

## Association between Diabetic Neuropathy and Neutrophil Lymphocyte Ratio amongst Type 2 Diabetics

Dr. JL Wadhvani<sup>1</sup>, Dr. Sachin chittawar<sup>2</sup>, Dr. Upendra Gedam<sup>3\*</sup>, Dr. Sagar Khandare<sup>4</sup>

<sup>1</sup>Associate Professor, MD Medicine, Department of Medicine, Gandhi Medical College Bhopal, Sultania Rd, near Hamidia Hospital, Royal Market, Bhopal, Madhya Pradesh 462001, India

<sup>2</sup>DM Endocrinology, Department of Medicine, Gandhi Medical College Bhopal, Sultania Rd, near Hamidia Hospital, Royal Market, Bhopal, Madhya Pradesh 462001, India

<sup>3</sup>PG Student, Department of Medicine, Gandhi Medical College Bhopal, Sultania Rd, near Hamidia Hospital, Royal Market, Bhopal, Madhya Pradesh 462001, India

<sup>4</sup>MD Medicine, SR Department of Medicine, Gandhi Medical College Bhopal, Sultania Rd, near Hamidia Hospital, Royal Market, Bhopal, Madhya Pradesh 462001, India

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\*Corresponding author: Dr. Upendra Gedam

### Abstract

### Original Research Article

**Background:** The study aimed to evaluate the relationship between Diabetic neuropathy and neutrophil lymphocyte ratio amongst patients with type 2 diabetes. **Methodology:** The study was conducted as a cross sectional study in outpatient Department of Medicine, Hamidia Hospital Bhopal for a period of 6 months. All the 100 known cases of type 2 diabetes belonging to age group of 18 to 80 years and giving consent were included in the study. Detailed data regarding sociodemographic variables, diabetes duration and treatment was obtained and entered in questionnaire. Height, weight, BMI was recorded. CBC, FBS, PPBS and HbA1c was also conducted. **Results:** The present study observed no statistically significant association between various baseline variables and Neutrophil to lymphocyte ratio ( $p>0.05$ ). Neutrophil to lymphocyte ratio were significantly associated with duration of diabetes and presence of neuropathy i.e. NLR were significantly higher in patients with neuropathy and patients with longer duration of diabetes ( $p<0.05$ ). Diabetic neuropathy was observed to be significantly correlated with neutrophil to lymphocyte ratio and duration of diabetes ( $p<0.01$ ). **Conclusion:** Higher neutrophil to lymphocyte ratio may be considered as a prognostic indicator of diabetic neuropathy. This is a cost effective marker that is easily available and can be used in community settings as well as resource poor settings.

**Keywords:** Diabetic neuropathy, NLR, BMI, correlation, HbA1c.

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## INTRODUCTION

According to WHO report 2018, the prevalence of diabetes has been rising more rapidly in world and more so in middle- and low-income countries [1]. WHO estimated that the global prevalence of diabetes among adults over 18 years of age had almost doubled from 4.7% in 1980 to 8.5% in 2014 [2]. It is well established that patients with diabetes mellitus usually develop various chronic vascular complications; both macrovascular i.e. heart disease, stroke and peripheral vascular disease as well as microvascular i.e. retinopathy, neuropathy and nephropathy [3]. Literature suggest that it is the subclinical inflammatory process which is responsible for pathogenesis of type 2 diabetes and various associated vascular complications [4]. Apart from the role in development of these complications, chronic inflammation has role in insulin resistance and

also accelerate the microangiopathy and macroangiopathy in diabetic patients [5, 6].

Neutrophil-to-lymphocyte ratio (NLR) is a novel marker of chronic inflammatory disease that reflects a counterbalance between two complementary components of the immune system; neutrophils acting as active nonspecific indicator of inflammation, whereas lymphocytes representing the protective or regulatory component of inflammation [7].

Diabetic peripheral neuropathy is one of the most common chronic complications associated with diabetes mellitus. American Diabetes Association (ADA) in their study demonstrated that about 50% of peripheral neuropathy are asymptomatic whereas painful complicated diabetic neuropathy are observed in about 26.4% [8]. Furthermore, Diabetic neuropathy is

associated with other complications such as foot, ulcers, infection, and amputation [9]. Diabetic neuropathy is diagnosed clinically and other methods such as nerve condition study and electrophysiological methods [10]. These methods help in diagnosis usually in late stage of pathogenesis. Also these methods are costly and not available at every place. Complete blood picture is a basic investigation which is available at all levels of health care delivery. Thus NLR can be a cost effective and reliable predictor of the diabetic neuropathyespecially in resource poor setting. Therefore, the study aimed to evaluate the relationship between Diabetic neuropathy and neutrophil lymphocyte ratio amongst patients with type 2 diabetes.

## METHODOLOGY

The present study was conducted as a cross sectional study in outpatient Department of Medicine, Gandhi Medical College and associated Hamidia Hospital Bhopal for a period of 6 months i.e. from 1<sup>st</sup> December 2018 to 30<sup>th</sup> May 2019. All the 100 known cases of type 2 diabetes belonging to age group of 18 to 80 years and giving consent were included in the study. The exclusion criteria comprised of patients with type 1 diabetes; critically ill patients requiring immediate care; patients with infections or recent history of infections (bacterial/ viral/ fungal or parasitic) in the past 1 month; HIV positive patients; patients with known systemic disorder such as cardiovascular disease, chronic kidney disease, chronic liver disease, blood disorders, autoimmune disorders or malignancy; patients on anti-inflammatory drugs, systemic steroids or alcohol; patients with uncontrolled blood pressure.

Detailed data regarding sociodemographic variables was obtained from all the patients and entered in questionnaire. Apart from this, a detailed information about diabetes, its duration, and treatment was documented. All patients were subjected to detailed anthropometric measurements such as height, weight, body mass index [BMI] was recorded for all patients and entered in questionnaire.

CBC, FBS, PPBS and HbA1c was conducted for all the patients and the findings were recorded. To assess the status of diabetic peripheral neuropathy pin prick, vibration sense, ankle reflex, and knee reflex were checked.

Statistical analysis: Data was compiled using Ms Excel 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 included 100 patients during the study period with mean age of 50.66±11.14 (Range-30 to 76) years. Mean duration of diabetes was 5.05±5.29 years. Complication i.e. diabetic neuropathy was observed in 22% patients in present study. Mixed neuropathy was observed in majority of patients (14%) whereas motor and sensory neuropathy was observed in 6% and 2% patients respectively. Mean Neutrophil to lymphocyte ratio was 2.34±0.89.

**Table-1: Association of baseline variables with Neutrophil to lymphocyte ratio**

Variables	Neutrophil to lymphocyte ratio				P value
	0.85-1.71 (n=20)	1.71-2.1 (n=28)	2.1-2.6 (n=25)	>2.6 (n=27)	
Age (years)	52.65±12.19	46.86±11.27	52.16±10.73	51.74±10.2	0.20
Male:Female	9/11	6/22	13/12	13/14	0.09
Height (cm)	162±7.19	159.2±4.19	161.1±6.22	160.2±8.5	0.45
Weight (kg)	69.6±11.29	67.8±12.5	67.6±10.9	70.4±16.1	0.84
BMI (kg/m <sup>2</sup> )	26.4±3.6	26.7±4.5	26.04±4.3	27.2±4.2	0.77

The present study observed no statistically significant association between various baseline variables and Neutrophil to lymphocyte ratio (p>0.05).

**Table-2: Association of Neutrophil to lymphocyte ratio with diabetes**

Variables	Neutrophil to lymphocyte ratio				P value
	0.85-1.71 (n=20)	1.71-2.1 (n=28)	2.1-2.6 (n=25)	>2.6 (n=27)	
Duration of diabetes (years)	3.90±7.53	5.39±4.15	6.8±4.9	8.6±4.6	0.03
FBS	157.5±42.6	166.5±41.8	171.3±57.6	168.7±35.6	0.77
PPBS	215.2±50.8	242.8±85.4	226.5±71.9	241.5±77.7	0.54
HbA1c	8.20±1.27	7.64±1.39	8.55±2.12	8.14±1.17	0.5
Neuropathy	2	4	6	10	0.04

Neutrophil to lymphocyte ratio were significantly associated with duration of diabetes and presence of neuropathy.i.e. NLR were significantly higher in patients with neuropathy and patients with

longer duration of diabetes (p<0.05) whereas no such association was observed between other variables (p>0.05). Mean NLR amongst patients with no diabetic neuropathy was 1.49±0.54 whereas that amongst

patients with diabetic neuropathy was  $3.14 \pm 1.09$  and the observed difference was statistically significant ( $p < 0.05$ ).

**Table-3: Correlation of diabetic neuropathy with various variables**

Variables	Correlation coefficient	P value
Age	-0.08	0.32
Duration of diabetes	1.24	0.01
HbA1c	0.02	0.36
Neutrophil to lymphocyte ratio	2.68	0.001

Diabetic neuropathy was observed to be significantly correlated with neutrophil to lymphocyte ratio and duration of diabetes ( $p < 0.01$ ).

## DISCUSSION

It is now established that certain molecules combined chronic inflammatory process and underlying endothelial dysfunction play important role in development of insulin resistance, diabetes and associated complications [12, 13]. Neutrophilia or lymphopenia is associated with high NLR while lymphocytosis or neutropenia with low NLR [14]. Literature suggest that neutrophilia and relative lymphocytopenia are independent markers for diabetic neuropathy including neuropathy [15, 16].

Our study demonstrated that NLR were significantly higher in patients with diabetic neuropathy and patients with longer duration of diabetes ( $p < 0.05$ ) and also mean NLR was significantly higher in patients with diabetic neuropathy ( $p < 0.05$ ). The findings of preset study were supported by findings of Chittawar *et al.*, where number of microvascular complications were significantly higher in patients with a longer duration of diabetes and raised [17]. Fawad *et al.*, also reported findings similar to our study [18]. The findings of our study were also supported by an Egyptian study by Moursy *et al.*, in which significant increase was found in NLR between diabetic subjects with and without neuropathy [19].

Diabetic neuropathy develops as a result of hyperglycemia-induced local metabolic, enzymatic and microvascular changes. Endogenous TNF- $\alpha$  production acceleration has been observed in patients with diabetes which leads to increase in microvascular permeability, hypercoagulability and nerve damage, thus promoting the onset of characteristic lesions of diabetic polyneuropathy [20].

Our findings were contrasting to the finding of Fawad *et al.*, in which a significant correlation was observed between NLR and HbA1c whereas no such correlation was observed in our study [18]. Poor glycemic control is indicated by HbA1c levels and thus

increased HbA1c levels may correlate with increased risk of complications but no such correlation was observed in our study.

The study has certain limitations. Only single complication i.e. diabetic neuropathy were studied whereas other associated complications of diabetes were not studied. Diabetic neuropathy was diagnosed clinically in our study and that may have missed few cases of diabetic neuropathy. The study was conducted as a hospital based study, however a large multicentric community based study would yield better results.

## CONCLUSION

Higher neutrophil to lymphocyte ratio may be considered as a prognostic indicator of diabetic neuropathy. This is a cost effective marker that is easily available and can be used in community settings as well as resource poor settings.

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