Original Research Article

Neutrophil to Lymphocyte Ratio as a Denotative of Type II Diabetes Mellitus

Dr. Vaishnavi Selvaraju[1], Dr. R. Priya Dharshini[1*], Dr. Jayaganesh[2], Dr. Munazza Kaif, B. K[3]

[1]Postgraduate, Department of Pathology, Saveetha Medical College, Chennai, India
[2]Professor, Department of Pathology, Saveetha Medical College, Chennai, India
[3]Undergraduate, Department of Pathology, Saveetha Medical College, Chennai, India

*Corresponding author: Dr. R. Priya Dharshini
Postgraduate, Department of Pathology, Saveetha Medical College, Chennai, India

Abstract

Introduction: The neutrophil-lymphocyte ratio (NLR) is an economically accessible tool useful in cases of Type II Diabetes Mellitus (T2DM). It can be utilized as a laboratory index, indicating systemic inflammation. The sensitivity of NLR to HbA1c must be validated to utilize for its prognostic potential. Correlation of HbA1c with NLR and other parameters have been analyzed to assess the utility of NLR in chronic cases of T2DM, thereby evaluating the utility of NLR as a marker of systemic inflammation in diabetes. *Place and Duration of study*: Department of Pathology, Saveetha Medical College, Chennai, One year. *Objectives*: 1. To compare levels of NLR and other parameters in diabetics with those of healthy people and observe the nature of correlation between HbA1c and other parameters.2. To find the linear relationship between HbA1c and other parameters in the diabetic population. *Material and methods*: An observational study conducted at our Institute from January to October 2020. Blood profiles of 240 T2DM patients and 100 healthy controls were recorded. *Results*: The NLR (5.35) of T2DM group was significantly elevated (p 0.001) compared to NLR of control group (2.16). Urea and creatinine levels had positive regression coefficients with HbA1c indicating susceptibility of diabetic patients to diabetic nephropathy. *Conclusion*: NLR showed significance in T2DM. Increased NLR is associated with elevated HbA1c and poor glycemic control in patients with T2DM. It can be used as a prognostic tool during the follow up of diabetic patients.
Keywords: Diabetes Mellitus, Inflammation, Inflammatory markers, Neutrophil-lymphocyte ratio, HbA1c, Diabetic nephropathy.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder affecting individuals worldwide. It leads to multiple life-threatening complications including micro and macrovascular. Such complications result due to poor glycemic control and hence monitoring of glycemic level is significant. Few studies have suggested the activation of inflammatory pathways in Type II Diabetes mellitus [1, 2]. Plasma glycated hemoglobin (HbA1c) is helpful in determining long term glycemic level in diabetics. However glycated hemoglobin does not predict the inflammation and so other inflammatory markers are required. Neutrophil-lymphocyte ratio (NLR) has been shown to be markedly increased in diabetics and pre-diabetics [2]. The NLR is proposed to be a better indicator of type II diabetes mellitus (T2DM) as compared to other inflammatory markers. NLR is derived from routine hematological parameters by dividing neutrophil count by lymphocyte count. NLR is easily available, cost-effective tool and can be used on large scale basis for disease screening and monitoring. Further NLR has additional advantage as an economically accessible laboratory index. However, the kind of relationship between HbA1c and NLR requires a revisit. Hence it is relevant to study the relationship of other hematological parameters with the levels of HbA1c.

MATERIALS AND METHODS

Study design and participants: This is an observational study conducted after the approval of the Ethics committee during the period of January to October 2020 in Saveetha medical college and hospital, Tamil Nadu. NLR of patients with diabetes were compared with NLR of healthy controls and linear relationship of HbA1c with hematological parameters

were found out. Details of patients diagnosed as diabetics were obtained from the medical records. Hematological parameters were recorded from our hospital database. A total of 340 subjects were enrolled for our study, of whom 240 individuals were diagnosed to have T2DM and 100 were healthy individuals, who were enrolled from routine master health checkup.

Inclusion criteria: All gender, individuals > 18 years of age, individuals with gestational diabetes mellitus.

Exclusion criteria: Individuals < 18 years of age, active inflammation and infection in the past 2 weeks, any underlying malignancies.

Data collection instruments: Blood indices- Red Blood Cell count (RBC), Total leukocyte count (TLC) and differential count including Neutrophil and Lymphocyte count were generated from Sysmex XN 1000 autoanalyzer according to instructions provided by the manufacturer. NLR was obtained by dividing the above-mentioned neutrophil count by lymphocyte count generated by the autoanalyzer.

HbA1C level were obtained from BIORAD semiauto analysers Urea and creatinine values were obtained from VITROS integrated system 5600 auto analysers.

Statistical analysis: The data were expressed as mean ± SD. The significance of differences between the two groups was assessed using statistical techniques. A p value of < 0.05 was considered significant. Microsoft word and Excel were used to generate graphs, and tables.

RESULT
The study included 340 individuals, 240 with T2DM and 100 were healthy controls. Of 340 individuals, 210 were female and 130 were male. A p value of < 0.05 was considered significant. The NLR was observed to be predominantly higher in the age group of 45-55 years in the diabetic population under our study (Fig 1) and showed male predominance (Fig 2). The NLR of diabetic individuals were higher than healthy controls (Fig 3). The NLR of diabetic individual's (5.35) when compared to healthy controls (2.169) showed statistical significance (p 0.001).
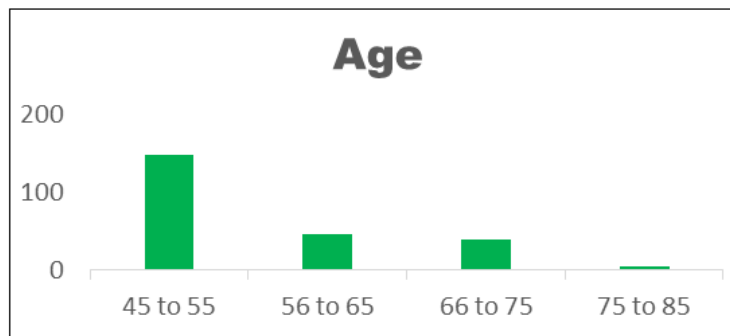

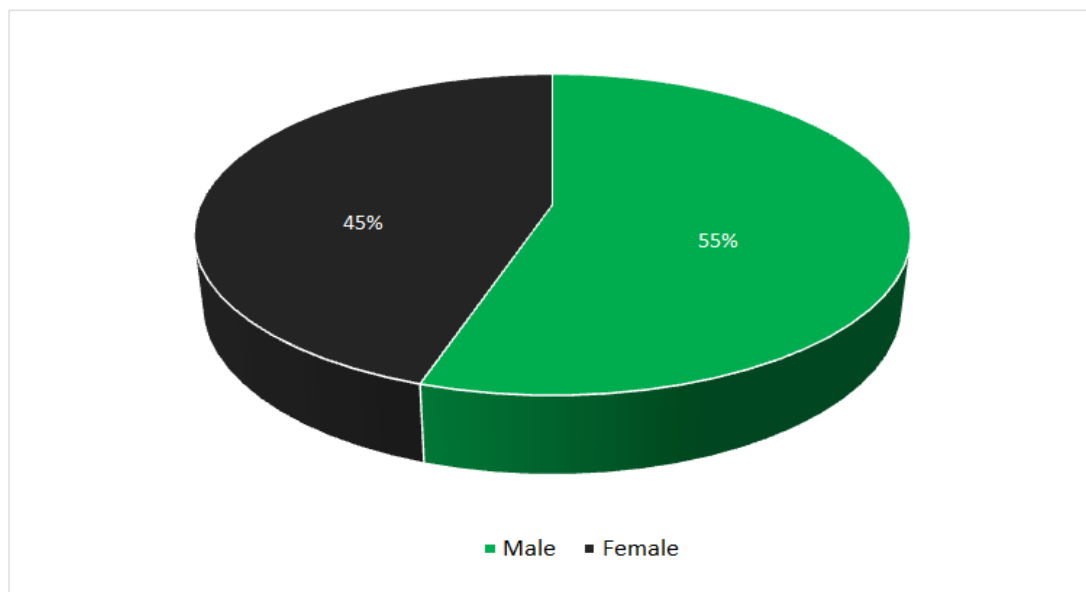**Figure 1: Age wise distribution of the diabetics with raised NLR showing predominance in 45 to 55 age group**

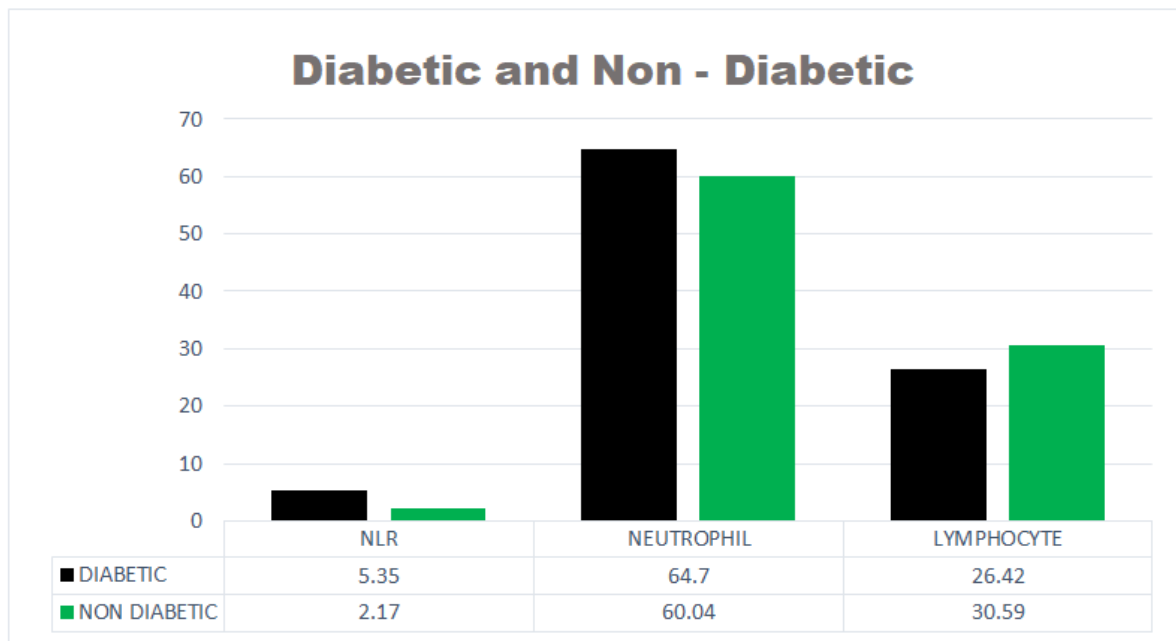**Figure 2: The gender distribution of increased NLR in diabetics**

Figure 3: Comparison of mean values of NLR, neutrophil and lymphocyte count in diabetics and control

The calculated p value for TLC, neutrophil count, lymphocyte count between the two groups showed increase in statistical significance (p 0.001) whereas RBC show significance (p 0.01) (Table 1).

Table 1: Regression on HbA1c as independent variable

Blood parameters	Diabetic population (mean ± SD)	Healthy controls (mean ± SD)	P value
RBC	4.417 ± 2.312	4.835 ± 0.638	0.01
TLC	10.102 ± 4.564	7.187 ± 1.626	0.001
Neutrophils	64.701 ± 12.176	60.043 ± 7.916	0.001
Lymphocytes	26.424 ± 10.886	30.596 ± 6.906	0.001
NLR	5.350 ± 3.75	2.169 ± 1.074	0.001

HbA1c and other blood parameter were recorded. In which HbA1c showed regression coefficient with urea and creatinine compared to other parameters. Urea and creatinine levels had positive regression coefficients with HBA1c, indicating susceptibility of diabetic patients to diabetic nephropathy (Table 2).

Table 2: Regression on HbA1c is significant with urea and creatinine

Parameters		Significance of regression
Urea	18.57 ±0.528*HbA1c	Significant
Creatinine	0.701 ±0096*HbA1c	Significant
NLR	5.350 ±0.1469*HbA1c	Not significant
Neutrophils	64.701 ±0.1516*HbA1c	Not significant
TLC	10.102 ± 0.0335*HbA1c	Not significant

DISCUSSION

In our study the NLR of diabetic individuals were significantly higher than the healthy control (p 0.001) and raised NLR in diabetic population showed a male predominance compared to the female population and same was observed in control group. WBC count and its components are classic inflammatory markers that are commonly available and inexpensive to measure. Whenever a diagnosis is made only based on a patient's WBC, neutrophil, or lymphocyte count, there are numerous biases involved. However, as a dynamic parameter, NLR has a better predictive value. NLR is a combination of two indicators, with lymphocytes serving as the regulatory or protective element of inflammation and neutrophils acting as the active nonspecific inflammatory mediator launching the first line of defense [3]. NLR is simple, easy to calculate and

in numerous researches on diabetic patients, NLR has been proven to have played a prominent role.

Our study also shows increase in TLC in diabetic population than the healthy control, which was in accordance with a study conducted by Oshitha *et al.,* [4]. PC Tong *et al.,* revealed that T2DM related macro and microvascular complications were linked to elevated WBC counts, even when they are within the normal range [5].

Our study shows regression on HbA1c is significant with urea and creatinine and thereby provides evidence about the association between the HbA1c level and diabetic nephropathy. Chronic hyperglycemia promotes the production of advanced glycation end products, which can increase the synthesis of growth factors and, in turn, cause extracellular protein deposition, mesangial enlargement, and progressive glomerular sclerosis, all of which can lower GFR [6, 7]. Accumulated evidence has implicated that chronic inflammation plays a dominant role in the development of diabetic complications. A study by B Azab *et al.,* revealed that NLR predicted a decline in renal function in diabetes patients [8]. Zhang J *et al.,* proved that in patients with T2DM, increased NLR impairs renal function and histologic lesions and may play a significant role in the development of DN [9]. NLR can be used as an inexpensive but an effective alternative marker as predictor of diabetic end organ damage.

CONCLUSION
NLR is significantly higher in type 2 diabetics as compared to the non-diabetic population. Poorly controlled diabetic status with increased HbA1C levels has a positive correlation with elevated NLR level. Hence it can be used as a disease monitoring tool during the follow up of diabetic patients.

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