

Association of Platelet Indices and Glycemic Control with Diabetic Retinopathy

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Abstract

Objective: Diabetic retinopathy (DR) is a major micro vascular complication of diabetes mellitus. It primarily driven by prolonged hyperglycemia, which results in vascular injury of the retina, neural impairment, and eventual vision loss. Among platelet indices, mean platelet volume (MPV) has frequently shown an association with DR, though evidence for platelet distribution width (PDW) and platelet large cell ratio (P-LCR) remains inconsistent. The present study was designed to assess the relationship between Platelet Indices with glycemic status in type 2 diabetes mellitus (T2DM) patients with and Without Diabetic Retinopathy. **Material and Methods:** Altogether, 200 subjects aged 35–75 years were included: 80 with DR, 60 with T2DM but no retinopathy, and 60 healthy controls. Fasting and postprandial blood glucose, HbA_{1c}, platelet counts, and platelet indices including MPV, PDW, P-LCR, and plateletcrit were measured and compared among the groups. **Results:** Patients with diabetes and those with DR exhibited significantly higher fasting and postprandial glucose levels and HbA_{1c} when compared with controls ($P < 0.01$). Platelet indices such as MPV, PDW, P-LCR were elevated in diabetics and DR patients, while plateletcrit showed no difference. Poor glycemic control (HbA_{1c} >7%) was associated with increased P-LCR and MPV and lower platelet count and plateletcrit ($P < 0.05$). **Conclusion:** Poor glycemic regulation and prolonged duration of diabetes showed a strong association with DR. Elevated HbA_{1c}, glucose, and platelet indices (MPV, PDW, P-LCR) correlated with disease severity, suggesting that routine monitoring of these parameters may aid early detection and risk stratification in type 2 diabetes.

Keywords: Type2 Diabetes mellitus, Diabetic Retinopathy, MPV, HBA_{1c}, Hypoglycemic drug

Introduction

Diabetes mellitus (DM) is a chronic metabolic disease marked by inadequate insulin secretion or by impaired insulin utilization. Insulin is essential for maintaining normal blood glucose levels and its dysfunction results in persistent hyperglycemia. Over time, uncontrolled diabetes damages several organ systems, including the renal, cardiovascular, and nervous systems, as well as the retina. The global burden of diabetes has risen sharply with affected individuals rising from about 200 million in 1990 to more than 830 million in 2022¹. At present, nearly one in seven adults has diabetes, with type T2DM accounting for over 95% of all cases. These numbers already exceed the earlier forecast of 783 million cases projected for 2045².

Chronic hyperglycemia is a central factor in the development of complication, particularly DR, a progressive microvascular disorder of the retina that remains a leading cause of blindness worldwide. The disease is primarily mediated through microvascular injury, resulting in complications such as diabetic maculopathy, proliferative diabetic retinopathy (PDR), tractional retinal detachment, vitreous hemorrhage, and neovascular glaucoma³. Worldwide, approximately 4% of the population is affected by DM, and almost half of these individuals develop DR during their lifetime. Prevalence estimates suggest that 9.3% of adults worldwide live with diabetes, compared with 15–19% in India, where DR affects roughly 16.9% of individuals with diabetes⁴. NPDR is marked by microaneurysms, capillary nonperfusion, and increased vascular permeability, which may lead to macular edema and vision impairment.

The development of DR is strongly linked to prolonged duration of diabetes, inadequately glycemic control, and hypertension⁵. Longitudinal studies show that after five years of type 1 diabetes, about 25% of patients develop DR and 2% progress to PDR. At 15 years, the risk rises to 80% for DR overall and to 25% for proliferative disease. Both persistent hyperglycemia, often measured by HbA_{1c}, and glycemic variability are linked to DR progression⁶. Additional risk factors include nephropathy, dyslipidemia, obesity, and elevated blood pressure.

HbA_{1c} serves as the key biomarker for long term glycemic control, and elevated levels are strongly correlated with DR prevalence and severity. Early detection of DR and timely therapeutic intervention remain critical in preventing irreversible vision loss⁷. In addition to glycemic markers, recent studies have investigated systemic inflammatory markers including neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR) and systemic immune-inflammation index (SII) as potential predictors of DR⁸. Platelet-based indices, including MPV, PDW, plateletcrit, and P-LCR, have also been examined, though findings have been inconsistent^{9, 10}.

Several reports highlight a positive association between MPV and DR, suggesting that larger platelets, which are metabolically more active, may contribute to vascular complications in diabetes¹¹. Increased MPV may result from hyperglycemia-induced osmotic changes and accelerated platelet turnover. Poor glycemic control appears to strengthen the association between MPV and microvascular damage. Pharmacological management also influences platelet parameters: metformin has demonstrated stronger antithrombotic properties com-

pared with sulfonylureas, although glimepiride may be more effective in certain diabetic complications such as foot ulcers ¹².

Complete blood count (CBC), a widely available diagnostic test, provides insights into red cell, white cell, and platelet parameters. However, evidence on the relationship between CBC-derived platelet indices (MPV, PDW, P-LCR, and PCT) and DR remains inconclusive. Therefore, in this study was undertaken to examine the association between platelet indices and hyperglycemia in patients with DR, focusing specifically on HbA_{1c} levels and platelet activation markers.

Material and Methods

Ethical Approval

The study was conducted in the Ophthalmology Outpatient Department of Sankara Eye Hospital, Chennai, between March 2024 and January 2025. Ethical approval was obtained from the Institutional Ethics Committee (Approval No. SEH/IEC/MOPT-11/2024, dated 21.02.2024) Written informed consent was obtained from all participants prior to enrollment, and patient confidentiality was strictly maintained. No identifying information is disclosed in the manuscript.

Sample size and study population

The sample size was calculated using Cochran's formula ($N = Z^2pq / d^2$). Based on the reported prevalence of diabetes in India at 7.3% (ICMR-INDIA Diabetes Study ¹³, applying a 95% confidence level ($Z = 1.96$) and a 5% error margin, the minimum required number of participants was estimated as 200. Recruitment was carried out using purposive sampling according to predefined inclusion and exclusion criteria.

Inclusion criteria

Participants between 30 and 75 years of age diagnosed with type 2 diabetes mellitus, with or without retinopathy, were eligible. Age- and sex-matched healthy individuals without T2DM or retinopathy served as the control group.

Exclusion criteria

Patients with hematological disorders, hepatic, renal, or cardiac failure, chronic infections, malignancies, anemia, thrombocytopenia, leukocytosis, or those receiving antiplatelet or anticoagulant therapy were excluded.

Study groups

Participants were categorized into three groups:

- **Group I:** Non-diabetic, healthy controls (n=60)
- **Group II:** Type 2 diabetes mellitus patients without retinopathy (n = 60)
- **Group III:** Diabetes mellitus with Retinopathy (n=80)

Groups II and III were further stratified by HbA_{1c} levels into: very good control (<7%) a and poor control (>7%).

Clinical and ophthalmological assessment

Demographic data, medical history (including duration of diabetes, comorbidities such as hypertension, and current treatment), height, weight, and BMI were recorded using a structured proforma. All diabetic participants underwent detailed ophthalmic evaluation, including evaluation of visual acuity and fundus examination using direct and indirect ophthalmoscopy along with slit-lamp bio microscopy.

Laboratory investigations

Blood samples were collected in EDTA tubes for HbA_{1c} and CBC analyses, and in plain tubes for biochemical parameters such as glucose. Using appropriate tubes minimized the risk of cross-contamination and ensured analytical precision. CBC was analyzed using the SYSMEX XP-100 automated three-part hematology analyzer (Sysmex Corporation, Kobe, Japan), based on the electronic impedance (Coulter) principle. HbA_{1c} was measured with the GH-900 Plus Hemoglobin A_{1c} Analyzer (Lifotronic Technology Co., Ltd., China), an automated HPLC-based system. Biochemical parameters were processed using the Vitros 250 Automatic Dry Chemistry Analyzer from Ortho Clinical Diagnostics, Raritan, NJ, USA.

Data management and statistical Method

Data were entered into Microsoft Excel and analyzed using SPSS for Windows. Continuous variables are expressed as mean $\pm$ standard deviation (SD), and categorical variables as frequencies and percentages. Comparisons of hematological parameters between groups were performed using one-way ANOVA, while categorical data were analyzed with the chi-square test. A p-value of less than 0.05 was considered statistically significant.

Result

A total of 200 participants aged 30–75 years were included in the study, comprising 90 males (45%) and 110 females (55%) (Figure 1). The distribution of age and sex across the three study groups was comparable. The mean ages were 51.13 ± 11.55 years for Group I (controls), 52.43 ± 11.57 years for Group II (diabetics without retinopathy), and 58.86 ± 6.41 years for Group III (diabetics with retinopathy) (Table 1).

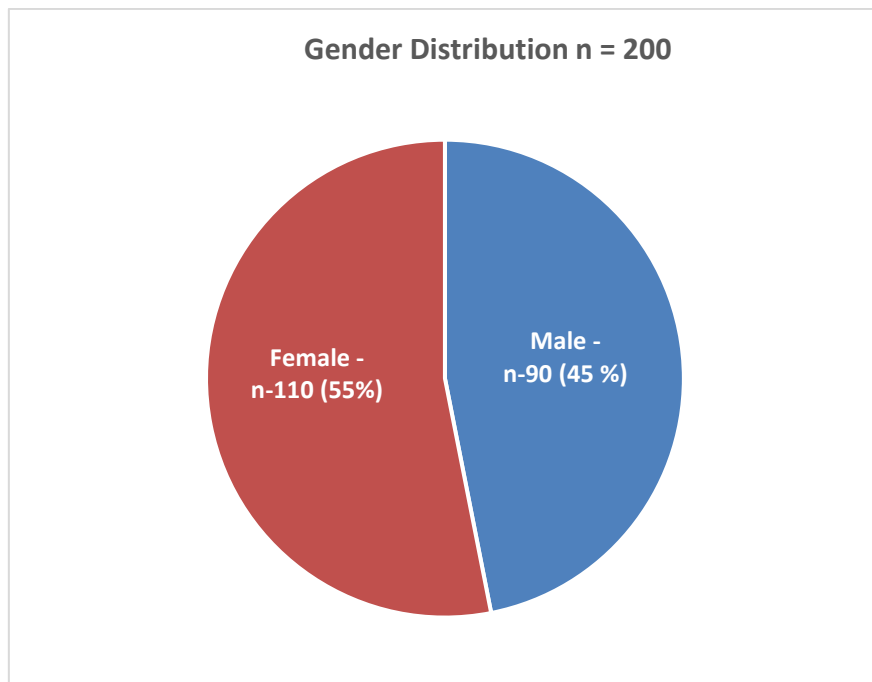


Figure 1. Gender distribution of study participants

Demographic Characteristics:

When gender distribution was assessed, 25 (41.7%) males and 35 (58.3%) females were observed in the control group. Group II comprised 29 males (48.3%) and 31 females (51.7%), while Group III included 36 males (45%) and 44 females (55%). The mean ages were 51.13 ± 11.55 years (Group I), 52.43 ± 11.57 years (Group II), and 58.86 ± 6.41 years (Group III), with an overall mean of 54.09 ± 9.84 years (Table 1).

Table 1: Participant Demographic characteristics in the three groups

Gender	Group - I Control no (%)	Group - II T2DM no (%)	Group - III T2DM + DR no (%)	Total no (%)
Average Age	51.13 ± 11.55	52.43 ± 11.57	58.86 ± 6.41	54.09 ± 9.84
Male	25 (41.7%)	29 (48.3%)	36 (45 %)	90 (45 %)
Female	35 (58.3%)	31 (51.7%)	44 (55 %)	110 (55%)
Total	60 (100%)	60 (100%)	80 (100 %)	200 (100%)
Abbreviations: T2DM: Type 2 Diabetes mellites; DR; Diabetic Retinopathy				

Age Distribution of participants:

The age of participants ranged between 30 and 75 years. Table 2 shows the distribution of participants across different age groups in the study population. Among controls (Group I), 21.6% were aged <40 years, 30% were between 41–50 years, 26.7% were between 51–60 years, and 21.6% were above 60 years. In Group II (T2DM without DR), 13.3% were <40 years, 35% were 41–50 years, 25% were 51–60 years, and 26.7% were >60 years. In Group III (T2DM with

DR), the majority of participants were in the older age categories, with only 1.2% below 40 years, 7.5% in 41–50 years, 48.8% in 51–60 years, and 42.5% above 60 years.

Table 2: Age distribution of study participants across groups

Ranging of Age	Group - I Control no (%)	Group - II T2DM no (%)	Group - III T2DM + DR no (%)	Total no (%)
< 40	13 (21.6)	8 (13.3)	1 (1.2)	22 (11)
41 - 50	18 (30)	21 (35)	6 (7.5)	45 (22.5)
51 - 60	16 (26.7)	15 (25)	39 (48.8)	70 (35)
> 60	13 (21.6)	16 (26.7)	34 (42.5)	63 (31.5)
	60 (100)	60 (100)	80 (100)	200 (100)

Comparison of biochemical and hematological parameters

Table 3 provide a summarizes the biochemical and hematological findings of the three study groups. The mean duration of diabetes was significantly longer in Group III (T2DM with DR, 11.34 ± 6.81 years) compared to Group II (T2DM without DR, 8.01 ± 4.55 years; $P = 0.0014$). BMI values were higher among diabetic groups compared with controls ($P = 0.0095$).

Glycemic parameters showed marked differences between groups. Both fasting and post-prandial glucose concentrations were significantly raised in diabetic groups, reaching their highest values in patients with DR (FBG: 158.49 ± 63.94 mg/dL; PPBG: 238.87 ± 96.19 mg/dL; $P < 0.0001$). HbA_{1c} followed a similar trend, being lowest in controls ($5.52 \pm 0.32\%$) and highest in DR patients ($8.85 \pm 1.95\%$; $P < 0.0001$).

In the present study, patients with diabetic retinopathy exhibited significantly higher platelet indices compared with diabetics without complications and healthy controls. MPV was highest in the retinopathy group (10.23 ± 1.05 fL) versus diabetics without complications (9.97 ± 0.79 fL) and controls (9.64 ± 0.97 fL; $p = 0.0032$). PDW and P-LCR followed similar trends, with PDW values of 13.30 ± 2.65 fL in DR patients compared with 12.44 ± 1.58 fL in diabetics without complications ($p = 0.0026$), and P-LCR of $27.28 \pm 7.97\%$ in DR versus $22.53 \pm 7.10\%$ in controls ($p = 0.0009$). Although mean platelet counts were lower in DR patients ($270.17 \pm 85.98 \times 10^3/\mu\text{L}$) Although the difference from controls was not statistically significant ($p = 0.2264$), MPV, PDW, and P-LCR were notably higher in diabetic retinopathy, indicating increased platelet activation and heterogeneity.

Table 3: Comprehensive analysis of biochemical and hematological parameters across study groups (Mean $\pm$ SD, One-way ANOVA)

Parameters	Control Group-I	T2DM Group-II	T2DM + DR Group-III	P-Values
Basic Demographic and biochemical Parameters				
Duration Of DM	NA	8.01 ± 4.55	11.34 ± 6.81	0.0014*
BMI	24.53 ± 3.07	25.94 ± 3.68	26.44 ± 4.07	0.0095*

FBG (mg/dl)	92.63 ± 10.3	143.56 ± 39.91	158.49 ± 63.94	< 0.0001*
PPBG (mg/dl)	118.30 ± 17.29	208.80 ± 59.28	238.87 ± 96.19	< 0.0001*
HbA1c (%)	5.52 ± 0.32	7.71 ± 1.41	8.85 ± 1.95	< 0.0001*
Platelets indices				
Platelets Count (10 ³ / uL)	292.26 ± 71.23	283.26 ± 65.59	270.17 ± 85.98	0.2264
MPV (fL)	9.64 ± 0.97	9.97 ± 0.79	10.23 ± 1.05	0.0032*
PDW (fL)	11.95 ± 1.85	12.44 ± 1.58	13.30 ± 2.65	0.0026*
P-LCR (%)	22.53 ± 7.10	24.32 ± 6.19	27.28 ± 7.97	0.0009*
PCT (%)	0.275 ± 0.06	0.277 ± 0.063	0.276 ± 0.066	0.9780
*Indicate P<0.05 for statistical significance.				
Abbreviations: FBG, Blood Glucose Levels after Fasting; PPBG, Blood; Glucose Levels after Eating HbA1c Glycosylated hemoglobin A1c T2-Type 2 diabetes (DM); Diabetic retinopathy (DR);; MPV (mean platelet volume), PDW (platelet distribution width), P-LCR (platelet large cell ratio), PCT (Plateletcrit).				

Comparison of Platelet Indices in Diabetic Patients with and Without Retinopathy

When comparing platelet indices between diabetics with and without retinopathy, P-LCR and PDW were significantly elevated in patients with DR (PDW: 13.30 ± 2.65 fL vs 12.44 ± 1.58 fL, P = 0.0272; P-LCR: 27.28 ± 7.97% vs 24.32 ± 6.19%, P = 0.0184). MPV and platelet counts were greater in diabetic retinopathy patients than in diabetics without retinopathy. but these differences did not reach statistical significance (MPV: 10.23 ± 1.05 fL vs 9.97 ± 0.79 fL, P = 0.0967; platelet count: 270.18 ± 85.98 vs 283.27 ± 65.59 ×10³/μL, P = 0.3270). Plateletcrit remained similar across both groups (P = 0.9276). as shown in Table 4.

Table 4: Comparison of platelet indices between diabetics with and without retinopathy

Platelets Indices	T2DM Group-II (n 60)	T2DM + DR Group-III (n 80)	t-Values	P Values
Platelets Count (10 ³ / uL)	283.27 ± 65.59	270.18 ± 85.98	-0.984	0.3270
MPV (fL)	9.97 ± 0.79	10.23 ± 1.05	1.672	0.0967
PDW (fL)	12.44 ± 1.58	13.30 ± 2.65	2.233	0.0272*
P-LCR (%)	24.32 ± 6.19	27.28 ± 7.97	2.386	0.0184*
PCT (%)	0.277 ± 0.062	0.276 ± 0.066	-0.091	0.9276
*Indicate P<0.05 for statistical significance.				

A strong association was found between elevated HbA1c levels and the presence of diabetic retinopathy (p = 0.0008). Among individuals with HbA1c ≥ 7%, 85% were diagnosed with

DR, whereas only 15% of those with HbA_{1c} < 7% had DR. Regarding duration of diabetes, retinopathy was more common in patients with longer disease history. More than half (53.8%) of DR cases had diabetes for over 10 years, compared with one-third (33.3%) of diabetics without retinopathy. In contrast, a shorter duration (<5 years) was more frequent among patients without retinopathy (40%) than among those with retinopathy (18.8%). The association reached statistical significance, P = 0.0126 (Table 5).

Table 5: Association of HbA_{1c} and duration of diabetes with and without diabetic retinopathy

Risk Factors	Risk Factors Variable	Total	T2DM Group-II		T2DM + DR Group-III		P. Values
		no (%)	no	%	no	%	
HBA1c (%)	<7.0 %	36 (25.7)	24	40	12	15	0.0008
	>7 %	104 (74.3)	36	60	68	85	
Duration of Diabetes	<5 Years	39 (27.9)	24	40	15	18.75	0.0126
	5 - 10 years	38 (27.1)	16	26.7	22	27.5	
	> 10 Years	63 (45)	20	33.3	43	53.75	
*Indicate P<0.05 for statistical significance.							

Table 6 shows the distribution of platelet indices among T2DM patients with diabetic retinopathy. Individuals with HbA_{1c} > 7% exhibited significantly elevated MPV and P-LCR were observed in patients with HbA_{1c} ≥ 7% (p = 0.004 each), while platelet count and PCT were higher in those with HbA_{1c} < 7% (p = 0.049 and p = 0.026, respectively). No significant variation in PDW was observed between the two groups.

Table 6. Platelet indices in T2DM patients with DR according to HbA_{1c} levels

Platelets Indices (Units)	HbA _{1c} <7% (Mean ± SD)	HbA _{1c} >7% (Mean ± SD)	P-value
Platelet Count (10 ³ /μL)	308.00 ± 93.40	274.88 ± 70.82	0.049*
MPV (fL)	9.84 ± 0.73	10.36 ± 1.02	0.004*
PDW (fL)	13.05 ± 3.81	13.56 ± 2.45	0.428
P-LCR (%)	24.29 ± 5.86	28.24 ± 7.47	0.004*
PCT (%)	0.30 ± 0.079	0.27 ± 0.05	0.026*
*Indicate P<0.05 for statistical significance.			

Discussion

In this study of 200 subjects, 80 had diabetic retinopathy, 60 had type 2 diabetes mellitus without DR, and 60 served as healthy controls, DR was present in 40% of diabetic patients, a prevalence higher than that reported in the CURES study (17.6%)¹⁴, but comparable to Saudi data (35.8%). The majority of DR cases occurred in individuals over 50 years, highlighting age as a major risk factor, consistent with observations by NabajaniDutta¹⁵ and Singh and Prasad¹⁶. A slight female predominance (55%) was noted among DR patients, which agrees with the findings of Long et al.¹⁷. Collectively, these results emphasize the role of poor glycemic control, advanced age, and female sex in the development of DR.

Our study highlights a consistent pattern: patients with diabetic retinopathy exhibited higher level of MPV, PDW, and P-LCR when compared to healthy controls. To further explore their role in retinopathy, we compared diabetics with and without the condition. Although MPV exhibited only a slight, non-significant increase, both PDW and P-LCR were markedly elevated in individuals with retinopathy. Hyperglycemia contributes to these changes by inducing platelet glycation, endothelial dysfunction, and inflammation, thereby enhancing platelet activity¹⁸. Monitoring platelet indices may therefore aid in the early detection of complications such as retinopathy. Elevated PDW, MPV, and P-LCR reflect the presence of larger, more active platelets and signal an increased risk of vascular complications, Providing a simple and cost-effective approach for identifying high-risk patients.

Platelet indices including MPV, PDW, P-LCR, and PCT are valuable markers of platelet activation and vascular risk in Type 2 diabetes. These routinely available hematological parameters reveal morphological and functional platelet changes that precede thrombotic events, making them useful tools for early detection and intervention. Elevated MPV is strongly associated with thrombotic risk, increased PDW indicates abnormal platelet production, and higher PCT reflects advancing atherosclerosis and thrombosis. Multiple studies support these findings: Ogbuaboret al.¹⁹ observed significantly raised MPV, PDW, and PCT in diabetics compared to controls, Shilpi and Potekar²⁰ reported higher MPV, PDW, and P-LCR among diabetics; and Khanna P. et al.²¹ confirmed that elevated platelet indices reliably predict early vascular complications. Collectively, this evidence highlights platelet indices as cost-effective, accessible, and clinically meaningful markers in the pathophysiology and management of diabetes.

The study highlights that inadequate glycemic control and longer duration of diabetes are major contributors to the development of DR. A strong link between HbA1c levels above 7% and DR underscores the role of persistent hyperglycemia in driving microvascular injury through processes such as glycation, oxidative stress, and endothelial dysfunction. The greater occurrence of DR in individuals with diabetes for over 10 years indicates the cumulative burden of chronic hyperglycemia on retinal vessels. These observations align with earlier research that emphasized HbA1c elevation and prolonged disease duration as critical factors in DR progression. Overall, the findings emphasize the need for optimal glycemic regulation and early intervention to reduce the risk or delay the onset of retinopathy.

In our study, elevated HbA1c levels were associated with altered platelet indices, reflecting a link between glycemic control and platelet activation. Among T2DM patients without DR,

There were no statistically significant variations in platelet count, MPV, PDW, P-LCR, or PCT when comparing patients with HbA_{1c} <7% to those with HbA_{1c} >7%, indicating that poor glycemic control alone may not substantially affect platelet activity in the absence of retinal changes. In contrast, among patients with DR, several platelet indices differed significantly between the HbA_{1c} groups. MPV, P-LCR, and PCT were increased in patients with HbA_{1c} >7%, while platelet count was higher in the HbA_{1c} <7% group, suggesting that poor glycemic control in individual with retinopathy is associated with heightened platelet activation. Our findings indicate that platelet abnormalities intensify with the development of microvascular complications, particularly diabetic retinopathy, underscoring the need to monitor glycemic control together with hematological markers in the management of diabetes.

Among patients with diabetic retinopathy, a significant increase was observed in MPV and P-LCR in those with poor glycemic control (HbA_{1c} >7%). MPV reflects platelet activation, whereas P-LCR indicates a higher proportion of large, reactive platelets. Their elevation in DR suggests enhanced platelet reactivity, which may aggravate microvascular damage and contribute to disease progression. Similar associations between raised MPV, P-LCR, and microvascular complications in diabetes have been documented by Walinjar et al.²² and Khanna et al.²³

Interestingly, patients with diabetic retinopathy and HbA_{1c} <7% showed higher platelet count and PCT values, suggesting a possible compensatory response or altered platelet turnover in advanced stages of retinopathy. Our observations align with those reported by Taderew et al.²⁴, who noted reduced platelet count but increased MPV in poorly controlled diabetic patients with retinopathy, indicating platelet consumption and release of younger, larger platelets. Overall, our findings demonstrate that poor glycemic control, longer disease duration, and changes in platelet indices are linked to the pathogenesis of diabetic retinopathy, suggesting that these parameters could serve as accessible and cost-effective markers for early risk assessment.

Strengths and Limitations of the Study

An important strength of the present study is its comprehensive assessment of glycemic status and platelet indices in relation to diabetic retinopathy, providing novel insights into the potential role of routine hematological markers in early risk stratification. The inclusion of healthy controls, diabetic patients without retinopathy, and diabetics with retinopathy allowed meaningful group comparisons that strengthen the validity of the findings.

However, this study has some limitations. As a single-center, cross-sectional study with a modest sample size, the findings may have limited generalizability and do not allow for establishing causality. Potential confounders such as treatment adherence, lifestyle factors, and comorbidities were not fully accounted for. In addition, only routine platelet indices were assessed.

Conclusion

The findings of this study indicate that poor glycemic regulation and a longer duration of diabetes are key contributors to the onset of diabetic retinopathy. Elevated glucose levels and higher HbA_{1c} were associated with more severe disease. Platelet indices, particularly MPV, PDW, P-LCR, and PCT, reflected early changes in platelet activation and vascular risk. Among these, PDW and P-LCR were significantly increased in patients with DR, while both MPV and P-LCR rose with poor glycemic control. These observations highlight that routine evaluation of glycemic markers together with platelet indices offers a practical and cost-effective approach for the early detection and may serve as useful markers for assessing the risk of complications in patients with type 2 diabetes.

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Conflicts of Interest

The authors declare no conflicts of interest.

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