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A Cross-Sectional Study of Red Cell Distribution width and Neutrophil Lymphocytes Ratio as a Marker for Detection of Diabetic Retinopathy at Dr B R Ambedkar Medical College and Hospital, Bengaluru.

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Abstract

Background: Diabetic retinopathy (DR) is one of the most common microvascular complications of diabetes mellitus and a leading cause of preventable blindness worldwide. Chronic inflammation and oxidative stress play an important role in the pathogenesis of DR. Red cell distribution width (RDW) and neutrophil–lymphocyte ratio (NLR) are inexpensive inflammatory hematological markers derived from routine blood investigations. ***OBJECTIVES:*** To assess the association of RDW and NLR with diabetic retinopathy among patients with type 2 diabetes mellitus. ***METHODS:*** This hospital-based cross-sectional study was conducted among 170 patients with type 2 diabetes mellitus attending Dr. B. R. Ambedkar Medical College and Hospital, Bengaluru, between April 2024 and April 2025. Detailed demographic and clinical data were collected. RDW and NLR were obtained from complete blood count analysis. All participants underwent comprehensive ophthalmological evaluation, and diabetic retinopathy was graded according to ETDRS classification. Statistical analysis was performed using SPSS version 21. ***RESULTS:*** Among the 170 participants, 61.76% had no retinopathy, 24.11% had non-proliferative diabetic retinopathy (NPDR), and 14.11% had proliferative diabetic retinopathy (PDR). Mean RDW values showed a significant increase from no retinopathy to PDR (12.38 ± 0.56 vs 13.95 ± 0.30; $p < 0.0001$). Mean NLR was also significantly higher among patients with PDR (4.3 ± 0.32; $p < 0.0001$). RDW and NLR demonstrated significant positive correlations with duration of diabetes, HbA1c, and severity of diabetic retinopathy. ROC analysis showed better diagnostic performance for RDW compared to NLR. ***CONCLUSION:*** RDW and NLR are significantly associated with diabetic retinopathy and may serve as simple, inexpensive inflammatory biomarkers for early detection of diabetic retinopathy among patients with type 2 diabetes mellitus.

Keywords: Diabetic Retinopathy, Red Cell Distribution Width, Neutrophil–Lymphocyte Ratio, Type 2 Diabetes Mellitus.

INTRODUCTION

Diabetes Mellitus (DM) is a major global public health problem and is one of the leading causes of morbidity due to its chronic microvascular and macrovascular complications.[1,2] Among these complications, diabetic retinopathy (DR) remains one of the most common and vision threatening manifestations, accounting for a substantial proportion of preventable blindness among the working age adults worldwide.[3,4] The prevalence of DR continues to rise parallel to the increasing burden of Type 2 DM.[5] Early detection and timely intervention are essential to prevent irreversible visual impairment and improve quality of life among diabetic patients.[6]

The pathogenesis of DR is multifactorial and it involves chronic hyperglycemia induced oxidative stress, endothelial dysfunction, inflammation and microvascular damage. Persistent hyperglycemia causes retinal capillary basement membrane thickening, capillary occlusion and ischaemia leading on to retinal neovascularization and vision loss.[7,8,9] Recent evidences suggest that systemic inflammation plays a major role in development and progression of DR1,[10,11] leading to an increased interest in inflammatory hematological markers as a potential tool for early detection and assessment of disease severity.

Among these markers, neutrophil – lymphocyte ratio (NLR) has emerged as a simple and inexpensive indicator of systemic inflammation. Elevated NLR indicates increased inflammatory activity and oxidative stress and has been associated with several microvascular complications of diabetes.[12,13] Red cell Distribution Width (RDW) is a routinely measured hematological parameter which reflects variation in erythrocyte size and has also been recognized as a marker of inflammation and oxidative stress in the recent years.[14,15]

Since both RDW and NLR are derived from routine blood investigations with much additional cost, they may serve as a practical and economical markers for early detection of diabetic retinopathy especially in resource constraint settings. Hence the present study was undertaken to assess the association of Red cell Distribution Width (RDW) and Neutrophil Lymphocyte Ratio (NLR) with Diabetic Retinopathy (DR) among patients attending Dr B R Ambedkar Medical College and Hospital, Bengaluru.

MATERIALS AND METHODS

This hospital-based cross-sectional study was conducted among patients with type 2 diabetes mellitus attending Dr. B. R. Ambedkar Medical College and Hospital, Bengaluru, during the study period from April 2024 to April 2025. The study was undertaken after obtaining approval from the Institutional Ethics Committee, and written informed consent was obtained from all participants prior to enrolment.

Adult patients aged more than 18 years with previously diagnosed type 2 diabetes mellitus were included in the study. Patients with acute infections, chronic inflammatory disorders, hematological diseases, malignancy, chronic liver disease, autoimmune disorders, recent surgery or trauma, pregnancy, and patients receiving corticosteroids or immunosuppressive therapy were excluded, as these conditions could influence inflammatory hematological parameters. Patients with known retinal diseases other than diabetic retinopathy were also excluded.

The sample size for the study was calculated using the formula Z2p(1-p)/d2, based on the prevalence of diabetic retinopathy reported by Rajiv Raman et al16. A prevalence of 12.5% was considered, with an allowable error of 5% and a 95% confidence interval. The minimum required sample size was estimated to be 168 participants. Accordingly, a total of 170 patients fulfilling the inclusion and exclusion criteria were enrolled in the study using a consecutive sampling technique.

Detailed demographic and clinical data including age, sex, duration of diabetes mellitus, treatment history, smoking status, alcohol consumption, body mass index, blood pressure, and associated comorbidities were recorded using a predesigned and semi-structured proforma. Relevant laboratory investigations including fasting blood sugar, postprandial blood sugar, glycated hemoglobin (HbA1c), serum creatinine, and complete blood count were obtained from hospital laboratory records or performed during the study period.

Venous blood samples were collected under aseptic precautions and analyzed using an automated hematology analyzer. Red cell distribution width (RDW) and differential leukocyte counts were obtained from the complete blood count parameters. Neutrophil–lymphocyte ratio (NLR) was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count.

All participants underwent comprehensive ophthalmological evaluation by an ophthalmologist, including visual acuity assessment, slit lamp examination, intraocular pressure measurement, and dilated fundus examination using indirect ophthalmoscopy and slit lamp biomicroscopy with a 90D lens. Diabetic retinopathy was graded according to the Early Treatment Diabetic Retinopathy Study (ETDRS) classification into no diabetic retinopathy, non-proliferative diabetic retinopathy, and proliferative diabetic retinopathy. Clinically significant macular edema was assessed where applicable.

The primary outcome measures of the study were RDW and NLR values among diabetic patients with and without diabetic retinopathy. The association between inflammatory hematological markers and severity of diabetic retinopathy was also assessed.

Data were entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) software version 21. Continuous variables were expressed as mean ± standard deviation or median with interquartile range depending on data distribution, while categorical variables were expressed as frequencies and percentages. Comparison between groups was performed using independent t-test or Mann–Whitney U test for continuous variables and Chi-square test or Fisher's exact test for categorical variables. One-way ANOVA or Kruskal–Wallis test was used for comparison across multiple groups wherever applicable. Correlation between variables was assessed using Pearson's or Spearman's correlation coefficient. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 170 patients with type 2 diabetes mellitus were included in the present study. The majority of the study participants belonged to the age group of 61–70 years (39.41%), followed by 71–80 years (24.11%) and 51–60 years (23.52%). The mean age of the study population was 63.14 ± 9.67 years. Male participants constituted 52.94% of the study population, while females accounted for 47.05% (Table 1).

Most of the participants were married (92.94%). With regard to body mass index, 41.76% had normal BMI, 37.64% were overweight, and 20% were obese. The mean duration of diabetes mellitus among the study participants was 14.42 ± 8.30 years, and the majority of patients (64.11%) had diabetes for more than 10 years. The mean HbA1c level of the study population was 9 ± 3.27, indicating poor glycemic control among many participants (Table 1).

Among the 170 participants, 105 (61.76%) had no evidence of diabetic retinopathy, 41 (24.11%) had non-proliferative diabetic retinopathy (NPDR), and 24 (14.11%) had proliferative diabetic retinopathy (PDR). Smoking and alcohol consumption were reported in 34.11% and 14.70% of participants, respectively. Hypertension and hyperlipidemia were present in 21.17% and 22.94% of the study population, respectively (Table 1).

Table 1: Baseline characteristics of the study population

Sl. No.	Variables	No. of Study Participants (%)
	Age	
1	31 – 40 Years	1 (0.58%)
2	41 – 50 Years	21 (12.35%)
3	51 – 60 Years	40 (23.52%)
4	61 – 70 Years	67 (39.41%)
5	71 – 80 Years	41 (24.11%)
	Mean Age	63.14 ± 9.67
	Gender	
1	Male	90 (52.94%)
2	Female	80 (47.05%)
	Marital Status	
1	Married	158 (92.94%)
2	Not Married	2 (1.17%)
3	Widowhood	10 (5.88%)
	Body Mass Index	
1	Underweight	1 (0.58%)
2	Normal	71 (41.76%)
3	Overweight	64 (37.64%)
4	Obese	34 (20%)
	Duration of Diabetes	
1	≤ 5 Years	31 (18.23%)
2	6 – 10 Years	30 (17.64%)
3	>10 Years	109 (64.11%)
	Mean Duration	14.42 ± 8.30
	Mean HbA1c	9 ± 3.27
	Retinopathy	
1	No Retinopathy	105 (61.76%)
2	Non Proliferative Diabetic Retinopathy (NPDR)	41 (24.11%)
3	Proliferative Diabetic Retinopathy (PDR)	24 (14.11%)
	Smoking	58 (34.11%)
	Alcohol	25 (14.70%)
	Hypertension	36 (21.17%)
	Hyperlipidemia	39 (22.94%)

The mean red cell distribution width (RDW) showed a progressive increase with increasing severity of diabetic retinopathy. Participants without retinopathy had a mean RDW of 12.38 ± 0.56, whereas patients with NPDR and PDR had mean RDW

values of 12.83 ± 0.94 and 13.95 ± 0.30, respectively. The difference was found to be statistically highly significant (F = 107.345, p < 0.0001) (Table 2).

Similarly, the neutrophil–lymphocyte ratio (NLR) was higher among patients with diabetic retinopathy compared to those without retinopathy. The mean NLR was 3.2 ± 0.68 in participants without retinopathy, 3.2 ± 0.72 among patients with NPDR, and 4.3 ± 0.32 among patients with PDR. The association between NLR and severity of diabetic retinopathy was also statistically highly significant (F = 29.256, p < 0.0001) (Table 2).

Table 2: Red cell distribution width and neutrophil lymphocyte ratio in the study population

Sl. No.	Hematological Parameter	No Retinopathy	NPDR	PDR	F value	P value
1	Red cell Distribution Width (RDW)	12.38 ± 0.56	12.83 ± 0.94	13.95 ± 0.3012	107.345	<0.0001*
2	Neutrophil Lymphocyte Ratio (NLR)	3.2 ± 0.68	3.2 ± 0.72	4.3 ± 0.32	29.256	<0.0001*

These findings suggest that both RDW and NLR increase with worsening severity of diabetic retinopathy and may serve as potential inflammatory biomarkers for detection and assessment of diabetic retinopathy among patients with type 2 diabetes mellitus.

Further analysis demonstrated a significant correlation between the inflammatory hematological markers and clinical parameters of diabetes mellitus. Red cell distribution width (RDW) showed a weak positive correlation with age (r = 0.162, p = 0.035) and a moderate positive correlation with duration of diabetes (r = 0.541, p < 0.0001), HbA1c levels (r = 0.473, p < 0.0001), and severity of diabetic retinopathy (r = 0.731, p < 0.0001). Similarly, neutrophil–lymphocyte ratio (NLR) demonstrated significant positive correlations with duration of diabetes (r = 0.428, p < 0.0001), HbA1c levels (r = 0.392, p < 0.0001), and severity of diabetic retinopathy (r = 0.512, p < 0.0001). However, no statistically significant correlation was observed between NLR and age (r = 0.118, p = 0.124). These findings indicate that increasing RDW and NLR values are associated with poorer glycemic control, longer duration of diabetes, and greater severity of diabetic retinopathy (Table 3).

Table 3: Logistic regression analysis for predictors of diabetic retinopathy

Sl. No.	Variable	Adjusted Odds Ratio (AOR)	95% Confidence Interval	P value
1	Duration of Diabetes	1.12	1.05 – 1.19	<0.0001*
2	HbA1c	1.36	1.11 – 1.67	0.003*
3	RDW	2.84	1.91 – 4.22	<0.0001*
4	NLR	1.92	1.23 – 3.01	0.004*
5	Hypertension	1.68	0.88 – 3.19	0.112
6	Hyperlipidemia	1.54	0.81 – 2.92	0.184

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic utility of RDW and NLR for detection of diabetic retinopathy. RDW demonstrated a sensitivity of 81.5% and specificity of 78.1% at a cut-off value of >12.95, with an area under the curve (AUC) of 0.842, indicating good diagnostic accuracy. NLR showed a sensitivity of 72.3% and specificity of 69.5% at a cut-off value of >3.45, with an AUC of 0.761, suggestive of acceptable diagnostic performance. Both RDW and NLR were found to be statistically significant predictors for detection of diabetic retinopathy (p < 0.0001). Among the two markers, RDW demonstrated comparatively better diagnostic performance (Table 4).

Table 4: ROC curve analysis of RDW and NLR for detection of diabetic retinopathy

Sl. No.	Parameter	Cut-off Value	Sensitivity (%)	Specificity (%)	AUC	P Value
1	RDW	>12.95	81.5	78.1	0.842	<0.0001*
2	NLR	>3.45	72.3	69.5	0.761	<0.0001*

DISCUSSION

The present study was undertaken to evaluate the role of red cell distribution width (RDW) and neutrophil–lymphocyte ratio (NLR) as inflammatory biomarkers for detection of diabetic retinopathy among patients with type 2 diabetes mellitus. Chronic hyperglycemia is known to induce oxidative stress, endothelial dysfunction, and inflammatory changes that contribute to retinal microvascular damage in diabetic patients.[7–10]

In the present study, the majority of participants belonged to the age group of 61–70 years, with a mean age of 63.14 ± 9.67 years. Similar findings were reported by Jain et al5 where diabetic retinopathy was predominantly observed among elderly diabetic individuals. The higher occurrence of diabetic retinopathy among older individuals may be attributed to prolonged exposure to hyperglycemia, progressive vascular endothelial damage, and age-related microvascular changes.

The present study also demonstrated that the majority of patients had diabetes mellitus for more than 10 years, with a mean duration of 14.42 ± 8.30 years. Logistic regression analysis further identified duration of diabetes as an independent predictor of diabetic retinopathy. Similar observations were reported by Raman et al16 who demonstrated increasing prevalence of diabetic retinopathy with longer duration of diabetes. Long-standing hyperglycemia causes accumulation of advanced glycation end products, oxidative stress, retinal capillary basement membrane thickening, and ischemic microvascular injury, thereby increasing the risk of development and progression of diabetic retinopathy.[7,8]

Poor glycemic control was another important finding in the present study, with a mean HbA1c value of 9 ± 3.27. HbA1c was found to be significantly associated with diabetic retinopathy on logistic regression analysis. Similar findings have been documented in previous studies, where uncontrolled diabetes was strongly associated with retinal vascular complications.[5,16] Persistent hyperglycemia induces inflammatory cytokine release, endothelial dysfunction, and retinal hypoxia, thereby contributing to progression of diabetic retinopathy.[7,10]

A major finding of the present study was the significant increase in RDW values with increasing severity of diabetic retinopathy. Patients with proliferative diabetic retinopathy showed markedly higher RDW values compared to patients without retinopathy and those with NPDR. Similar findings were reported by Kurtul et al[15] who observed significantly elevated RDW levels among diabetic retinopathy patients and suggested RDW as a useful inflammatory biomarker for retinal vascular involvement. Rehill et al.14 also reported significant associations between elevated RDW and diabetic vascular complications. The increase in RDW observed in the present study may be explained by chronic inflammation and oxidative stress interfering with erythropoiesis and reducing erythrocyte survival, resulting in increased heterogeneity in red blood cell size. Inflammatory mediators may additionally impair retinal microcirculation and aggravate retinal ischemia.[10,11]

The present study also demonstrated significantly elevated NLR values among patients with diabetic retinopathy, particularly in proliferative diabetic retinopathy. Similar observations were reported by Behera et al[12] and Mahajan et al[13] who demonstrated significant associations between elevated NLR and diabetic microvascular complications including diabetic retinopathy. NLR reflects the balance between neutrophil-mediated inflammatory activity and lymphocyte-mediated immune regulation. Chronic inflammatory activation in diabetes mellitus may lead to increased neutrophil counts, endothelial injury, release of inflammatory cytokines, and retinal capillary occlusion, thereby contributing to progression of diabetic retinopathy.[10]

Correlation analysis in the present study demonstrated significant positive correlations of RDW and NLR with duration of diabetes, HbA1c levels, and severity of diabetic retinopathy. These findings further support the role of systemic inflammation and oxidative stress in the pathogenesis of diabetic retinopathy. Deng et al11 similarly demonstrated significant associations between inflammatory hematological markers and different stages of diabetic retinopathy.

ROC curve analysis performed in the present study demonstrated good diagnostic accuracy of RDW and acceptable diagnostic accuracy of NLR for detection of diabetic retinopathy. RDW showed comparatively better sensitivity, specificity, and area under the curve than NLR, suggesting that RDW may serve as a superior inflammatory marker for identifying diabetic patients at higher risk of retinopathy. Since both RDW and NLR are routinely available through complete blood count analysis without additional financial burden, they may serve as practical and economical screening markers, especially in resource-limited settings.

However, the present study has certain limitations. Being a hospital-based cross-sectional study, causal relationships could not be established. The relatively small sample size and single-center design may limit generalizability of the findings. Nevertheless, the present study highlights the significant association of RDW and NLR with diabetic retinopathy and supports their potential role as simple inflammatory biomarkers for early detection and severity assessment of diabetic retinopathy among patients with type 2 diabetes mellitus.

CONCLUSION

The present study demonstrated a significant association between red cell distribution width (RDW), neutrophil–lymphocyte ratio (NLR), and diabetic retinopathy among patients with type 2 diabetes mellitus. Both RDW and NLR showed progressive elevation with increasing severity of diabetic retinopathy and were significantly associated with duration of diabetes and glycemic control. Among the two markers, RDW demonstrated comparatively better diagnostic

performance for detection of diabetic retinopathy. Since both parameters are inexpensive and routinely available through complete blood count analysis, they may serve as simple and practical inflammatory biomarkers for early identification of diabetic patients at increased risk of retinopathy, particularly in resource-limited settings.

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