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ORIGINAL ARTICLE

The Association and Clinical Implication of Hematological Inflammation Biomarkers and CRP in Diabetic Retinopathy Patients

N P Arul[1]*, Vasukidevi Ramachandran[2]

1 Department of Biochemistry, Bharath Institute of Higher Education and Research, Selaiyur, Chennai-600073, Tamil Nadu, India
2 Department of Bio-Tech & Microbiology, Bharath Institute of Higher Education and Research, Selaiyur, Chennai-600073, Tamil Nadu, India

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* **Corresponding author**.

dhasannavan@gmail.com

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Abstract

Objective: Diabetic retinopathy (DR) is a major complication of diabetes, arising from chronic hyperglycemia that damages retinal blood vessels and can lead to blindness. While inflammation is implicated, its role remains unclear. This study aimed to investigate the relationship between haematological inflammation markers and C-reactive protein (CRP) in DR patients. **Methods:** A total of 175 participants (aged 25–75 years; 82 males, 93 females) were enrolled. Group I included DR patients (n = 75; mean age 59.33 $\pm$ 6.35 years), Group II comprised diabetic patients without retinopathy (n = 50; mean age 53.92 $\pm$ 11.79 years), and Group III consisted of age- and sex-matched controls (n = 50; mean age 50.28 $\pm$ 11.96 years). Hematological parameters and CRP were measured and compared across groups. **Findings:** DR patients exhibited significantly higher neutrophil-to-lymphocyte ratio (NLR: 2.724 $\pm$ 0.93; p < 0.0001) compared with controls. Absolute neutrophil count (ANC), red cell distribution width (RDW-SD), mean platelet volume (MPV), platelet large cell ratio (P-LCR), and CRP levels were also elevated in DR patients. A positive correlation was observed between NLR and CRP. **Novelty:** Complete blood count (CBC) tests, which measure red blood cell, white blood cell, and platelet parameters, are routinely performed in all healthcare settings. NLR reflects an imbalance between pro-inflammatory neutrophils and protective lymphocytes, while elevated CRP indicates vascular inflammation, both contributing to retinal damage DR. This study investigates associations of CBC-derived inflammatory markers (RDW, ANC, ALC, NLR, MPV, PDW, P-LCR) and CRP with DR, and further explores their relationships with HbA1c and diabetes duration to support early detection and monitoring of inflammation in DR.

Keywords: ANC; C-reactive protein; Diabetic Retinopathy; NLR; Type 2 Diabetes mellitus

1 Introduction

Diabetic retinopathy is a chronic microvascular complication of diabetes, in which prolonged hyperglycemia results in progressive retinal vessel injury and eventual vision impairment[1]. Globally, diabetes prevalence is estimated at 9.3%, with Indian prevalence ranging between 15–19%[2]. In India, type 2 diabetes mellitus (T2DM) affects approximately 8.9% of the population, and the SMART India study reported a national prevalence of DR of 12.5%, with vision-threatening DR (VTDR) accounting for 4.0–4.8%[3].

Diabetic retinopathy progresses through two main stages: non-proliferative (NPDR) and proliferative (PDR). NPDR is characterized by microaneurysms resulting from abnormal capillary permeability and non-perfusion. Fluid leakage can lead to macular edema, a major cause of vision impairment. PDR develops when extensive capillary occlusion induces retinal ischemia, stimulating the growth of fragile neovascular vessels prone to hemorrhage. Blood accumulation in the vitreous cavity may severely compromise vision and, in advanced cases, cause tractional retinal detachment[4]. In recent years, there has been growing interest in hematological and inflammatory biomarkers that may elucidate the pathophysiology and progression of DR. Among these, the NLR and PLR have emerged as simple indicators of systemic inflammation and immune dysregulation. NLR reflects the balance between pro-inflammatory neutrophils and protective lymphocytes, whereas PLR highlights the interplay between platelets and lymphocytes[5]. Inflammatory processes typically elevate total white blood cell (WBC) and neutrophil counts while suppressing lymphocyte levels[6]. Additionally, studies have reported a positive association between MPV and DR, while platelet distribution width (PDW), another marker of platelet activation, has shown inconsistent findings[7].

CRP is an important acute-phase protein and is commonly used as an indicator of systemic inflammation. It has established diagnostic and prognostic value in musculoskeletal, hepatic, and renal disorders, but its role in diabetes and its complications remains less clearly defined. In the context of DR, CRP is particularly relevant because of its association with endothelial dysfunction, an important early event in microvascular injury. CRP is synthesized primarily in hepatocytes under the stimulation of pro-inflammatory cytokines, especially those derived from adipocytes in response to hyperglycemia. Raised CRP concentrations have been associated with the development of type 2 diabetes and its complications, including a possible role in DR[8]. However, clinical studies evaluating the relationship between CRP and DR have produced inconsistent findings. While CRP has been shown to correlate with hyperglycemia and HbA1c levels, it is not consistently elevated in all DR patients, limiting its reliability as a standalone screening marker. These discrepancies suggest that CRP may serve better as part of a combined biomarker panel rather than an isolated indicator. Larger, longitudinal studies are therefore needed to validate its predictive value and to identify complementary inflammatory markers that may enhance the early detection of DR[9].

Diabetic retinopathy is a leading cause of global vision loss. Naveen Nishal G et al[10] reported an association between CRP and DR severity. While some studies link CRP levels to DR stages in type 2 diabetes mellitus, others suggest that higher CRP and BMI may correlate with reduced DR risk. Such inconsistencies may reflect ethnic variations in CRP/BMI, as well as unaccounted factors such as diabetes duration and environmental influences.

Conventional hemogram-derived biomarkers such as RDW, ANC, ALC, NLR, MPV, PDW, P-LCR serve as potential indicators of inflammation and diabetes progression[11]. MPV, an indicator of platelet activation, tends to be higher in individuals with type 2 diabetes mellitus and diabetic nephropathy, and its elevation is linked to greater cardiovascular risk[12]. RDW, reflecting variability in red blood cell size, indicates inflammation and oxidative stress across several conditions, including poorly controlled diabetes[13]. NLR, a marker of systemic inflammation, is elevated in chronic inflammatory states such as T2DM and correlates with insulin resistance and diabetic complications, making it a valuable prognostic indicator[14].

Markers such as ANC, NLR, and CRP are simple and inexpensive to measure; their correlation with DR progression remains inconsistent, limiting their routine clinical use[15]. More sensitive and specific biomarkers are therefore needed to enhance risk stratification and long-term disease management. Addressing this gap, the present study investigates the combined utility of CRP and NLR in relation to key risk factors, including diabetes duration and HbA1c. Such combined inflammatory markers may improve predictive accuracy, aid in identifying high-risk patients, and serve as valuable tools for monitoring therapeutic outcomes.

A complete blood count, routinely performed in healthcare settings, provides red cell, white cell, and platelet indices. However, studies assessing the impact of diabetic retinopathy on these hematological parameters have produced conflicting results. Research on markers such as ANC, NLR, and CRP in T2DM-related retinopathy remains limited, particularly in developing regions like India. This study evaluates the association of hematological inflammatory markers (ANC, ALC, NLR, RDW-SD, MPV, PDW, and P-LCR) and CRP in T2DM patients with and without DR compared to healthy controls, with the aim of identifying cost-effective diagnostic indicators. It further examines the correlation of CRP with NLR, HbA1c, and diabetes duration across CRP quartiles to improve risk prediction. This novel approach may provide a framework for early diagnosis and assessment of inflammatory burden in DR. This study is, to our knowledge, the first of its kind to be conducted in a tertiary eye care centre in South Chennai.

2 Methodology

A cross-sectional study was performed at the ophthalmology outpatient department of Sankara Eye Hospital, Chennai, covering the period from March 2024 to January 2025. Ethical clearance was obtained from the Institutional Ethics Committee (SEH/IEC/MOPT-11/2024; dated 21.02.2024), and the research was conducted in line with institutional ethical principles. Written informed consent was secured from all study subjects.

Sample size determination was performed using the formula $n = (Z^2 \times P \times (1-P))/d^2$, where Z denotes the standard normal variate corresponding to the desired confidence level (1.96 for 95%), P represents the assumed prevalence of diabetic retinopathy (13%), and d indicates the allowable error (5%). On substitution, the calculation yielded $n = (1.96^2 \times 0.13 \times 0.87)/0.05^2 \approx 174$, which was rounded up to 175 participants.

Participants were split into three groups-

Group I: Type2 diabetics with retinopathy (n=75)

Group II: Type2 diabetics without retinopathy (n=50)

Group III: Non-diabetic age/sex-matched controls (n=50)

Additionally, the study examined the relationship between CRP levels and the risk factors associated with the development of retinopathy across three separate quartiles categorized by CRP concentration: normal (Q1, <10 mg/L), mild elevation (Q2, 10–20 mg/L), and moderate elevation (Q3, >30 mg/L).

The present research investigates hematological inflammatory markers and CRP in individuals with and without diabetic retinopathy, compared to control subjects. A purposive sampling strategy was applied, yielding 175 participants who met specific inclusion and exclusion criteria.

2.1 Inclusion Criteria

This study including both male and female type 2 diabetes patients, 25-75 years old, with and without diabetic retinopathy

2.2 Exclusion Criteria

- Type 1 diabetes
- T2DM with acute or chronic inflammatory conditions (e.g., fever, bronchitis, asthma, tuberculosis, rheumatoid arthritis, psoriasis)
- History of cataract surgery, glaucoma, thrombocytopenia, or platelet disorders
- Gestational diabetes mellitus
- Chronic kidney disease

All eligible participants underwent a comprehensive clinical evaluation, including demographic details, diabetes duration, treatment history with oral hypoglycemic agents, and comorbidities such as hypertension. Each patient received a complete ophthalmic examination comprising visual acuity assessment and detailed fundus evaluation using both direct and indirect ophthalmoscopy. The control group (non-diabetics without retinopathy) was not re-examined during the 11-month study period, consistent with established screening protocols[16].

2.3 Laboratory Investigations

Blood samples were collected in in EDTA (ethylenediaminetetraacetic acid) tubes for HbA1c and CBC tests, and in plain tubes for biochemical assays, including glucose and C-reactive protein (CRP). Appropriate collection tubes were used to prevent cross-contamination and ensure analytical accuracy. CBC was performed using the SYSMEX XP-100 three-part automated cell counter based on electronic impedance-Coulter technology. HbA1c levels were measured with the GH-900 plus Hemoglobin A1C Analyzer, a fully automated HPLC system, while biochemical assays and CRP estimation were carried out using the Vitros 250 Automatic Dry Chemistry Analyzer employing micro slide technology. This sophisticated equipment's ensured reliable and accurate laboratory results.

2.4 Statistical Analysis

Clinical data were documented using a structured proforma and entered into Microsoft Excel. Statistical analyses were performed with Social Science Statistics for Windows. Continuous variables are presented as mean $\pm$ standard deviation (SD), while categorical variables are shown as frequencies and percentages. Comparisons between groups were made using

the Chi-square test for categorical data and one-way ANOVA for continuous data. A p-value < 0.05 was regarded as statistically significant.

3 Results and Discussion

3.1 Base line demographic and Clinical Characteristics

This study included 175 participants aged 25–75 years, comprising 82 males (46.9%) and 93 females (53.1%) (Figure 1). No significant differences in age or sex distribution were observed across the three study groups. The gender-wise distribution of participants within each group is presented in Figure 2.

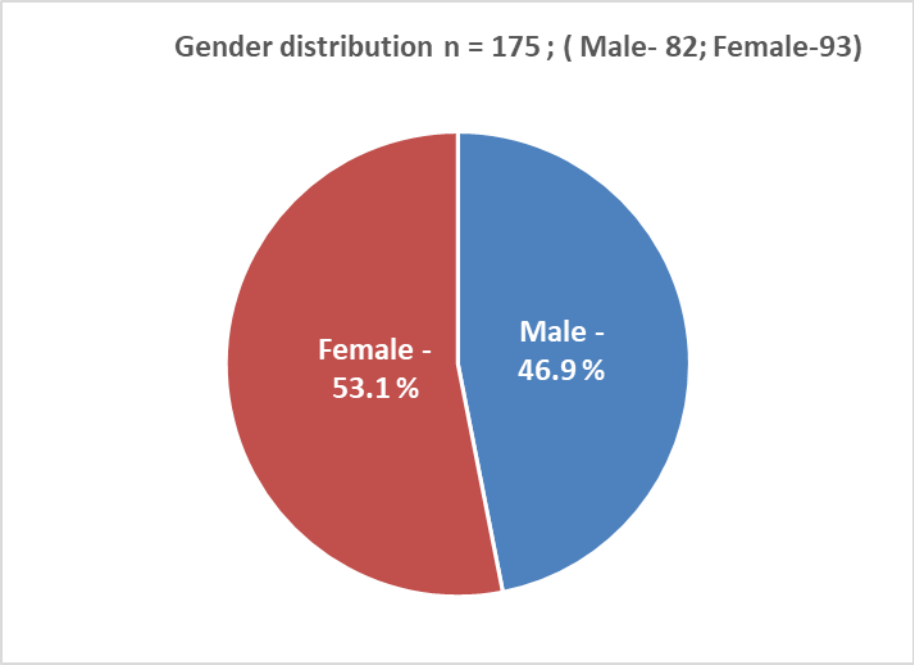

Fig 1. Gender distribution of the study population

The mean age of patients with diabetic retinopathy was 59.33 ± 6.35 years, compared to 50.28 ± 11.96 years in the control group. Among diabetic patients without retinopathy, the mean age was 53.92 ± 11.79 years. Body mass index (BMI) was significantly higher in individuals with type 2 diabetes mellitus, particularly in those with retinopathy (27.11 ± 4.55 kg/m^2), compared to diabetics without retinopathy (26.37 ± 3.99 kg/m^2) and healthy controls (24.37 ± 3.20 kg/m^2), as shown in Table 1.

Table 1. Demographic characteristics of each group

Parameter	Group – I T2 DM + DR	Group – II T2DM	Group – III Control	Total no & (%)
Age (Years) Mean / SD	59.33 ± 6.35	53.92 ± 11.79	50.28 ± 11.96	
Male (n & %)	36 (48%)	22 (44%)	24 (48%)	82 (46.86%)
Female (n & %)	39 (52 %)	28 (56%)	26 (52%)	93 (53.14%)
BMI (Mean / SD)	27.11 ± 4.55	26.3657 ± 3.99	24.37 ± 3.20	175 (100%)

Abbreviations: *T2DM: Type 2 Diabetes mellitus; DR: Diabetic Retinopathy BMI: Body Mass Index*

The age distribution of the 175 participants was as follows: 5 participants (2.9%) were in the 25–34 year group, 23 (13.1%) in the 35–44 year group and 47 (26.9%) in the 45–54 year group. The largest proportion was observed in the 55–64-year group, comprising 68 participants (38.9%), while 32 participants (18.3%) were in the 65–75-year group. Among participants with T2DM and retinopathy (Group I), most were in the 55–64 year age group (23.4%), followed by 9.1% in the 65–75 year group.

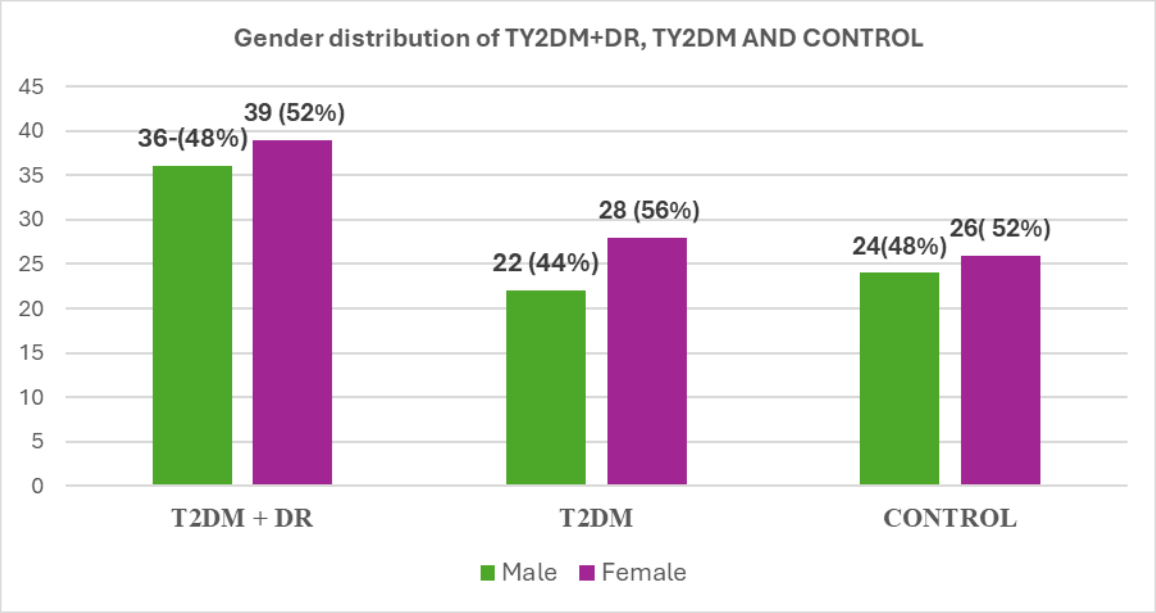

Fig 2. Gender distribution among study groups

In contrast, healthy controls (Group III) were predominantly clustered in the 35–44 year range (9.1%), with relatively fewer individuals aged $\geq$ 65 years. These distributions are summarized in Table 2.

Table 2. Distribution of age groups

Ranging of Age	Group – I T2DM + DR	Group – II T2DM	Group – III Control	Total no (%)
25-34	0	3 (1.71)	2 (1.14)	5 (2.85)
35-44	1 (0.57)	6 (3.43)	16 (9.14)	23 (13.14)
45-54	17 (9.72)	15 (8.57)	15 (8.57)	47 (26.86)
55-64	41 (23.43)	18 (10.29)	9 (5.15)	68 (38.86)
65-75	16 (9.14)	8 (4.57)	8 (4.57)	32 (18.29)
	75	**50**	**50**	**175 (100)**

3.2 Biochemistry Baseline Parameters

Healthy controls demonstrated mean fasting and postprandial glucose levels of 92.0 $\pm$ 10.72 mg/dL and 117.79 $\pm$ 17.86 mg/dL, respectively. In contrast, patients with type 2 diabetes exhibited significantly elevated values (fasting: 146.87 $\pm$ 42.84 mg/dL; postprandial: 215.67 $\pm$ 67.46 mg/dL). Participants with diabetic retinopathy showed the highest levels (fasting: 151.75 $\pm$ 51.81 mg/dL; postprandial: 224.98 $\pm$ 84.75 mg/dL), with $P < 0.0001$ for both comparisons. Similarly, HbA1c levels were markedly different across groups: 5.54 $\pm$ 0.31% in controls, 8.10 $\pm$ 1.69% in diabetics without retinopathy, and 8.38 $\pm$ 1.71% in those with retinopathy ($P < 0.001$) as illustrate is Table 3.

Our findings indicate a consistent pattern in glycemic control, with normoglycemia in controls, hyperglycemia in diabetic patients, and the highest levels in those with retinopathy. The HbA1c results reinforce this trend, highlighting its utility as a reliable biomarker of chronic glycemic control. Our results are consistent with the findings of Chirag Singh et al.[17], who demonstrated a significant association between HbA1c levels and both the occurrence and severity of retinopathy. Compared with isolated glucose measurements, HbA1c provides a more robust indicator of long-term glycemic exposure and its role in retinopathy progression.

Table 3. Mean and SD values of biochemical and hematological parameters, and CRP using one-way ANOVA

Parameter	Group – I T2DM + DR	Group – II T2DM	Group – III Control	P-Values
Biochemical Baseline Parameters for Diabetes				
FBG (mg/dl)	151.75 ± 51.81	146.87 ± 42.84	92.0 ± 10.72	< **0.0001***
PPBG (mg/dl)	224.98 ± 84.75	215.67 ± 67.46	117.79 ± 17.86	< **0.0001***
HBA1c (%)	8.38 ± 1.71	8.10 ± 1.69	5.54 ± 0.31	< **0.0001***
RBC Indices				
MCV (fL)	88.10 ± 6.37	84.53 ± 11.22	86.50 ± 13.50	0.1673
MCH (pg)	28.11 ± 2.91	26.91 ± 3.6	27.71 ± 3.68	0.1541
MCHC (g/dl)	31.84 ± 1.70	30.89 ± 1.79	31.06 ± 1.67	**0.0045***
RDW SD (fL)	46.07 ± 4.38	44.74 ± 3.26	43.40 ± 2.42	**0.0003***
RDW-CV (%)	13.84 ± 4.38	13.7 ± 1.76	13.44 ± 4.38	0.4045
WBC Indices				
Total WBC (10^3 / uL)	9.05 ± 3.34	8.26 ± 1.56	7.41 ± 1.70	0.0006*
ANC (10^3 / uL)	5.80 ± 1.69	5.07 ± 1.26	4.35 ± 1.23	< **0.0001***
ALC (10^3 / uL)	2.24 ± 0.65	2.51 ± 0.62	2.46 ± 0.56	**0.0298***
N to L Ratio	2.724 ± 0.93	2.11 ± 0.64	1.81 ± 0.54	< **0.0001***
Platelets indices				
Platelets Count (10^3 / uL)	277.64 ± 83.1	278.21 ± 81.72	302.83 ± 106.05	0.2551
MPV (fL)	10.22 ± 1.17	9.96 ± 0.79	9.71 ± 0.93	**0 .0213***
PDW (fL)	13.30 ± 2.99	12.519 ± 1.6	12.08 ± 1.82	**0.0155***
P-LCR (%)	27.08 ± 9.03	24.36 ± 6.25	22.81 ± 6.91	**0.0086***
C-Reactive Protein				
CRP (mg/L)	19.61 ± 9.5	16.66 ± 6.75	9.47 ± 5.2	< **0.0001***

* 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); Mean corpuscular volume (MCV); Mean Corpuscular Hemoglobin (MCH); Mean Corpuscular Hemoglobin Concentration (MCHC); Red cell distribution width (RDW); White Blood Cell (WBC) :ANC (Absolute Neutrophils Count).ALC, Absolute Lymphocytes Count; N to L Ratio N/L, neutrophil/lymphocyte; MPV (mean platelet volume), PDW (platelet distribution width), P-LCR (platelet large cell ratio), CRP (C-Reactive Protein).

3.3 RBC indices

Significant differences were observed in red blood cell indices between groups. DR patients showed higher MCHC (31.84 ± 1.70, $P = 0.0045$) and RDW-SD (31.84 ± 1.70, $P = 0.0003$) compared to controls. In contrast, MCV (88.10 ± 6.37, $P = 0.167$) and MCH (28.11 ± 2.91, $P = 0.1541$) were slightly higher in DR patients but did not reach statistical significance (P = 0.167 and P = 0.1541) (Table 3).

These findings highlight the clinical relevance of specific RBC parameters in the context of diabetic retinopathy. While MCV and MCH showed no meaningful differences, the significant elevations in RDW-SD and MCHC suggest altered erythropoiesis and underlying inflammatory processes. Elevated HbA1c has been strongly associated with increased variability in red blood cell size, reflecting erythropoietic stress [18], [19]. Furthermore, inflammation a hallmark of diabetes plays a key role in modulating RDW values, thereby contributing to disease progression [20]. Previous studies have shown that poorly controlled diabetes is frequently accompanied by elevated RDW, which is associated with complications including retinopathy, nephropathy, and cardiovascular disease [21]. Taken together, our results indicate that RDW-SD, in particular, may serve as a valuable hematological marker for assessing diabetic retinopathy and could complement existing diagnostic approaches.

3.4 WBC Indices

Patients with diabetic retinopathy demonstrated significantly reduced ALC levels (2.24 ± 0.65; P = 0.0298) compared to controls. Conversely, total WBC count (9.05 ± 3.34; P = 0.0006), ANC (5.80 ± 1.69; P < 0.0001), and NLR (2.72 ± 0.93; P < 0.0001) were markedly elevated in DR patients (Table 3).

Our findings highlight the role of white blood cell indices in the inflammatory profile of diabetic retinopathy. Elevated ANC and NLR in DR patients compared to healthy controls suggest an enhanced systemic inflammatory response. Notably, the reduction in ALC further contributes to this imbalance. The NLR, in particular, offers a simple and cost-effective alternative to cytokine assays (e.g., interleukin-6) for assessing inflammation. According to a 2023 review by Rafaqat and Rafaqat[22] emphasized its potential as a practical biomarker for systemic inflammation and diabetes severity. Similarly, increased neutrophil counts have been linked to both the presence and progression of DR, reinforcing inflammation's central role in its pathogenesis. Taken together, our results support the clinical utility of ANC and NLR as accessible hematological indicators that may complement traditional markers in the assessment of diabetic retinopathy.

3.5 Platelets indices

Platelet indices demonstrated elevated mean values in cases compared to controls: MPV (10.22 ± 1.17; P = 0.0213), PDW (13.30 ± 2.99; P = 0.0155), and P-LCR (27.08 ± 9.03; P = 0.0086). Among patients with DR, the mean platelet count (277.64 ± 83.1) was lower than that of the control group; however, the difference was not statistically significant (p = 0.2551) (Table 3).

Our study identified significant increases in platelet activation markers such as MPV, PDW, and P-LCR among individuals with diabetic retinopathy compared to healthy controls. These findings align with prior studies by Waghale and Khot[23], who also reported elevated MPV and P-LCR in patients with T2DM. Notably, DR patients exhibited higher values than diabetics without retinopathy, supporting the association between platelet dysfunction and micro vascular complications. The P-LCR, which reflects the proportion of large platelets (>12 fl), is particularly relevant, as elevated values of P-LCR and PDW may indicate increased peripheral platelet destruction and turnover. This suggests enhanced platelet activation in DR, a phenomenon previously linked to hyperglycemia-induced glycation, endothelial dysfunction, and inflammatory stress[24].

Overall, these findings suggest that platelet indices may serve as affordable markers for the early identification of complications in T2DM. Regular assessment of MPV, PDW, and P-LCR could help detect individuals at increased risk of retinopathy, facilitating timely interventions and better disease management.

3.6 CRP

Mean CRP levels (mg/L) were significantly elevated in patients with diabetic retinopathy (19.61 ± 9.5) compared with those without retinopathy (16.66 ± 6.75) and healthy controls (9.47 ± 5.2; P < 0.0001) (Table 3). Moreover, CRP levels showed a positive correlation with NLR (r = 0.28, R^2 = 0.08, P = 0.014), indicating a positive association between elevated CRP and NLR in patients with diabetic retinopathy (Figure 3).

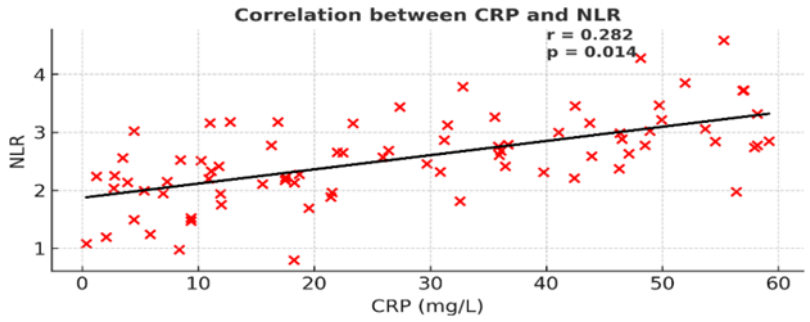

Fig 3. Correlation between CRP and NLR among study participants

The Chi-square analysis demonstrated a significant association between CRP levels and the presence of DR. The duration of diabetes was also significantly related to CRP distribution, with patients having diabetes for >10 years showing a higher proportion with CRP >20 mg/L compared with those with <10 years' duration (57.1% vs. 31.6%; p = 0.0167). Similarly, patients with DR exhibited higher CRP levels, with 40% falling into the >20 mg/L group compared with 30% of diabetics without DR (p

= 0.0060). In contrast, no significant difference in CRP distribution was observed between NPDR and PDR stages (p = 0.4763) (Table 4).

Table 4. Association of CRP levels (mg/L) with duration of diabetes and diabetic retinopathy status using Chi-square test

Risk Factor	Variable	Total n (%)	CRP < 10.0 n (%)	CRP 10–20 n (%)	CRP >20.0 n (%)	P-values
Duration of Diabetics	<10 Years	76 (60.8)	10 (13.2)	42 (55.2)	24 (31.6)	0.0167*
	>10 Years	49(39.2)	5 (10.2)	16 (32.7)	28 (57.1)	
T2DM and DR	DM no DR	50 (40)	17 (34)	18 (36)	15 (30)	0.0060*
	DR	75 (60)	8 (10.7)	37 (49.3)	30 (40)	
Stages of Retinopathy	NPDR	51 (68)	6 (11.76)	27 (52.94)	18 (35.3)	0.4763
	PDR	24 (32)	2 (8.33)	10 (41.67)	12 (50)	

** Indicate P<0.05 for statistical significance*

Abbreviations: *CRP: C-reactive protein; DM: diabetes mellitus; DR: diabetic retinopathy; NPDR: non-proliferative diabetic retinopathy; PDR: proliferative diabetic retinopathy*

Among the glycemic indices, HbA1c levels showed a significant increase across CRP quartiles (7.51 ± 0.69 in Q1, 8.23 ± 1.50 in Q2, and 9.03 ± 1.96 in Q3; $P = 0.0373$). Similarly, NLR was significantly higher in patients with elevated CRP (1.99 ± 0.49 in Q1 vs. 2.91 ± 0.81 in Q3; $P = 0.0419$). Although ANC tended to rise and ALC declined with increasing CRP levels, these trends did not reach statistical significance (Table 5).

Table 5. Comparison of biochemical and hematological parameters across CRP categories (mg/L) using one-way ANOVA test

Parameter	Q1- CRP <10.0 mg/L	Q2- CRP 10–20 mg/L.	Q3 - CRP >20 mg/L	F-Values	P-Values
Duration of DM	10 ± 4.81	10.41 ± 6.73	11.3 ± 7.10	1.82	0.8230
FBG (mg/dl)	137 ± 26.7	149.62 ± 56.2	157.16 ± 51.93	0.50656	0.6046
PPBG (mg/dl)	198.67 ± 41.47	220.12 ± 80.73	234.88 ± 90.37	0.63968	0.5304
HBA1C (%)	7.51 ± 0.69	8.23 ± 1.50	9.03 ± 1.96	3.4411	**0.0373***
ANC (10^3 / uL)	5.1 ± 1.47	5.83 ± 1.70	6.01 ± 1.73	0.90694	0.4083
ALC (10^3 / uL)	2.7 ± 1.17	2.22 ± 0.57	2.12 ± 0.51	2.58014	0.0827
NLR	1.99 ± 0.49	2.75 ± 1.01	2.91 ± 0.81	3.3149	**0.0419***

** Indicate P<0.05 for statistical significance*

CRP is a readily measurable marker of inflammation and has been extensively investigated for its association with systemic diseases. Elevated CRP levels are consistently linked to an increased risk of atherosclerosis, cardiovascular disease, and diabetes. Our findings demonstrate a clear association between inflammation and the severity of diabetes. Patients with elevated CRP levels (>20.0 mg/L) showed worse clinical outcomes, including longer disease duration, poorer glycemic control (higher fasting glucose and HbA1c), and impaired immune function. Conversely, lower CRP levels (<10 mg/L) were associated with better metabolic and immunological profiles, suggesting that inflammation contributes to diabetes progression. While many parameters exhibited consistent trends, significant differences in HbA1c, NLR, and diabetic retinopathy provide strong evidence of inflammation's impact on immune dysregulation in diabetes. Previous studies by Yang XF et al.[25] and Chavda PB et al. similarly reported significant associations between elevated CRP and increased HbA1c. Our study further identified correlations between HbA1c and NLR across CRP strata, as well as relationships among CRP, NLR, and HbA1c levels in patients with and without DR. Comparable findings were reported by Nishal DG et al.[26], emphasizing NLR's influence across varying levels of glycemic control.

Our study demonstrates that an elevated NLR, characterized by reduced lymphocytes and increased neutrophils, is directly correlated with CRP levels in patients with diabetic retinopathy. This association was most evident among those with poorly controlled diabetes. These findings extend prior research, which largely focused on CRP in relation to general leukocyte indices, by highlighting NLR and CRP as predictive biomarkers of inflammation and potential complications in inadequately controlled diabetes, rather than merely as indicators of glycemic status. Furthermore, our results indicate that MCV, MCH, and platelet counts are not sensitive markers for DR, consistent with the observations of Ginoudis et al.

Diabetic retinopathy is a microvascular complication of diabetes characterized by damage to the retinal vessels, with inflammation playing a pivotal role in its onset and progression [27]. Previous studies have reported significantly higher RDW levels in patients with DR compared with diabetics without retinopathy. NLR, an established marker of systemic inflammation, has also been linked to an elevated risk of DR [28]. Furthermore, elevated platelet indices such as MPV, PDW, and P-LCR may serve as early indicators of vascular complications in type 2 diabetes mellitus [29].

Our findings align with previous studies showing that hematological indices including RDW, ANC, ALC, NLR, MPV, PDW, and P-LCR are significantly associated with diabetic retinopathy. We also observed a notable correlation between CRP and NLR, supporting the role of inflammation in DR pathogenesis. Furthermore, longer diabetes duration and poor glycemic control were linked to an increased risk of retinopathy. These inflammatory markers may enhance risk assessment and monitoring, providing valuable tools for evaluating disease progression. Notably, routine, low-cost tests such as CBC and CRP offer accessible biomarkers for the early detection and management of DR.

This study has two main limitations. First, the relatively small sample size may restrict the generalizability of our findings. Second, we did not evaluate the relationship between CRP levels and the different stages of diabetic retinopathy (mild, moderate, and severe), which could offer further insight into disease progression

4 Conclusion

This study highlights that the prolonged duration of diabetes and poor glycemic control are primary risk factors for the development of diabetic retinopathy. Significant associations were also observed between DR and hematological inflammatory markers, including RDW, MPV, PDW, P-LCR, ALC, ANC, NLR, and CRP, underscoring their potential value as indicators of both disease onset and progression. Notably, the strong correlation between CRP and NLR further supports the role of subclinical systemic inflammation in DR pathogenesis. Therefore, routine assessment of these inflammatory markers, together with glucose and HbA1c monitoring, may provide a simple, cost-effective strategy for earlier detection, improved risk stratification, and slowing the progression of diabetic retinopathy.

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