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Assessment of Relationship of Neutrophil Lymphocyte Ratio with Diabetic Retinopathy among Patients with Type 2 Diabetes

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ABSTRACT

Background: Diabetes is metabolic disorder which is responsible for several long-term complications including both microvascular and macrovascular.
Aims and Objectives: The present study was conducted to assess the relationship between Diabetic retinopathy and neutrophil lymphocyte ratio amongst type 2 diabetics.
Methodology: This study was conducted as a cross sectional study in OPD settings at tertiary care Hospital on 150 patients for a period of 1 year. All the cases of type 2 diabetes recently or previously diagnosed, belonging to age group of 18 to 80 years were included. Detailed information regarding sociodemographic variables, diabetes, its duration, and treatment was obtained. Digital fundus photography with the help of ophthalmologist was done to assess diabetic retinopathy.
Results: The present study was conducted on a total of 150 patients of type 2 diabetes with mean age of 50.5±11.5 years. The present study observed statistically significant association and correlation of diabetic retinopathy with NLR ratio ($p<0.03$).
Conclusion: Our study highlighted the importance of NLR as a cheap, reliable, easily available and affordable predictor of the occurrence of diabetic retinopathy in patients with T2DM. The NLR ratios are significantly increased in the setting of diabetic retinopathy and they also correlate well with the severity of diabetic retinopathy. Thus early detection of these abnormal ratio levels will be helpful to detect diabetic retinopathy and also to assess the progression of the disease in diabetic patients.

Keywords: Diabetic retinopathy, NLR, diabetes, microvascular complications.

INTRODUCTION

Diabetes is now recognized as a global health burden and morbidity as well mortality due to diabetes are increasing especially in low and middle income countries such as India. [1] Prevalence of diabetes is rising rapidly in India and our country is regarded as the diabetes capital of the world. The prevalence of diabetes and prediabetes in India are 9% and 11-14%, respectively. [2] Type 2 Diabetes usually starts in middle age or in the elderly and is more commonly encountered type in approximately 80% cases. It is due to either impaired insulin secretion or resistance to the action of insulin at its targets cells. [3]

Diabetes is metabolic disorder which is responsible for several long-term complications including both microvascular and macrovascular. Diabetic retinopathy is one such microvascular complication which develops in patients with long standing diabetes and has been considered as the major cause of blindness. [4] It was estimated that approximately 28.5 to 40.3% of patients with type II diabetes mellitus (T2DM) develop diabetic retinopathy. [5,6,7] Thus, it is important to elucidate pathogenesis of DR and identify high-risk patients. Previous studies have indicated that in patients with obesity and type II diabetes, components of the immune system

are altered and various inflammatory markers such as interleukin 6 (IL6) and C-reactive protein (CRP) are raised. [8,9]

Neutrophil: lymphocyte ratio (NLR) has been observed to be raised in numerous chronic inflammatory disease and recently gained importance in biological and medical research. [10,11] NLR represents a combination of two markers i.e. neutrophils and lymphocytes- Neutrophils represent the active nonspecific inflammatory mediator initiating the first line of defense and lymphocytes represent the regulatory or protective component of inflammation. Recently, several studies have suggested that NLR could play a predictive role for assessing the development of microvascular complications of diabetes. NLR which is a component of complete blood picture is both accessible as well as affordable in resource poor setting such as India and it thus has been increasingly used in clinical trials and research studies. Thus NLR can be a cost effective and reliable predictor of the diabetic retinopathy especially in resource poor setting. Therefore, the present study was conducted to assess the relationship between Diabetic retinopathy and neutrophil lymphocyte ratio amongst type 2 diabetics.

METHODOLOGY

Present cross sectional study was performed on 150 patients using Questionnaire in Out Patients Department (OPD) of Department of Medicine, Gandhi Medical College and associated Hamidia Hospital Bhopal from 1st December 2018 to 30th November 2019.

Inclusion criteria: All the cases of type 2 diabetes recently or previously diagnosed, belonging to age group of 18 to 80 years and giving consent.

Exclusion criteria: Patients with type 1 diabetes; patients with diabetes and presenting with infections or recent history of infections (bacterial/ viral/ fungal or parasitic) in the past 1 month; HIV positive patients; critically ill patients requiring admission; patients with known systemic disorder or other chronic disorders such as cardiovascular disease, chronic kidney disease, chronic liver disease, blood disorders, autoimmune disorders or malignancy; type 2 diabetics on anti-inflammatory drugs, systemic steroids or alcohol; patients with uncontrolled blood pressure.

All the patients were explained about the nature and purpose of the study and those willing to participate were included. An informed consent was obtained from all the study participants. The study tool was so designed as to obtain detailed information regarding sociodemographic variables, detailed information about diabetes, its duration, and treatment. All patients were further subjected to anthropometric measurements including height, weight, body mass index [BMI]. Fasting and postprandial blood glucose along with HbA1c levels was assessed.

CBC, FBS, PPBS and HbA1c were conducted for all the patients and the findings were recorded. Diabetes was diagnosed by WHO criteria. Digital fundus photography with the help of ophthalmologist was done to assess diabetic retinopathy. Diabetic retinopathy was diagnosed using the Early Treatment Diabetic Retinopathy Study criteria. [12]

Statistical analysis- Data was compiled using MsExcel and analysed using IBM SPSS software version 20. Descriptive variables were expressed as mean and ANOVA test was applied. P value <0.05 was considered significant whereas $p<0.01$ was considered highly significant.

RESULTS

The present study was conducted on a total of 150 patients of type 2 diabetes with mean age of 50.5±11.5 years.

In present study, majority of patients belonged to 45 to 55 years of age (30%) followed by 25.3% and 22% patients belonging to age group of 36 to 45 and 56 to 65 years respectively. Female

preponderance in a female: male ratio of 1.5:1 was observed in present study with females constituting 59.3% of the study population. Mean duration of diabetes were 4.98±5.2 years and majority of patients were recently diagnosed i.e. duration of diabetes was 5 or less years. HbA1c was raised in 56% population whereas HbA1c could not be done in 42% patients.

Neutrophil to lymphocyte ratio were grouped and NLR was>2.6 in majority of patients (29.3%). Mild moderate and severe NPDR was observed in 44%, 13.3%, and 16.7% patients respectively whereas PDR was observed in 2% patients.

Table 1- Distribution according to baseline characteristics of patients

Baseline characteristics		Frequency	Percentage
Age (years)	≤35	18	12.0
	36-45	38	25.3
	46-55	45	30.0
	56-65	33	22.0
	>65	16	10.7
Gender	Male	61	40.7
	Female	89	59.3
Duration of diabetes (years)	≤5	107	71.3
	6-10	22	14.7
	11-15	15	10.0
	>15	6	4.0
HbA1C (%)	≤6.5	3	2.0
	>6.5	84	56
	NA	63	42
NLR	0.85-1.71	29	19.3
	1.71-2.1	43	28.7
	2.1-2.6	34	22.7
	>2.6	44	29.3
Fundus	Normal	36	24.0
	Mild NPDR	66	44.0
	Moderate NPDR	20	13.3
	Severe NPDR	25	16.7
	PDR	3	2.0

Table 2- Association of NLR with diabetic Retinopathy

Diabetic Retinopathy	Neutrophil to lymphocyte ratio				P value
	0.85-1.71 (n=29)	1.71-2.1 (n=43)	2.1-2.6 (n=34)	>2.6 (n=44)	
Normal	13 (44.8)	9 (20.9)	6 (17.6)	8 (18.2)	0.03
Mild NPDR	11 (37.9)	22 (51.3)	18 (52.9)	15 (34.1)	
Moderate NPDR	4 (13.9)	6 (13.9)	4 (11.8)	6 (13.6)	
Severe NPDR	1 (3.4)	6 (13.9)	5 (14.7)	13 (29.5)	
PDR	0 (0)	0 (0)	1 (2.9)	2 (4.5)	

The present study observed statistically significant association of diabetic retinopathy with NLR ratio i.e. NLR ratio were significantly higher as the diabetic retinopathy advanced from mild NPDR towards PDR (p<0.03).

Table 3: Correlation of diabetic retinopathy with NLR ratio

R	R Square	Adjusted R Square	Std. Error of the Estimate	F	Sig.
0.193	0.037	0.031	0.920	5.748	0.018

The present study observed statistically significant positive correlation between diabetic retinopathy and NLR ratio i.e. as the retinopathy progressed, NLR increased (r^2=0.037; p=0.018). (Figure 1)

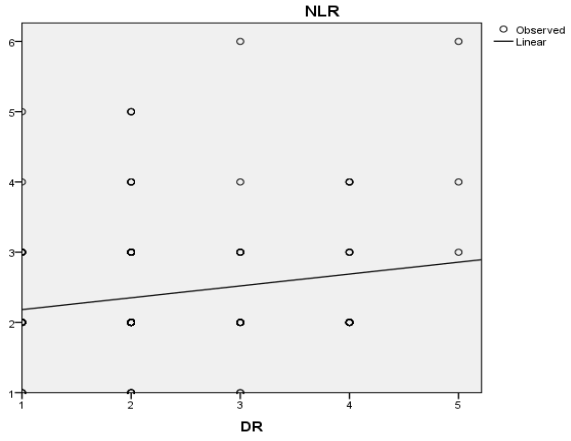

Figure 1: Correlation of diabetic retinopathy with NLR ratio

DISCUSSION

The etiopathogenesis underlying insulin resistance, diabetes and other complications with diabetes have been attributed to certain molecules combined chronic inflammatory process and associated endothelial dysfunction. [13] NLR reflects both the lymphocyte and neutrophil counts. Neutrophilia due to any cause or lymphopenia will obviously increase NLR ratio; similarly conditions causing neutropenia or lymphocytosis will reduce NLR. [14]

Diabetic retinopathy is a microvascular complication of diabetes involving series of multiple events. Powell et al., has reported that some anti inflammatory agents may prevent the

disease occurrence, showing that inflammation play a role in diabetic retinopathy pathogenesis. [15] The present study observed that NLR were significantly higher in patients with diabetic retinopathy. The findings of preset study were supported by findings of Yue et al in which patients with diabetic retinopathy had increased NLR values as compared to diabetics who did not have retinopathy. [16] Ulu et al also documented higher NLR amongst patients with diabetic retinopathy and concluded NLR to be a quick and reliable prognostic marker for diabetic retinopathy and its severity. [17] Moursy et al also replicated similar results i.e. NLR among subjects with retinopathy was significantly higher than among diabetic patients without retinopathy. [18]

A statistically significant correlation of NLR ratio with severity of diabetic retinopathy was observed in present study. These findings were supported by various studies, [16-18] however; Wang et al reported contrasting results. They observed no association of NLR with severity of diabetic retinopathy. [19]

The mechanism responsible for microvascular complications among diabetics could be attributed to hyperglycemia induced local metabolic and enzymatic changes. In certain clinical studies, increased levels of proinflammatory cytokines in the vitreous fluid of patients diagnosed with type 2 diabetes with proliferative diabetic retinopathy are an indicator of the progression of retinal injury. [20]

CONCLUSION

Our study highlighted the importance of NLR as a cheap, reliable, easily available and affordable predictor of the occurrence of diabetic retinopathy in patients with T2DM. The NLR ratios are significantly increased in the setting of diabetic retinopathy and they also correlate well with the severity of diabetic retinopathy. Thus early detection of these abnormal ratio levels will be helpful to detect diabetic retinopathy and also to assess the progression of the disease in diabetic patients.

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