(International Print/Online Journal)

SJIF IMPACT FACTOR: 5.565
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume 6, Issue 1 , Page No: 292-299
January-February 2023

IJMSCR

A Cross Sectional Study To Estimate The Prevalence Of Diabetic Retinopathy And Its Association With Neutrophil Lymphocyte Ratio Among Diabetics Attending A Tertiary Care Hospital In Chennai, Tamilnadu

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Type of Publication: Original Research Paper
Conflicts of Interest: Nil

Abstract

Background: Diabetes Mellitus is a highly prevalent metabolic syndrome associated with various Ocular complications like Diabetic Retinopathy and blindness. Incidence and progression of DR is affected by various factors. There is a need for markers for early detection and management of DR.

Objective: To determine the association between Hematological parameters like WBC counts,Neutrophil Lymphocyte ratio (NLR) in diabetic patients with severity of DR.

Materials and methods: A Comparative cross-sectional study was conducted in Chettinad Hospital and Research Institute. 150 participants with DM are included in this study. Complete Ophthalmic examination with staging of DR with estimation of haematological parameters like Hb, WBC, NLR were done in all patients.

Results - Various parameters were evaluated and the following variables were significantly associated ($p<0.05$) with the Group BCVA (Best-corrected visual acuity) Distance (Worse Eye), Visual Acuity Near Worse Eye, Amsler Grid Worse Eye, Anterior Segment Worse Eye, Grading of Diabetic Retinopathy with Haemoglobin (g/dL), HCT (%), TLC (/cu.mm), NLR Category.

Conclusion – NLR is an indicator which aids the early identification and referral of Diabetic patients to manage Retinopathy to prevent morbidity.

Keywords: DM, Retinopathy, NLR.

Introduction

Given that there are already 62 million diabetics in India, the disease is quickly reaching the status of a possible epidemic. Untreated and uncontrolled diabetes can damage end organs and result in considerable mortality and morbidity. Diabetes is a syndromic condition that causes a variety of macro and microvascular consequences.[1] FPG less than 7.0 mmol/l (126 mg/dl) or a 2 hour PG level less than 11.1 mmol/l (200 mg/dl) are the current WHO diagnostic criteria for diabetes mellitus.[2] The most prominent microvascular complication of DM is DR, which is one of the leading causes of blindness worldwide and causes significant morbidity in patients.

The DM pandemic is now being caused by the extremely high incidence of DM in the world. By 2030, the WHO projects that there will be over 500 million people with diabetes worldwide [3,4]. DM is found not only in wealthy industrialised nations but also in underdeveloped nations. Dietary choices, a high BMI, and very little physical activity are major

problems. Patients who have DM run the chance of getting DR. [5] . Microvascular changes in the DR disease cause reduced retinal blood flow, retinal blood vessel leak, new retinal blood vessel development, and macula oedema[6].

In nations like the USA and the UK, DR is a highly prevalent cause of vision loss in all age groups, has a significant impact on daily living, and places a significant financial burden on healthcare systems. [7] treating DM, several departments are involved, and collaboration between staff members with different specialties is essential. To give patients the best care possible, medical retina, general ophthalmologists, and endocrinologists must learn to collaborate[8]. The current study's goal is to classify DR in DM patients and evaluate the severity by looking at the retina and its relationship to micronutrients[9].

The quality of life for diabetic people is significantly impacted by DR. Early identification and classification of patients with DR, especially those with severe NPDR who are at high risk of visual loss, is essential since a sizable portion of vision loss can be avoided with laser, pharmaceutical, or surgical treatment.[10].

A microvascular consequence of Type-2 DM, DR is the main factor in adult blindness. DR is associated to the chronic inflammation that results from the activation of inflammatory markers in DM patients. According to studies, abnormal white blood cell function in DM may contribute to the impairment of microvascular circulation and the development of DR. [11] One of the most accurate measures of inflammation in the body is the neutrophil-to-lymphocyte ratio (NLR). When screening diabetes patients for DR [12]. higher NLR scores may be a meaningful indicator. The severity and development of DR are highly correlated with higher NLR [13]. In the presence of DR, the Platelet-Lymphocyte Ratio and NLR are dramatically elevated [14].

In view of this background, this study was aimed to estimate the prevalence of diabetic retinopathy among diabetics and determine its association with neutrophil lymphocyte ratio .

Materials And Methods

Study design: Descriptive Comparative Cross-sectional study

Study area: This study was conducted in a private hospital setting in Chennai, Tamilnadu

Study Period: The study was conducted for 6months

Study Population: Study was conducted among diabetic patients attending ophthalmology OPD in private college in Chennai.

Inclusion Criteria: study respondents were selected on the following criteria

- Diagnosed type 2 diabetic cases on regular treatment with OHA or insulin or both.
- Newly diagnosed Type 2 diabetic individuals (FPG-126mg/dl or more; PPG-200mg/dl or more; RBS- 200mg/dl or more)

Exclusion Criteria

Those patients who are chronic diarrhoeal diseases, alcoholics, those with reduced renal functions, those on supplementations and those patients on diuretics were excluded from the study.

Sampling method: Purposive sampling

Sample Size: Sample size was calculated to be 150 and data was collected till the desired sample size was achieved

Data collection method:

Detailed history: A detailed patient history and symptoms were enquired. Any DM medication taken in the past, as well as a family history of comparable problems.

Symptomatic complaints: Diminution of vision, floaters, diplopia and history on any medication in past were noted.

General and systemic examination

Detailed examination of eyes

1. Visual acuity: unaided, aided, and pin hole measurements were taken.
2. Almer's Grid was checked using chart.
3. Any other lid, lacrimal apparatus, or ocular movement findings were recorded.
4. Conjunctiva, sclera, cornea, iris, anterior chamber, pupil, lens, anterior vitreous face, and any evidence of uveitis were examined under high magnification of slit lamp.

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5. Fundus examination indirect ophthalmoscope with Slit-lamp bio-microscopy with + 78 D & + 90 D Lens after dilatation of pupil was done
6. Intraocular pressure was recorded with Topcon noncontact
7. Tonometer.

Blood investigations:

Diagnosed cases of diabetes after history and ocular examination underwent blood investigations like CBC from which **Neutrophil Lymphocyte ratio was calculated**, fasting blood sugar, post prandial blood sugar

Data Analysis: Data entry was done in MS excel. Data were analysed using SPSS software version 22.

Informed Consent At the start of study, informed consent was obtained from all respondents.

Ethical Clearance Ethical proposal was presented before the Institutional Ethical Committee (IEC) and approval was obtained before conducting the study

Results:

Form the study participants, various details were collected and are tabulated as figures and tables below. Prevalence of Diabetic retinopathy was estimated to be 50% among the total study respondents. Out of the 150 study participants with diabetics, half of them (75) were diagnosed to have diabetic retinopathy. Sociodemographic characteristics like age, gender was compared among those with and without DR. the results are tabulated below. For tabulation purpose. Those with diabetic retinopathy were considered as group 1 and those without diabetic retinopathy were considered as group 2.

Age

In this study, 75 respondents with diabetes were compared with those without DR. The mean of Age in the group 1 was 55.49 (9.96). The mean of Age in the group 2 was 55.67 (9.39). The median of Age in the group 1 was 56 (50-62.5). The median of Age in the group 2 was 55 (50-61.5). The Age in the Group 1ranged from 27 - 76. The Age (Years) in the Group 2 ranged from 35 - 75. Results are

Table - 1: Comparing Study respondents with and without DR in Terms of Age (Years)

Age (Years)	Group		t-test	
	1	2	t	p-value
Mean (SD)	55.49 (9.96)	55.67 (9.39)	-0.110	0.913
Median (IQR)	56 (50-62.5)	55 (50-61.5)		
Range	27 - 76	35 - 75		

Figure 1: Association between Study groups and age

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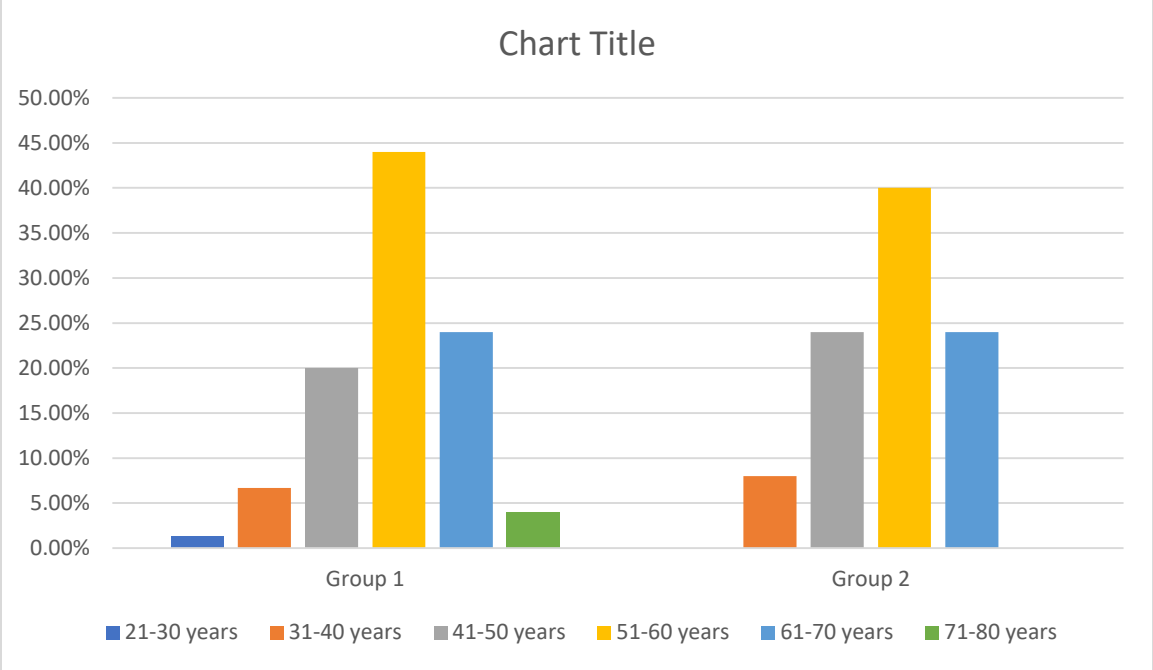

Strength of association between the two variables (Cramer's V) = 0.1 (Little/No Association)

Strength of association between the two variables (Bias Corrected Cramer's V) = 0 (Little/No Association) 1.3% of the participants in the group 1 had Age 21-30 Yrs. 6.7% of the participants in the group 1 Age 31-40 Yrs. 20.0% of the participants in the Group 1 are 41-50 Yrs . 44.0% subjects in the group 1 51-60 Yrs . 24.0% of the participants in the Group 1 had Aged 61-70 Yrs . 4.0% of the participants in the group 1 had Aged 71-80 Yrs . 8.0% of the participants in the group 2 had Aged 31-40 Yrs. 24.0% of the participants in the group 2 had Age: 41-50 Yrs . 40.0% of the participants in the group 2 had Aged 51-60 Yrs . 24.0% of the participants in the group 2 had Aged 61-70 Yrs. 4.0% of the participants in the group 2 had Age 71-80 Yrs.

Gender

57.3% of the participants in the group 1 are Males. 42.7% are female. 42.7% of the participants in the group 2 are Males. 57.3% of the participants in the group 2 are Female.

Table 2: Association Between Group and Gender (n = 150)

Gender	Group			Chi-Squared Test	
	1	2	Total	χ2	P Value
Male	43 (57.3%)	32 (42.7%)	75 (50.0%)	3.227	0.072
Female	32 (42.7%)	43 (57.3%)	75 (50.0%)		
Total	75 (100.0%)	75 (100.0%)	150 (100.0%)		

BEST CORRECTED VISUAL ACUITY (BCVA)

Table 3: Association Between Group and Vision Involvement

BCVA (Distance)	Group	Chi-Squared Test

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(Involvement)	Group 1	Group 2	Total	χ2	P Value
Unilateral	16 (42.1%)	14 (31.8%)	30 (36.6%)	0.930	0.335
Bilateral	22 (57.9%)	30 (68.2%)	52 (63.4%)		
Total	38 (100.0%)	44 (100.0%)	82 (100.0%)		
VA (Near) (Worse Eye)				**Fisher's Exact Test**	
	Group 1	**Group 2**	**Total**	**χ2**	**P Value**
N6	34 (45.3%)	75 (100.0%)	109 (72.7%)	56.422	<0.001
N8	5 (6.7%)	0 (0.0%)	5 (3.3%)		
N10	10 (13.3%)	0 (0.0%)	10 (6.7%)		
N12	5 (6.7%)	0 (0.0%)	5 (3.3%)		
N18	10 (13.3%)	0 (0.0%)	10 (6.7%)		
N36	11 (14.7%)	0 (0.0%)	11 (7.3%)		
Amsler Grid (Worse Eye)	**Group 1**	**Group 2**	**Total**	**Chi-Squared Test**	
				χ2	**P value**
Normal	34 (45.3%)	75 (100.0%)	109 (72.7%)	56.422	<0.001
Defective	41 (54.7%)	0 (0.0%)	41 (27.3%)		

Results show a significant difference between the two groups for BCVA. 24.0% of the participants in the group 1 had BCVA 6\6. 5.3% of the participants in the group 1 had BCVA 6\9. 12.0% of the participants in the group 1 had BCVA 6\12. 5.3% of the participants in the group 1 had BCVA 6\18. 10.7% of the participants in the group c1 had BCVA 6\24. 8.0% of the participants in the group 1 had BCVA 6\36. 13.3% of the participants in the group 1 had BCVA 6\60. 12.0% of the participants in the group 1 had BCVA 5\60. 1.3% of the participants in the group 1 had BCVA (Distance) 4\60. 4.0% of the participants in the group 1 had BCVA 3\60. 4.0% of the participants in the group 1 had BCVA 2\60. There was a significant difference between the groups in terms of distribution of VA (Near) (Worse Eye) . 45.3% of the participants in the group 1 had VA Worse Eye N6. 6.7% of the participants in the group 1 had VA Near in Worse Eye N8. 13.3% of the participants in the group 1 had VA near Worse Eye N10. 6.7% of the participants in the group 1 had VA: N12]. 13.3% of the participants in the group 1 had VA N18. 14.7% of the participants in the group 1had VA N36.

45.3% of the participants in the group 1 had Amsler Grid Worse Eye Normal. 54.7% of the participants in the group 1 had Amsler Grid Worse Eye Defective. 100.0% of the participants in the group Group 2 had Amsler Grid Worse Eye Normal. Participants in the group Group 2 had the larger proportion of Amsler Grid Worse Eye Normal. Participants in the group Group 1 had the larger proportion of Amsler Grid Worse Eye Defective

Table 4: DR TYPE AND COMPARISON

SNo	Characteristic	Frequency	Percentage (%)
1	**Type of DR**		
	NPDR	61	81.3
	PDR	14	18.7
2	**Severity of DR**		

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	Mild NPDR	18	24.0
	Moderate NPDR	27	36.0
	Severe NPDR	16	21.3
	PDR	14	18.7

Table: 5 Association of Diabetic retinopathy with NLR

SNo	**NLR**	**Characteristic**				**Test used**	
		Group					
		I	**II**	**Total**		**χ2**	**P-Value**
1	≤3.5	13 (17.3%)	75 (100.0%)	88 (58.7%)		105.682	<0.001
	>3.5	62 (82.7%)	0 (0.0%)	62 (41.3%)			
2	NLR	**DR Severity**				**Kruskal Wallis Test**	
		Mild NPDR	**Moderate NPDR**	**Severe NPDR**	**PDR**	**χ2**	**p value**
	Mean (SD)	3.54 (0.23)	4.36 (0.49)	4.82 (0.92)	4.84 (0.55)	33.381	<0.001
	Median (IQR)	3.55 (3.5-3.6)	4.5 (4.1-4.65)	5.05 (4-5.62)	5 (4.45-5.22)		
	Range	3 - 4	3.1 - 5	3.1 - 5.9	3.6 - 5.6		
3	NLR	**DR Type**					
		NPDR	**PDR**			**W**	**p-value**
	Mean (SD)	4.24 (0.76)	4.84 (0.55)			212.500	0.004
	Median (IQR)	4.2 (3.6-4.7)	5 (4.45-5.22)				
	Range	3 - 5.9	3.6 - 5.6				
4	NLR	**Variable Group**				**W**	**p-value**
		Group 1	Group 2				
	Mean (SD)	4.35 (0.76)	1.92 (0.43)			5620.000	<0.001
	Median (IQR)	4.4 (3.6-4.95)	2 (1.6-2.1)				
	Range	3 - 5.9	1.3 - 3.2				

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The mean of NLR in the group 1 was 4.35 (0.76). The mean of NLR in the group 2 was 1.92 The significant difference, 2 groups in terms of NLR (W = 5620.000, p = <0.001), with the median NLR being highest in the Group: 1 The significant difference, 2 groups in terms of NLR (W = 212.500, p = 0.004), with the median NLR being highest in the DR Type: PDR group.

Table 6 : Pairwise comparison of subcategories of DR severity.

Pairwise Comparison of Subcategories of DR Severity	Adjusted P-Value
Mild NPDR - Moderate NPDR	0.001
Mild NPDR - PDR	<0.001
Moderate NPDR - PDR	0.221
Mild NPDR - Severe NPDR	<0.001
Moderate NPDR - Severe NPDR	0.447
PDR - Severe NPDR	0.999

The significant difference, 4 groups in terms of NLR with the median NLR being very high in the DR Severity: Severe NPDR group.

Discussion

In this cross-sectional study total number of study respondents were 150 Diabetic patients of which 75 of them were diagnosed to have DR and 75 were without DR. in this comparative cross-sectional study, Neutrophil lymphocyte ratio was measures and its association in both diabetic patients with and without diabetic retinopathy was evaluated.

A study done by M Cahill et al[15] concluded that the prevalence of DR in elderly type II diabetics is lower than patients with early diagnosed type II diabetes. But in our study the p value obtained for age of the patient and development of DR was 0.9 which was statistically insignificant. A study done by Raman et al [16] suggest that male gender is a significant risk factor for DR whereas in our study there was no association of gender and DR with p value of 0.07. A study done by P H Scanlon et al[17] stated that other than DR, other reasons account for the bulk of vision loss in a diabetic population. BCVA is not a viable criterion for predicting DR on its own which was similar to our study having p value of 3.335.

Threshold Amsler Grid (TAG) is an important method in the estimation of maculopathy and retinal involvement in patients with DR. Its simple non-invasive technique and high sensitive technique make it very use full in distant settings where high-end retinal imaging techniques are not available. A study done by Wolf and sadun et [18] concluded that amsler grid was a rapid and inexpensive tool to assess maculopathy in DR patients which was similar to the results in our study showing a statistical significance with p value of 0.001.

In this study for the both the groups haemoglobin, haematocrit, and total WBC count were evaluated and compared. Haemoglobin and haematocrit were found to be statistically significant in group 1 vs group 2 with p value of 0.001 which was in concordance with the study by Qiao et al [19] which concluded that severe retinopathy was more common in anaemic participants on insulin therapy or who had diabetes for a long time. Higher WBC count was present in the group 1 as compared to the group 2 and total WBC count were statistically significant with p value of 0.001 between the group 1 and 2 but no correlation was seen with severity of DR. Study done I vermes et.al suggested that in DM Altered white blood cell function may act as an additional factor in the impairment of microvascular circulation and leads to DR progression[11] A high WBC count can predict acute and chronic inflammation. Inflammation is one of the pathogenesis of DR.

Sena Memnunu Ulu and others We are aware of no other study that examines the connection between an inflammatory marker called NLR and the severity of DR.[20] In our study, higher NLR values were found to

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have a statistically significant p value of 0.001, suggesting that they may be a useful marker for assessing diabetes patients in terms of DR.In this study by Rui-tao Wang et al, it was discovered that patients with Type 2 DM and DR had greater NLR levels.[21] Early detection of abnormal NLR levels in Type 2-DM and DR patients may help in the hunt for subclinical atherosclerosis.

According to a study by Song Yue et al, the Platelet-Lymphocyte Ratio and NLR are significantly increased in the presence of DR. After taking into consideration any potential confounding variables, it was shown that the monocyte-lymphocyte ratio represents a risk factor for DR. [22]The Monocyte-Lymphocyte Ratio may be clinically and pathophysiological significant in DR, however it has a low level of predictability. In line with the previously mentioned study, the DR in our study exhibits a statistically significant positive association with NLR, with a p value of 0.004; additionally, NLR exhibits a statistically significant correlation with the severity of DR in DM patients, with a p value of 0.001.

Conclusion

In this study, it was found that NLR correlates with DR severity and progression, as well as the inflammatory status of the patients. This study's findings suggest that to avoid serious vision loss, DM patients should have routine eye exams to check for retinal and other ocular problems. Patients with high NLR should be sent to an ophthalmologist for additional testing and treated for early eye problems by their doctors.

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