

EARLY PREDICTION OF DIABETIC RETINOPATHY BY NEUTROPHIL-LYMPHOCYTE RATIO IN TYPE 2 DIABETES MELLITUS PATIENTS

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Abstract: Background & objectives: Diabetes Mellitus (DM) is the most prevalent endocrinal disorder distinguished by hyperglycaemia arising from faults in insulin secretion, insulin action or both and is related with remarkable morbidity and mortality. Diabetic retinopathy is a serious microvascular complication which can seriously affect vision in diabetic patients. Neutrophil-Lymphocyte ratio has close association with development and progression of diabetic retinopathy. The objective of this study was to study Neutrophil-Lymphocyte ratio (NLR) in Type 2 diabetics with and without complications of diabetic retinopathy. **Methods:** A cross sectional study was conducted on 75 Type 2 diabetes patients. Detailed clinical history regarding duration, and complications was taken. NLR was obtained using automated cell counter. Fasting blood glucose, HbA1c were also obtained. Diabetics were further categorized into patients with complications and without complications of diabetic retinopathy. Statistical analysis was performed by Statistical Package for the Social Sciences Version 16 (Chicago, IL), the Chi-square test and the Unpaired t-test. **Results and Interpretation:** NLR were significantly ($p=0.001$) higher among patients with retinopathy than without retinopathy. **Conclusion:** NLR is significant in microvascular complication diabetic retinopathy in type 2 diabetes patients and can be considered as predictive marker of diabetic microvascular complication

Key Words: Diabetes mellitus, diabetic retinopathy, NLR.

Abbreviations: AUC : Area under the curve, EDTA: Ethylene diamine tetra acetic acid, NPV: Negative predictive value, PPV: Positive predictive value, NLR: Neutrophil-lymphocyte ratio

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INTRODUCTION:

Diabetes Mellitus (DM) is the most prevalent endocrinal disorder distinguished by hyperglycaemia arising from faults in insulin secretion, insulin action or both and is related with remarkable morbidity and mortality.

Diabetic Retinopathy is one of the most serious complications of type 2 DM and also the ocular manifestation of end-organ damage and has subsequently become the major cause of vision loss resulting in irreversible blindness among adults.^{1,2} Microvascular complication like diabetic retinopathy eventually determine the mortality of diabetes and is a burden on the health care system. Studies have shown that inflammation play a key part in the evolution of Diabetes Mellitus.³ Glycated proteins cause damage to cells and impair their function, which induces the production of inflammatory cytokines like C-Reactive Protein, Tumour Necrosis Factor-alpha (TNF- α), interleukin - 6 (IL-6) and free radicals. Activation of inflammatory processes appears to be one of the major

mechanisms responsible for vascular damage leading to clinically well recognized complications of diabetes mellitus.⁴

NLR is a novel marker of chronic inflammation that manifests a balance of two interdependent components of the immune system; neutrophils, which mediate the first line of inflammatory defence, while lymphocytes are the regulatory and protective component of inflammation.⁵

An index has thus been subsequently generated to reflect both neutrophilia, which accompanies the acute state of inflammation, and lymphopenia, which is a response to physiological stress. This index, which is the Neutrophil-Lymphocyte Ratio (NLR), has been demonstrated to be a reliable indicator of the inflammatory status.⁶

Particularly, an increasing proof has shown that NLR is also closely related to the development and progression of Diabetic retinopathy.^{7,8,9} So due to its easily availability and inexpensive method of determination, NLR is coming up as an easy parameter to evaluate inflammatory status of a

patient in contrast to estimation of interleukin-1, interleukin-6, TNF-alpha, etc which are exorbitant and clumsy. Since there are not many Indian studies concerning evaluation of Neutrophil- Lymphocyte Ratio in type 2 DM patients having microvascular complication diabetic retinopathy, this study has been undertaken to assess Neutrophil-Lymphocyte Ratio and its association with microvascular complications in type 2 diabetic patients.

Material and Methods:This study was conducted in Department of Medicine, SGT Medical College, SGTUniversity, Gurugram, Haryana, India. 75 patients in the age group 35 years to 70 years wereselected for the study. NLR was studied in the cases and were correlated withdiabetic retinopathy to evaluate the predictive values of NLR in predictingdiabetic retinopathy.Laboratory results in these patients were analysed & frequency of abnormal results was evaluated. Consent was taken from the patients prior to involving them in the study on a consent form. Correct procedure of the test was well explained to all the patients. After taking permission from the ethical committee of SGT medical college and written consent of patients, a cross-sectional study was carried out in the medicine department of SGT medical college and hospital.

Blood sample was taken under all aseptic precautions from the ante-cubital vein by a clean puncture avoiding bubbles and froth. About 2 ml of blood sample was collected in EDTA, fluoride bulb, and plain bulb each. Complete hemogram was performed by using automatic blood counter (Sysmex XN-550, USA) from EDTA bulb. Differential leucocyte count (DLC) was recorded and neutrophil-lymphocyte ratio was determined.

The data collected was entered into the M-S excel sheet and SPSS. The results were analysed using software Statistical Software Package of Social Sciences (SPSS) 16.0 version (Chicago, Inc., USA).The results were presented in percentages and mean \pm SD. The Chi-square test was used to compare categorical variables. The Unpaired t-test was used to compare continuous variables. The receiving operating curve (ROC) analysis was carried out. The area under the curve (AUC) was calculated. The sensitivity, specificity, positive predictive value

(PPV) and negative predictive value (NPV) were calculated. P value <0.05 was considered significant and p value < 0.01 was considered as very significant.

RESULT:

Table:1 Comparison of NLR with and without Retinopathy.

Retinopathy	NLR (Mean \pm SD)
Present	4.66 \pm 1.51
Absent	3.79 \pm 1.35
p-value ¹	0.01*

¹Unpaired t-test, Significant

Table-1 shows the comparison of NLR with between with and without retinopathy. NLR was significantly ($p=0.01$) higher among patients with retinopathy (4.66 \pm 1.51) than without retinopathy (3.79 \pm 1.35).

Table-2: Predictive values of NLR in predicting retinopathy.

NLR	Retinopathy				Total	
	Present		Absent			
	No.	%	No.	%		
>3.90	20	26.7	17	22.7	37	49.3
\leq 3.90	8	10.7	30	40.0	38	50.7
Total	28	37.3	47	62.7	75	100.0

AUC	Sensitivity	Specificity	PPV	NPV
0.70	71.4	63.8	54.1	78.9

Table-2 and Fig. 1 shows NLR >3.90 correctly predicted retinopathy in 26.7% patients with sensitivity and specificity of 71.4% and 63.8% respectively.

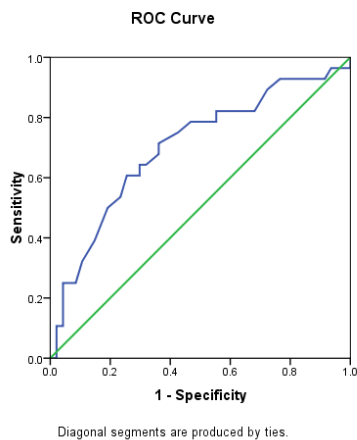


Fig. 1: ROC curve showing sensitivity and specificity of NLR in predicting retinopathy

DISCUSSION:

Our findings are in accordance with the previous studies where high NLR were associated with microvascular complications like diabetic retinopathy, thus implicating the role of inflammation in the pathogenesis of microvascular complications.

A study by Woo et al.¹⁰ showed that neutrophil count in circulation was higher in patients with diabetic retinopathy, and was closely associated with diabetic retinopathy grades, indicating the considerable role of neutrophil mediated inflammation in the development and progression of diabetic retinopathy. Furthermore, several recent studies have proposed that NLR, as a novel inflammation marker, was found to be more in patients with diabetic retinopathy and is associated with severity of diabetic retinopathy.^{11,12,13,14}

A study by Chittawar et al found NLR to be the best predictor of nephropathy followed by retinopathy¹². Similar to our finding, Moursey et al also found NLR to be an independent predictor of all diabetic microvascular complications.¹⁵ A recent study in Egyptian patients has shown that NLR values were significantly higher in diabetic patients with retinopathy ($P < 0.001$), than those of diabetic patients without any microvascular complications and healthy controls.¹⁵

So NLR can be used as a cheaper and easily available predictor of microvascular complication diabetic retinopathy in diabetic patients.

CONCLUSION: NLR was significantly ($p=0.01$) higher among patients with retinopathy than without nephropathy in our study.

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Conflict of Interest : None