Original Research Article

Neutrophil Lymphocyte Ratio: A Marker of Glycemic Status and Proinflammatory State in Patients with Type 2 Diabetes Mellitus

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Abstract

Background: The aim of present study was establishing NLR levels of type 2 diabetic subjects. We also aimed to find out possible correlation between NLR and HbA1c in type 2 DM.

Methods: In this Hospital based observational study, we studied 140 patients with type 2 diabetes mellitus, aged above 30 years presenting to the Medicine out-patient service and those admitted to the medical wards, between September 2021 and September 2022 at the JLN Hospital, a part of the Medical College in Ajmer, conducted with the aim of establishing subclinical inflammation as indicated by neutrophil lymphocyte ratio, and it's association with glycemic control in type 2 diabetes mellitus.

Results: In the present study mean ± SD of the neutrophil count was 82.78 ± 6.95 where 97.14% cases had high neutrophil count; the mean ± SD of lymphocytes count was 13.53 ± 5.43, with 88.57 % having low, 7.14% having normal, and 4.28% having high counts. The mean ± SD of the neutrophil lymphocyte ratio was 4.80 ± 2.02. The mean ± SD of fasting plasma glucose was 187.35 ± 58.01 mg/dL. The mean ± SD of HbA1c was 8.39 ± 1.87 %. A statistically significant positive correlation was found between NLR and fasting blood sugar (r = 0.425, p value <0.001) as well as HbA1c (r = 0.516, p value <0.001).

Conclusion: NLR is a marker a systemic inflammation. Elevated NLR in otherwise healthy subjects with type 2 diabetes mellitus may be indicative of underlying impaired glucose metabolism and moreover, NLR should be used as a marker of diabetic control level in addition to HbA1c in type 2 diabetic subjects.

Keywords: DM, NLR, FBS.

Introduction

Diabetes mellitus prevalence is rising most quickly, as per WHO, in low- and middle-income nations. The key drivers of the global rise in the diabetes mellitus epidemic are the quick socioeconomic change, urbanisation, and industrialization, with other risk factors like population expansion, unhealthful eating patterns, and a sedentary lifestyle also playing a significant part.[1] Diabetes mellitus is becoming more prevalent day by day. Both industrialized and developing nations are experiencing a diabetes mellitus epidemic.

Novel inflammatory markers derived from standard blood count test are in demand nowadays. One of these derived novel inflammatory markers is neutrophil to lymphocyte ratio (NLR), which is obtained by simple division of neutrophil count by lymphocyte count in hemogram. It reflects high inflammatory burden of certain diseases [4]. It is observed that NLR is significantly elevated in subjects with type 2 diabetes mellitus. Latest studies in literature have found significant association between NLR and many conditions [2-3].

The aim of present study was establishing NLR levels of diabetic subjects. We also aimed to find out possible correlation between NLR and HbA1c in patients with type 2 DM.

Material and method

Study Type: Cross sectional observational study.

Study Centre: Department of Medicine, JLN Medical College and Hospital, Ajmer.

Sample Size: For 95% confidence level (alpha=0.05), desired sample size is estimated as under:

$n = pq/(Z/d)^2$

n= sample size needed

p = prevalence rate from earlier studies.

q = (1-p)

z = the value from the table of probabilities of standard normal distribution for desired level of confidence.

d = allowable error (taken as) pacing values-
$n = (0.10) \times (0.90) \times / (1.96/0.05)^2 = 138$.

140 patients were examined between September 2021 and September 2022 at the JLN Hospital, a part of the Medical College in Ajmer, while taking into account inclusion and exclusion criteria.

Patient Selection Inclusion Criteria

1. Patients with type 2 diabetes mellitus including those with recently diagnosed diabetes mellitus and those who were already diabetic and taking insulin or oral antidiabetic drugs.
2. Between the ages of 30 and 70.

Exclusion Criteria

1. Patients with acute infections.
2. Patients with chronic inflammatory conditions like inflammatory bowel disease, osteoarthritis, rheumatoid arthritis, gout, bronchial asthma and chronic hepatitis.
3. Patients with acute myocardial infarction, cerebral infarction.
4. Patients with chronic kidney disease.
5. Patients with chronic liver disease.
6. Patients with malignancy.
7. Pregnant females.

Methodology

After receiving approval from the ethical committee and taking into account the inclusion and exclusion criteria, the current study was carried out on patients attending at the Jawahar Lal Nehru Hospital, attached to JLN Medical College, in Ajmer, aged above

30 years presenting to the Medicine out-patient service and those admitted to the medical wards.

The data were recorded from each subject with an in-person interview by administering a specific questionnaire, after taking consent from patient and / or relative. Qualifying patient underwent detailed history, clinical examination, routine investigation, special investigation.

Statistical Analysis

Statistical analyses were done using computer software (SPSS Trial Version 23 and Primer). The qualitative data were expressed in proportions and percentages, and the quantitative data (continuous data) were expressed as means and standard deviations. The difference in proportion was analysed using the chi-square test, and the difference in means among the groups was analysed using the student's t-test. Correlation between quantitative outcomes was assessed using Pearson correlation coefficient. For all statistical analyses, a 5% probability level was considered statistically significant, i.e., p 0.05.

Results

Table 1: General characteristics

Mean±SD	49.4±9.67
Male: female	56:84
FBS (mg/dl)	187.35±58.01 (98.0.0to 302.0)
PPBS (mg/dl)	359.85±133.10 (130 to 592.0)
Hb1Ac (%)	8.39±1.87 (6.10 to 14.3)
Neutrophils	82.78±6.95
Lymphocyte	13.53±5.43
Neutrophil lymphocyte ratio	4.8±2.02

Table 2: Correlation of NLR with fasting plasma glucose

	Mean	SD	Pearson Correlation	Sig. (2-tailed)
FBS (mg/dL)	187.35	58.01		
NLR	4.80	2.02	0.425	<0.001

The above table depicts the correlation of NLR with fasting plasma glucose. The mean ± SD of NLR and fasting plasma glucose were 4.80 ± 2.02 and 187.35 ± 58.01 mg/dL respectively. This table shows that NLR was positively correlated with fasting plasma glucose (r = 0.425, p value <0.001).

Table 3: Correlation between NLR and HbA1c

	Mean	SD	Pearson Correlation	Sig. (2-tailed)
NLR	4.80	2.02		
HbA1c (%)	8.39	1.87	0.516	<0.001

The above table depicts the correlation of NLR with HbA1c. The mean ± SD of NLR and HbA1c were 4.80 ± 2.02 and 8.39 ± 1.87 % respectively. Pearson correlation was found to be significant (r = 0.516, p value <0.001).

Discussion

In the present study mean ± SD of the neutrophil count was 82.78 ± 6.95 where 97.14% cases had high neutrophil count; the mean ± SD of lymphocytes count was 13.53 ± 5.43, with 88.57 % having low, 7.14% having normal, and 4.28% having high counts. The mean ± SD of the neutrophil lymphocyte ratio was 4.8 ± 2.02. The mean ± SD of fasting plasma glucose was 187.35 ± 58.01 mg/dL. The mean ± SD of HbA1c was 8.39 ± 1.87 %. A statistically significant positive correlation was found between NLR and fasting blood sugar (r = 0.425, p value <0.001) as well as HbA1c (r = 0.516, p value <0.001). The absolute counts of white blood cells, the differential counts, and their ratios are useful in signifying any ongoing inflammatory process.

As described in many studies, diabetes mellitus, its complications, and even its pathogenesis have been attributed to chronic low-grade inflammation. In our study, high level of neutrophils, low level of lymphocytes leading to high level of neutrophil to lymphocyte ratio were observed, which is consistent with Mazhar Hussain *et al*. (2017),[3] who observed that patients with the worst control (Group C) demonstrated a high leukocyte count (p.001), a high neutrophil count (p.003), and a reduced lymphocyte count (p.44) in comparison to patients with good control (Group A). They found that the NLR value was considerably higher in the diabetic groups with the worst control (Group C) as compared to poor control (Group B), and excellent control (Group A) (4.3 ± 2.8, 2.7 ± 1.0, and 2.0 ± 0.5).

According to a study by Imtiaz *et al*. (2012)[4], systemic inflammation, measured by NLR, is strongly associated with chronic illnesses including diabetes mellitus and hypertension. Fatih Sefil *et al*. (2014)[5] observed that the NLR ratio was significantly higher in group 2 compared with group 1 (1.97 ± 0.57 versus 1.45 ± 0.56, respectively; P <0.001). (HbA1c levels, 7%; n = 34) and group 2 (HbA1c levels, >7%; n = 37). Guo X *et al*. (2015)[6] found in their, "Chronic Low-Grade Systemic Inflammation and Health Cohort Study", that NLR, but not leukocyte, neutrophil, or lymphocyte counts, was positively related to the incidence of type 2 diabetes mellitus in a reasonably sized sample of urban Chinese adults. They concluded that NLR was significantly increased in diabetic patients and might serve as a biomarker with efficiency and accuracy for predicting T2DM. Wang R.T. *et al*. (2015)[6] found an increase in NLR in T2DM patients. Demirtas L*et al*. (2015)[7] found that NLR levels were an independent predictor of impaired glucose regulation in diabetic patients.

Multiple studies have established that inflammatory markers such as neutrophilia and relative lymphocytopenia are independent markers of many diseases, especially complications of DM, such as Diabetic nephropathy. However, establishing a diagnosis individually based on WBC, neutrophil, or lymphocyte counts has its own biases, unlike NLR, which is a dynamic parameter that has a higher prognostic value.

Conclusion

NLR is a marker a systemic inflammation. In our study there was significant positive correlation between NLR and glycemic status, indicating diabetes mellitus as a state of subclinical inflammation. Elevated NLR in otherwise healthy subjects with type 2 diabetes mellitus may be indicative of underlying impaired glucose metabolism and moreover, NLR should be used as a marker of diabetic control level in addition to HbA1c in type 2 diabetic subjects.

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