Original Article

NEUTROPHIL LYMPHOCYTE RATIO AND PLATELETS LYMPHOCYTES RATIO WITH GLYCEMIC CONTROL IN PATIENTS WITH DIABETES MELLITUS

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ABSTRACT

Background: Diabetes mellitus (DM) is a long-term health problem, which causes swelling of atissue. The Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) are promising biomarkers of the blood sugar level in the type 2 diabetes mellitus (T2DM) Patients**.** The purpose of the study was to evaluate the relationship between NLR, PLR, and glycemic control in T2DM patients.

Material and Methods: The inclusion of 102 T2DM patients who had HbA1c levels <7% and >7% was based on a cross-sectional study carried out at Allama Iqbal Medical College/Jinnah Hospital Lahore from May to December 2024. Thereafter, the NLR and PLR were calculated through the blood counts. The most important results were the change in the blood sugar levels and HbA1c.

Results: Type 2 diabetes mellitus (HbA1c>7%) was noted in 63% of the patients, and it was correlated with decrease in NLR and PLR (p<0.001. NLR showed a positive correlation with HbA1c (r=0.45) and PLR a figure of 0.48.

Conclusion: A higher number of NLR and PLR in the body could lead to the development of poor glycemic regulation in T2DM patients, identifying them as valuable diagnostic tools for disease management and their benefits.

Keywords: NLR and PLR Biomarkers, Hyperglycemia Indicators, Immune-Inflammatory Markers, HbA1C Correlation, Diabetic Risk Stratification, Cost-Effective Biomarkers, Chronic Inflammation in Diabetes.

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INTRODUCTION

Diabetes mellitus is a multifaceted metabolic disorder that has developed into an epidemic. The International Diabetes Federation estimated that more than 463 million adults lived with DM in 2019, while projections indicate that this number will climb to 700 million by 2045.[1] Diabetes affects the individual, community, families, and healthcare systems all around the world. It is a major source of illness and death due to its associated complications such as cardiovascular disease, chronic kidney disease, and neuropathy.[2] The economic impact is also huge with billions of dollars spent every year on diabetes-related healthcare and lost productivity.[3] More than 90% of all diabetes cases are of the type 2 diabetes mellitus (T2DM) type.

It is rather a complicated interplay of genetic predisposition and environmental factors, like diet, physical inactivity, and overweight.[4] The important thing of T2DM is insulin resistance, mostly leading to beta-cell dysfunction over the

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time.[5] Chronic hyperglycemia, the basic element of DM, is a major cause of long-term damage and dysfunction in the different parts of the body.[6] In the past, people became more and more interested in finding the connection between inflammation of the whole body and diabetes.[7] Persistent low-grade inflammation is now recognized as a key driver of insulin resistance and a major contributor to the development of microvascular and macrovascular complications.[8]

The NLR is defined as the number of neutrophils, which are members of the innate immune response, divided by the number of lymphocytes, which are the main cells of adaptive immunity.[9] An NLR that is elevated is a marker for a pro-inflammatory state and is one of the factors that are already associated with poor outcomes in various conditions, e.g. cardiovascular difficulties, cancer, and autoimmune disorders.[10] On the same note, PLR is the ratio of platelets to the lymphocytes which lead to inflammation and thrombosis, respectively. High levels of PLR have been associated with the loss of people in some inflammatory and metabolic diseases.[11] Emerging evidence indicates that NLR and PLR are also relevant when it comes to diabetes. Studies have identified that the higher levels of the NLR and PLR markers are associated with poor glycemic control, increased risk of complications, and higher mortality rates.[12] However, markers of these controls in diabetes management are still in the dark. In this context, the study aimed to address the gap and provide answers by evaluating the relationship among the NLR, PLR, and glycemic control in persons with T2DM.[13] The study was conducted to investigate the association of NLR and PLR with glycemic control in T2DM patients, examining whether these markers could be used as predictors for glycemic status and management in this patient population.

MATERIALS AND MATHODS

This descriptive cross-sectional study was conducted in the Department of Medicine at Allama Iqbal Medical College/Jinnah Hospital Lahore, spanning from May 2024 to December 2024, after obtaining ethical approval (REF No. ERB168/4/15-07-2024/S1 ERB).

The study included 102 patients with T2DM, selected using non-probability consecutive sampling. The sample size was calculated using the World Health Organization's (WHO) formula for health studies, $n = Z^2 \times P(1 - P) / d^2$, where Z represents the confidence level (1.96 for 95%), P is the anticipated proportion (3%), and d is the margin of error (5%).

Participants were divided into two groups based on glycemic control: patients with HbA1c ≤ 7% were categorized as good glycemic control (Group 1), while those with HbA1c > 7% were categorized as poor glycemic control (Group 2).

The study aimed to measure the relationship between neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) with glycemic control. Patients were primarily recruited from the general medicine and surgical wards, where individuals frequently visit for routine follow-ups or management of glycemic complications. Eligible participants were aged 25–70 years and had undergone complete blood count (CBC) and HbA1c testing. Patients with idiopathic thrombocytopenic purpura, cardiac or stroke conditions, liver cell failure, myeloproliferative neoplasms, acute or chronic infections, or those on anticoagulant or antiplatelet drugs, immunosuppressive therapy, or active inflammation in the past two weeks were excluded to avoid confounding results.

Pregnant or lactating females were also excluded. Informed consent was obtained from all participants, and data collection included detailed medical histories, clinical examinations, and laboratory investigations.

Blood samples (5 ml) were collected in EDTA tubes under aseptic conditions, and HbA1c, NLR, and PLR were calculated using standard methods. NLR was determined by dividing the absolute neutrophil count by the absolute lymphocyte count, and PLR was calculated by

dividing the platelet count by the absolute lymphocyte count. The laboratory analyses were conducted using a Sysmex XN-1000 hematology analyzer for CBC and the high-performance liquid chromatography (HPLC) method with an Abbott Architect Analyzer for HbA1c measurement.

Baseline characteristics such as age, gender, HbA1c levels, and hematological parameters were summarized using descriptive statistics. Mean ± standard deviation or median with the range of interquartiles were employed to represent continuous variables, with frequencies and percentages being the mode of presentation of the categorical variables.

Gender distribution revealed higher proportion males (~60%), and this imbalance was accounted for during analysis. Independent samples t-tests were used to compare continuous variables between low and high NLR/PLR groups, and stratification for age, BMI, and duration of diabetes was performed to control effect modifiers. Pearson's correlation coefficients were calculated to assess the relationships among the NLR, PLR, HbA1c, and other clinical parameters such as hemoglobin, white blood cell counts, and platelet counts. Statistical analyses were performed based on The SPSS version 25.0 for windows with the p-value ≤ 0.05 level of the significance adopted.

RESULTS

The mean age of the 102 participant's was 50 yeas. The cohort consisted of 55% males and 45% females. The mean HbA1C level was 7.8% ± 1.5%, with 63% of patients having poor glycemic control (HbA1C ≥7%). Hematological parameters showed hemoglobin levels of 13.2 g/dL, white blood cell counts of 7,500 cells/µL on average, and platelet counts of 200,000 cells/µL on average. The median NLR was 2.5 (interquartile range: 1.8–3.2), and the median PLR was 120 (interquartile range: 95–150). (Table 1)

Table 1: Baseline Characteristics of the Study Population

Characteristic	Value (Median [Range])
Age (years)	50 (13–95)
Hemoglobin (Hb, g/dL)	13.2 (11–25)
Platelet Count (x10⁹/L)	200,000 (115000–465000)
Neutrophil-to-Lymphocyte Ratio (NLR)	1.82 (0.92–2.32)
Platelet-to-Lymphocyte Ratio (PLR)	6000 (2577.78–0628.57)
Hematocrit (HCT, %)	43.6 (36–86)
Mean Corpuscular Volume (MCV, fL)	90.6 (56–100)
Mean Corpuscular Hemoglobin (MCH, pg)	27.3 (6–36)
Mean Corpuscular Hemoglobin Concentration (MCHC, g/dL)	31.05 (28–35)
HbA1C (%)	7.8 (5–14)
Neutrophils (%)	60 (43–65)
Lymphocytes (%)	33 (28–48)
Monocytes (%)	5.0 (3–9)
Eosinophils (%)	2.0 (1–2)

Using a 3.0 cut-off point, the patients were divided into low and high NLR groups, whereas PLR groups were also divided by the use of a cut-off value of 150. These groups showed significant differences in several clinical parameters when compared with one another. Patients with high NLR had markedly higher percentages of neutrophils 63.8% ± 6.5% vs. 55.2% ± 5.0%, $p < 0.001$) and lymphocyte percentages (28.5% ± 4.2% vs. 38.8% ± 5.5%, $p < 0.001$) than those with low NLR. High PLR was connected with an increased number of platelets (260,000 ± 50,000 cells/µL vs. 170,000 ± 25,000 cells/µL, $p < 0.001$) and reduced numbers of lymphocytes (30.5% ± 4.7% vs. 39.1% ± 5.0%, $p = 0.001$).(Table 2)

Table 2: Patient Characteristics by Neutrophil-to-Lymphocyte Ratio Groups

Characteristics	Low NLR (n=71, Mean ± SD)	High NLR (n=31, Mean ± SD)	p-value
Age (years)	50.10 ± 11.50	54.70 ± 12.80	0.11
Hb (g/dL)	14.10 ± 1.80	12.80 ± 1.10	0.030*
WBC (cells/µL)	7500.50 ± 1600.00	9100.00 ± 1900.50	0.002*
RBC (millions/µL)	5.20 ± 0.40	4.80 ± 0.35	0.012*
HCT (%)	44.90 ± 4.50	41.70 ± 3.30	0.050*
MCV (fL)	87.50 ± 8.00	92.00 ± 10.50	0.030*
Platelet count (cells/µL)	200500 ± 30000	210400 ± 45000	0.4
MCH (pg)	27.50 ± 3.00	26.90 ± 2.60	0.28
MCHC (g/dL)	31.30 ± 1.10	30.00 ± 1.00	0.010*
Neutrophils (%)	55.20 ± 5.00	63.80 ± 6.50	0.001*
Lymphocytes (%)	38.80 ± 5.50	28.50 ± 4.20	0.001*
Monocytes (%)	5.10 ± 0.70	5.20 ± 0.60	0.25
Eosinophils (%)	1.70 ± 0.40	2.00 ± 0.00	0.001*
HbA1C (%)	6.80 ± 1.20	8.10 ± 1.30	0.020*

Table 3: Patient Characteristics by Platelet-to-Lymphocyte Ratio (PLR) Groups

Characteristic	Low PLR (n=52, Mean ± SD)	High PLR (n=50, Mean ± SD)	p-value
Age (years)	49.80 ± 10.20	55.10 ± 13.70	0.08
Hb (g/dL)	14.20 ± 1.70	12.60 ± 1.20	0.015*
WBC (cells/µL)	7600.00 ± 1500.00	8900.50 ± 2000.00	0.010*
RBC (millions/µL)	5.10 ± 0.35	4.75 ± 0.45	0.010*
HCT (%)	45.00 ± 3.90	40.90 ± 4.20	0.004*
MCV (fL)	89.00 ± 7.50	92.50 ± 8.20	0.06
Platelet count (cells/µL)	170000 ± 25000	260000 ± 50000	0.001*
MCH (pg)	28.00 ± 2.80	26.50 ± 2.40	0.09
MCHC (g/dL)	31.20 ± 1.00	30.10 ± 1.10	0.015*
Neutrophils (%)	56.10 ± 4.90	62.50 ± 5.80	0.004*
Lymphocytes (%)	39.10 ± 5.00	30.50 ± 4.70	0.001*
Monocytes (%)	4.80 ± 0.70	5.40 ± 0.80	0.030*
Eosinophils (%)	1.60 ± 0.40	2.00 ± 0.00	0.001*
HbA1C (%)	6.70 ± 1.30	8.20 ± 1.10	0.005*

Correlation analysis was undertaken, which reported a moderate positive correlation between HbA1C and both NLR ($r = 0.45$, $p < 0.001$) and PLR ($r = 0.48$, $p < 0.001$). These observations point on raising glycemic index that follows the progression of NLR and PLR (Table 3). Analysis of logistic regression demonstrates that NLR as well as PLR play key roles in poor glycemic control. The other factors are age and gender that are independent as well

DISCUSSION

In the current study, we investigated the relationship between the Neutrophil-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio, and glycemic control in patients with Type 2 Diabetes Mellitus (T2DM). Our results suggest that elevated NLR and PLR were associated with poor glycemic control, as indicated by higher HbA1c levels in patients with increased values of these ratios. A study by Ahmed et al. (2021) explored the relationship between NLR, PLR, and blood glucose regulation in T2DM patients. They found that patients with poor glycemic control had elevated NLR and PLR levels, indicating a potential link between these markers.[14] The mean NLR in patients with poor glycemic control was significantly higher compared to those with good glycemic control, aligning with the findings of previous studies.[15] Our study found a mean NLR of 3.2 (±1.1) in patients with poor glycemic control and 1.8 (±0.6) in those with good control shows that results are consistent with the study by Li et al. (2023), who reported that elevated NLR was significantly correlated with poor glycemic control in T2DM patients, with patients having higher HbA1c levels associated with higher NLR values.[16] The association between elevated PLR and poor glycemic control could reflect underlying metabolic dysfunction and platelet activation are consistent with the work of Rahman et al. (2021), who found that elevated PLR was linked to poor glycemic control and an increased risk of complications in T2DM patients.[17] Such results also indicated that PLR might become a pivotal sign of the presence of patients who are at a higher risk of having a permanent diabetes-related issue.[18] Given the simplicity and availability of complete blood count tests, NLR and PLR could be useful markers for early detection of patients at risk for complications related to poorly controlled diabetes.[19] Monitoring these markers may help identify patients who require more intensive management to prevent the progression of diabetes-related complications. In our study, we also observed significant correlations between other clinical parameters, such as age and hemoglobin levels, with NLR and PLR.[20] The results of our study have significant implications for clinical practice, especially in resource-constrained settings. By incorporating simple, accessible biomarkers such as NLR and PLR into routine clinical assessments, healthcare providers can better identify high-risk patients and intervene early to prevent complications. Given that NLR and PLR are derived from routine blood tests, they are both cost-effective and easily accessible, making them suitable for widespread use in various healthcare settings.

LIMITATIONS:

Despite the promising findings, this study has several limitations. The cross-sectional design limits our ability to establish causal relationships between NLR, PLR, and glycemic control. Future research needs to include long-term research to identify the possibility of predicting diabetes-related complications and long-term results by these markers. Additionally, we did not assess factors such as medication adherence, lifestyle habits, or comorbidities, all of which could influence the results. Future studies should take these factors into account to provide a more comprehensive understanding of the role of NLR and PLR in diabetes management.

CONCLUSION:

In conclusion, this study supports the growing body of evidence indicating that NLR and PLR are valuable markers for assessing glycemic control in T2DM patients. These markers were associated with poor glycemic control and may help identify patients at higher risk for complications. Given their ease of measurement and clinical relevance, NLR and PLR have the potential to be integrated into routine diabetes care to improve patient outcomes

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CONFLICT OF INTEREST

None.

AUTHOR'S CONTRIBUTION

SG: Research Proposal,
IU: Review of Article,
TF: Review of Article, Supervision of project
NT: Data Analysis and Result Writing
HA: Data Analysis and Result Writing

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