM with NPDR or PDR), after detailed screening and dilated fundus examination. The study aimed to determine the relationship of MPV and P-LCR with DR and assess their variation across severity grades. Since both indices are routinely available on standard CBC tests, establishing their value may support low-cost screening, earlier referrals, and better monitoring in settings with limited ophthalmic resources.

In this study age distribution was similar across groups (p = 0.08), minimizing confounding by age. Most participants were 61–70 years, followed by 51–60 years. Mean age was 58.95±10.16 years in cases and 60.12±11.41 years in controls; the overall mean was 59.54±10.79 years. These values mirror prior reports Shah *et al.* [6] (58.6±9.3 years) and Al-Rubeaan *et al.* [7] (59.4±11.7 years) and align with the well-described concentration of DR in the sixth to seventh decades of life [8]. Sex distribution was also comparable (males: 60.00% cases vs 61.53% controls; p = 0.07). The predominance of men among T2DM patients with microvascular complications is consistent with earlier Indian cohorts (e.g., Mishra *et al*., 66:34 [9]; Ranjan *et al*., 65.6% male [10].

Disease duration differed markedly between groups 10.65±7.18 years in cases vs 4.88±2.99 years in controls (*p*< 0.001), reinforcing duration of diabetes as a major determinant of DR risk. This is concordant with the global literature Yau *et al*. showed >60% 10-year cumulative risk with long-standing diabetes [11], and the SN-DREAMS data similarly documented a sharp rise beyond 10 years [12].

Glycemia was consistently worse among DR cases. Fasting blood sugar was higher in cases (183±27.13 mg/dL) than controls (162.58±18.65 mg/dL; *p*< 0.01. Post-prandial levels showed the same pattern (271.92±47.85 mg/dL vs 221.61±5.93 mg/dL; *p*< 0.01. HbA1c reflecting chronic glycemic exposure—was substantially elevated in cases (8.7±1.23%) compared with controls (6.03±0.58%; *p*< 0.01). These findings echo UKPDS, where tighter control reduced microvascular outcomes [12], and more recent evidence showing higher HbA1c among DR patients (typically >8%) than non-DR diabetics (<7%) [13].

Treatment patterns also differed. Insulin use was more frequent in cases (16.92% vs 4.62%; p = 0.02), while OHA use was more common in controls (95.38% vs 83.07%; p = 0.04), suggesting that patients requiring insulin often have longer or more severe disease and are therefore at greater risk of DR findings consistent with Pradeepa *et al.* [14].

Stage distribution showed that moderate NPDR was most prevalent (40%), followed by mild NPDR (33.08%), severe NPDR (16.92%) and PDR (10.76%). This profile underscores the clinical value of routine fundus screening to capture disease in earlier, more treatable stages and aligns with Indian data from SN-DREAMS (NPDR 15.1%, PDR 0.9%) [15] and CURES (DR 17.6%, mainly NPDR) [16], as well as global estimates from Yau *et al.* (overall DR 34.6%; NPDR 28.4%; PDR 6.96%) [17].

MPV an accessible marker of platelet size and activation was significantly higher in DR (12.27±2.04 fL) than in controls (9.32±0.77 fL; *p*< 0.01), indicating platelet hyperreactivity that may aggravate microvascular injury. MPV also rose stepwise with DR severity 10.05±1.06 fL (mild NPDR), 12.56±0.71 fL (moderate NPDR), 13.25±0.46 fL (severe NPDR), and 14.19±0.93 fL (PDR). These gradients are consistent with multiple studies reporting higher MPV in DR than non-DR diabetes Moinul *et al.* [18], Teklioglu *et al.* [19], Yilmaz *et al.* [20], Cirik *et al.* [21], and Demirtas *et al.* [22] with additional support from Papana *et al.* [23] and Dundar *et al.* [24]. Although a few analyses Liu *et al.* [25]; Zhou *et al.* [26] did not detect differences, the weight of evidence favors a positive MPV–DR association.

P-LCR was likewise elevated in DR (35.02±4.23%) versus controls (21.96±2.08%; *p*< 0.01), consistent with a higher proportion of larger, more thrombogenic platelets. By stage P-LCR increased numerically from mild NPDR (33.08±5.66%) to moderate (35.6±7.49%), severe (37.2±8.05%), and PDR (39.4±7.4%). While the trend did not achieve conventional statistical significance, the directional rise is biologically plausible and broadly supported by literature demonstrating higher P-LCR in DR and progressive increases with severity: Demirtas *et al.* [22], Koseoglu *et al.* [27], Uslu *et al.* [3], Karaman *et al.* [4], and Kocak *et al.* [5].

Duration of diabetes correlated strongly with DR severity (*p*< 0.001), matching the natural history of cumulative microvascular injury. Parallel increases in MPV and P-LCR with advancing stage and longer duration reinforce platelet-mediated endothelial dysfunction as a key mechanistic thread. Although insulin therapy tended to be more common in advanced DR this did not reach statistical significance (p = 0.078), likely reflecting the intertwined effects of poorer control and longer disease exposure.

Our study shows that both MPV and P-LCR are higher in DR than in diabetes without retinopathy and that MPV—more robustly, and P-LCR directionally—track with disease severity. Given their availability on routine CBCs, these indices are practical, inexpensive adjuncts for early detection, monitoring, and risk stratification of DR in T2DM, particularly where access to specialty care is constrained.

Conclusion

This study confirms that Mean Platelet Volume (MPV) and Platelet-Large Cell Ratio (P-LCR) are significantly associated with both the presence and severity of diabetic retinopathy in type 2 diabetes mellitus. MPV and P-LCR were consistently higher in patients with DR and showed a clear rise with advancing disease stages, indicating

increased platelet activation in DR pathogenesis.
Because these indices are readily available from routine CBC testing, they offer simple, low-cost markers that can support early detection and risk stratification, especially where ophthalmologic services are limited. Incorporating MPV and P-LCR into regular diabetes monitoring may enable earlier identification of high-risk individuals and improve access to timely intervention, helping reduce preventable vision loss in underserved populations.

Conflict of Interest
Not available

Financial Support
Not available

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