GMR
The Original

ASSOCIATION OF NEUTROPHIL-TO-LYMPHOCYTE RATIO WITH GLYCEMIC CONTROL IN PATIENTS WITH TYPE 2 DIABETES MELLITUS: A CROSS-SECTIONAL STUDY

Dr. Shivani Saini[1], Dr. Ayush Jain[2]*, Dr. Bimal k. Agrawal [3]

[1]Associate professor, Department of General Medicine, MM Institute of Medical Sciences and Research, Mullana , Ambala, Haryana, India
[2]Junior resident 3, Department of General Medicine MM Institute of Medical Sciences and Research, Mullana , Ambala, Haryana, India, Email- ayushshrishrimal16@gmail.com
[3]Principal and professor Department of General Medicine MM Institute of Medical Sciences and Research, Mullana , Ambala, Haryana, India

ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by persistent hyperglycemia and low-grade systemic inflammation. Increasing evidence suggests that inflammatory biomarkers play an important role in the pathogenesis and progression of diabetes and its complications. The neutrophil-to-lymphocyte ratio (NLR), an inexpensive and readily available marker derived from routine blood counts, has emerged as a potential indicator of systemic inflammation.

Objective: To evaluate NLR in patients with T2DM and determine its association with glycemic parameters.

Methods: A hospital-based cross-sectional study was conducted among 100 patients with T2DM attending a tertiary care center. Clinical details, hematological parameters, fasting blood sugar (FBS), random blood sugar (RBS), and glycated hemoglobin (HbA1c) were recorded. NLR was calculated from complete blood count parameters, and its correlation with glycemic indices was assessed.

Results: Among the study participants, 43% had NLR <3, 16% had NLR between 3–5, and 41% had NLR >5. NLR demonstrated a significant positive correlation with HbA1c ($r=0.44$, $p<0.001$), FBS ($r=0.36$, $p<0.001$), and RBS ($r=0.30$, $p=0.003$). Higher NLR values were associated with poorer glycemic control.

Conclusion: NLR showed a significant association with glycemic parameters in patients with T2DM and may serve as a simple, cost-effective inflammatory marker for assessing glycemic status and disease severity.

KEYWORDS: Type 2 diabetes mellitus, Neutrophil-to-lymphocyte ratio, HbA1c, Inflammation, Glycemic control.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic condition characterized by elevated blood glucose levels caused by insulin resistance together with progressive dysfunction of pancreatic β-cells.The disease is associated with disturbances in carbohydrate, lipid, and protein metabolism and remains a major contributor to cardiovascular morbidity and mortality worldwide.[1–5]

Growing evidence indicates that chronic low-grade inflammation is a key contributor to the development and progression of type 2 diabetes mellitus (T2DM).Hyperglycemia, insulin resistance, and adipose tissue dysfunction promote the release of pro-inflammatory cytokines and reactive oxygen species, resulting in endothelial dysfunction, oxidative stress, and vascular injury.[6–9] These inflammatory mechanisms contribute not only to impaired glucose metabolism but also to the development of diabetic microvascular and macrovascular complications.[10–13]

Neutrophils and lymphocytes are important components of the immune response and are significantly influenced by metabolic and inflammatory alterations associated with diabetes.[14-18] Persistent hyperglycemia has been shown to enhance neutrophil activation, prolong neutrophil survival, and increase the release of inflammatory mediators, while simultaneously affecting lymphocyte function and immune regulation.[19–22] Consequently, alterations in circulating neutrophil and lymphocyte counts may reflect the underlying inflammatory burden in patients with T2DM.

The neutrophil-to-lymphocyte ratio (NLR), calculated from routine complete blood count parameters, has emerged as a simple, inexpensive, and readily available marker of systemic inflammation.[23-24]NLR reflects the balance between innate inflammatory activity and adaptive immune regulation and has been investigated in various inflammatory, cardiovascular, and metabolic disorders.[25–26] In patients with T2DM, elevated NLR has been associated with poor glycemic control, endothelial dysfunction, vascular inflammation, and increased risk of diabetes-related complications.[27-28]

Since NLR can be derived from a routine hematological investigation without additional cost, it may serve as a practical biomarker for assessing inflammatory status in diabetic patients. However, data regarding its relationship with glycemic parameters in the local population remain limited. Therefore, the present study was undertaken to evaluate the neutrophil-to-lymphocyte ratio in patients with Type 2 diabetes mellitus and to assess its association with glycemic status.

REVIEW OF LITERATURE

The neutrophil-to-lymphocyte ratio (NLR), derived from the absolute neutrophil and lymphocyte counts, serves as a practical and cost-effective marker for assessing systemic inflammatory status.Increasing evidence suggests that NLR reflects the inflammatory burden associated with diabetes mellitus and its complications. Chronic inflammation is a major factor in the pathogenesis of both type 1 and type 2 diabetes, where it contributes to the development of insulin resistance, β-cell dysfunction, and vascular complications. Elevated NLR has been associated with poor glycemic control, increased insulin resistance, and a higher risk of diabetic complications.[29-30]

Several studies have demonstrated a positive correlation between NLR and HbA1c levels, indicating that higher inflammatory activity is associated with poorer glycemic control. Elevated NLR has also been linked to increased fasting blood glucose levels and worsening insulin sensitivity.[31-32]

NLR has emerged as a potential predictor of both microvascular and macrovascular diabetic complications. Higher NLR values have been reported in patients with diabetic nephropathy, retinopathy, neuropathy, cardiovascular disease, and diabetic foot ulcers, suggesting its usefulness as a prognostic biomarker.[33–35]

Studies on NLR in Diabetes Mellitus

Sefil et al. (2014) reported a significant positive association between NLR and HbA1c levels in patients with type 2 diabetes mellitus, suggesting that elevated NLR reflects poor glycemic control.[36]

Shiny et al. (2014) found significantly higher NLR values in diabetic individuals compared with subjects having impaired glucose tolerance or normal glucose tolerance. NLR showed positive correlations with fasting plasma glucose, HbA1c, and insulin resistance.[37]

Kahraman et al. (2014) demonstrated that patients with diabetic foot ulcers had significantly higher NLR values, indicating its potential role as an inexpensive marker of systemic inflammation in these patients.[38]

Huang et al. (2015) observed significantly elevated NLR levels in patients with diabetic nephropathy andidentified NLR as an independent predictor of nephropathy development.[39]

Verdoia et al. (2015) concluded that an elevated rise in NLR was associated with both the prevalence and severity of coronary artery disease among diabetic patients.[40]

Lou et al. (2015) found a strong association between NLR and insulin resistance, suggesting that NLR may serve as a useful marker for identifying patients at risk of metabolic deterioration. [41]

Hussain et al. (2017) demonstrated that NLR increased progressively with worsening glycemic control and could be used as a monitoring tool in diabetes management.[42]

Wang et al. (2020) identified NLR as an independent risk factor for diabetic retinopathy and showed that its inclusion improved risk prediction models. [43]

Chen et al. (2024) reported that elevated NLR was significantly associated with an increased risk of type 2 diabetes mellitus in a large population-based analysis, reinforcing its role as an inflammatory biomarker in diabetes.[44]

MATERIALS AND METHODS

Study Design and Setting

This observational cross-sectional study was carried out in the Department of General Medicine at a tertiary care teaching hospital. The study was conducted over a period extending from November 2024 to May 2026.

The study was initiated only after receiving approval from the Institutional Ethics Committee. Written informed consent was obtained from each participant before inclusion in the study. The study was conducted in compliance with established ethical standards governing biomedical research involving human subjects.

Study Population

The study included 100 patients diagnosed with Type 2 Diabetes Mellitus (T2DM). Participants were recruited from the outpatient department, inpatient wards, and intensive care unit of the Department of General Medicine.

Diagnosis of T2DM was established according to the American Diabetes Association (ADA) criteria, which included fasting plasma glucose ≥126 mg/dL, 2-hour plasma glucose ≥200 mg/dL during an oral glucose tolerance test, HbA1c ≥6.5%, or random plasma glucose ≥200 mg/dL in the presence of classical symptoms of hyperglycemia. Eligible participants of either gender were considered for inclusion.

Study Duration

The study was conducted from November 2024 to May 2026.

Source of Data

Primary data were collected directly from enrolled patients using a predesigned and structured case record proforma. Relevant demographic details, clinical history, laboratory findings, and other necessary information were documented by the investigator.

Sample Size
A total of 100 patients with Type 2 Diabetes Mellitus were included in the study.
Inclusion Criteria
The following patients were included:
- Patients diagnosed with Type 2 Diabetes Mellitus according to ADA criteria.
- Patients willing to provide written informed consent.
- Patients of either gender.

Exclusion Criteria
Patients with the following conditions were excluded from the study:
- Acute or chronic liver disease
- Anemia
- Acute infectious illnesses
- Inflammatory bowel disease
- Osteoarthritis
- Rheumatoid arthritis
- Gout
- Bronchial asthma
- Hepatitis
- Acute myocardial infarction
- Cerebral infarction
- Acute kidney injury
- Chronic kidney disease
- Pregnancy

METHODOLOGY
This hospital-based cross-sectional study enrolled 100 patients with Type 2 Diabetes Mellitus who fulfilled the predefined inclusion and exclusion criteria.
After obtaining informed consent, detailed demographic and clinical information was recorded. Venous blood samples were collected under aseptic precautions and subjected to laboratory investigations.
Laboratory Investigations
Complete Blood Count (CBC)
Complete blood count analysis was performed using a six-part automated hematologyanalyzer (Sysmex XN-1000, Sysmex Corporation, Kobe, Japan). A Sysmex SQ-320 three-part hematologyanalyzer was utilized when required. Instrument calibration, quality control procedures, and sample processing were carried out according to the manufacturer's recommendations.
For study purposes, hemoglobin values greater than 8 g/dL and total leukocyte counts between 4–11 × 10^3/mm^3 were considered acceptable.
Neutrophil-to-Lymphocyte Ratio (NLR)
The neutrophil-to-lymphocyte ratio (NLR) was determined by dividing the absolute neutrophil percentage by the absolute lymphocyte percentage obtained from the complete blood count (CBC).
Glycated Hemoglobin (HbA1c)
HbA1c estimation was performed using High-Performance Liquid Chromatography (HPLC) on the BIORAD D-10 system. Calibration, standardization, quality assurance, and sample processing procedures were conducted according to manufacturer guidelines.
HbA1c levels were categorized as follows:
- Normal: 2.00–5.97%
- Good glycemic control: 5.97–6.81%
- Fair glycemic control: 6.81–7.65%
- Poor glycemic control: 7.65–14.0%

Blood Glucose Estimation
Fasting Blood Sugar (FBS) and Random Blood Sugar (RBS) levels were measured using automated chemistry analyzers (ERBA EM-360 and COBAS C311). All analyses were performed according to standard operating procedures and manufacturer instructions.
Renal and Liver Function Tests
Renal function tests (RFT) and liver function tests (LFT) were performed using an automated clinical chemistry analyzer.
Reference ranges considered were:
Renal Function Parameters
- Blood urea: 18–40 mg/dL
- Serum creatinine: 0.7–1.2 mg/dL
- Sodium: 135–145 mEq/L

- Potassium: 3.5–5.5 mEq/L
- Chloride: 96–106 mEq/L

Liver Function Parameters

- Total bilirubin: 0.2–1.0 mg/dL
- Serum albumin: 3.5–5.3 g/dL

Study Variables

The following variables were assessed:

- Age
- Gender
- Duration of diabetes mellitus
- Complete blood count parameters
- Neutrophil-to-lymphocyte ratio (NLR)
- Glycated hemoglobin (HbA1c)
- Fasting blood sugar (FBS)
- Random blood sugar (RBS)

Statistical Analysis

The collected data were recorded in Microsoft Excel and subsequently analyzed using the Statistical Package for the Social Sciences (SPSS) version 20.0.

Continuous variables were summarized as mean ± standard deviation (SD), while categorical variables were expressed as frequencies and percentages. Statistical analyses were performed using appropriate tests to examine associations between variables. A p-value <0.05 was considered indicative of statistical significance

Ethical Considerations

Ethical clearance was obtained from the Institutional Ethics Committee before commencement of the study. The study adhered to the ethical principles outlined for biomedical research involving human participants.

Written informed consent was obtained from all participants prior to enrolment. Confidentiality and privacy of patient information were maintained throughout the study. Participation was entirely voluntary, and participants were informed of their right to withdraw from the study at any stage without affecting their ongoing medical care or treatment.

RESULTS

Out of the 100 patients included in the study, the largest proportion was from the 60–69 years age group (42%). This was followed by those aged 50–59 years and ≥70 years, each accounting for 25% of the cases, while the least representation was observed in patients younger than 50 years (8%) as shown in Table 1.

Table 1: Table1.Distributionofstudyparticipantsaccordingtoage(n=100)

Agegroup (years)	Frequency	Percentage
<50	8	8.0
50–59	25	25.0
60–69	42	42.0
≥70	25	25.0
Total	100	100

We also observed that 52% were males and 48% were females, indicating a slightly higher proportion of male participants compared to female participants.

The participants showed vital signs within generally normal ranges. The mean pulse rate was 82.40 ± 12.10 beats/min (range: 60–110), while the mean systolic blood pressure was 122.10 ± 18.20 mmHg (100–140). The mean diastolic blood pressure was 80.15 ± 8.45 mmHg (60–100). Respiratory rate averaged 17.20 ± 1.80 breaths/min (14–22), and the mean body temperature was 98.42 ± 0.30°F (98.0–99.0) as depicted in Table 2.

Table 2: Clinicalparameters(n=100)

Parameter	Mean±SD	Minimum	Maximum
Pulse rate	82.40 ± 12.10	60	110
SBP(mmHg)	122.10 ± 18.20	100	140
DBP(mmHg)	80.15 ± 8.45	60	100
RespiratoryRate	17.20 ± 1.80	14	22

Temperature	98.42 ± 0.30	98.0	99.0

The mean hemoglobin level among participants was 11.85 ± 1.45 g/dL (range: 8.1–15.2 g/dL). The average total leukocyte count was 8.32 ± 1.40, while the mean platelet count was 220.15 ± 75.25 ×10³ (range: 90–500 ×10³). Neutrophils constituted a mean of 71.20 ± 11.20%, and lymphocytes accounted for 21.10 ± 9.80%. The mean neutrophil-to-lymphocyte ratio (NLR) was 4.85 ± 2.80, with values ranging from 1.10 to 12.20 as shown in table 3.

Table 3: Hematologicalparameters(n=100)

Parameter	Mean±SD	Minimum	Maximum
Hemoglobin(g/dL)	11.85±1.45	8.1	15.2
TLC	8.32 ± 1.40	4.5	9.8
Platelet(×10³)	220.15 ± 75.25	90	500
Neutrophil(%)	71.20 ± 11.20	45	90
Lymphocyte(%)	21.10 ± 9.80	5	40
NLR	4.85 ± 2.80	1.10	12.20

The glycemic profile of the participants indicated elevated blood glucose levels. The mean HbA1c was 8.92 ± 1.95% (range: 6.5–14.5%), while the mean fasting blood sugar level was 118.20 ± 20.40 mg/dL (75–260 mg/dL). The mean random blood sugar level was 205.30 ± 50.20 mg/dL, with values ranging from 110 to 420 mg/dL. Similarly our studies also reported the renal function parameters were largely within normal limits. The mean serum urea level was 31.50 ± 10.80 mg/dL, ranging from 12 to 65 mg/dL, while the mean serum creatinine level was 0.89 ± 0.18 mg/dL, with values between 0.5 and 1.19 mg/dL

The electrolyte profile of the participants was generally within normal ranges. The mean serum sodium level was 138.10 ± 3.95 mEq/L (range: 130–148 mEq/L), the mean potassium level was 4.22 ± 0.55 mEq/L (3.3–5.5 mEq/L), and the mean chloride level was 100.25 ± 3.85 mEq/L, with values ranging from 92 to 110 mEq/L. Liver function was evaluated using serum bilirubin and albumin levels, as hepatic involvement is frequently associated with Type II Diabetes Mellitus. The mean serum bilirubin level was 0.46 ± 0.18 mg/dL (range: 0.1–1.1 mg/dL), indicating that most participants had normal bilirubin values. The mean serum albumin level was 3.52 ± 0.42 g/dL, with values ranging from 2.5 to 4.6 g/dL, reflecting generally preserved liver synthetic function.

Our study also found that among the total participants, 43% had NLR values less than 3, 16% had NLR values between 3 and 5, and 41% had NLR values greater than 5 as shown in Table 4.

Table 4: NLRcategory(n=100)

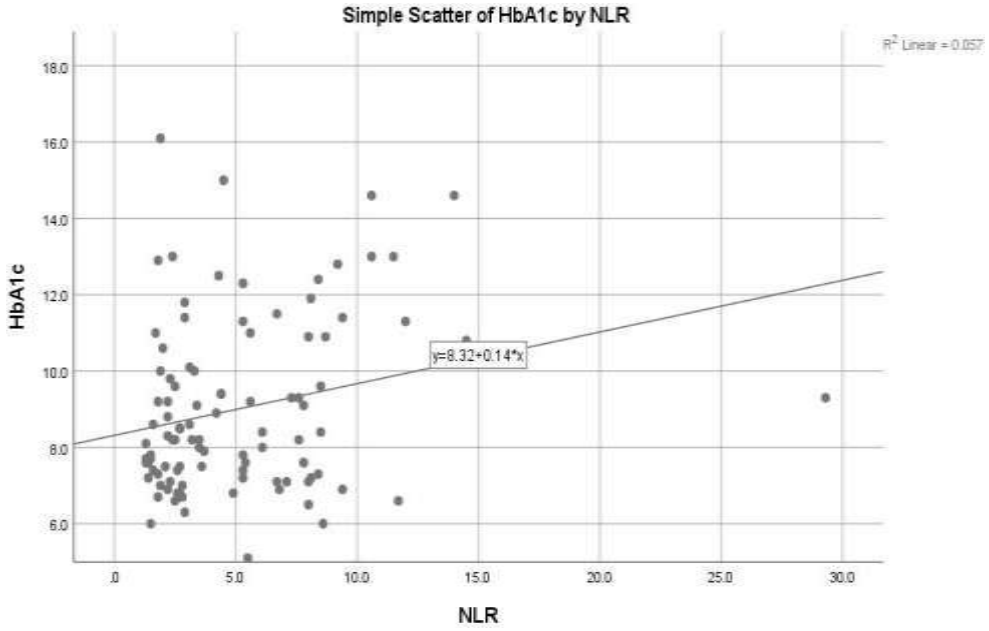
NLRcategory	Frequency	Percentage
<3	43	43.0
3–5	16	16.0
>5	41	41.0
Total	100	100

A statistically significant positive correlation was observed between NLR and all glycemic parameters. NLR showed a moderate positive correlation with HbA1c ($r = 0.44$, $p < 0.001$), followed by fasting blood sugar ($r = 0.36$, $p < 0.001$) and random blood sugar ($r = 0.30$, $p = 0.003$) as depicted in table 5 and graph 1. These findings indicate that higher NLR values were associated with poorer glycemic control.

Table 5: CorrelationbetweenNLRandglycemicparameters(n=100)

Parameter	Correlation(r)	p-value
HbA1c	0.44	<0.001
FBS	0.36	<0.001
RBS	0.30	0.003

Graph 1: Simple Scatter Graph of HBA1c by NLR

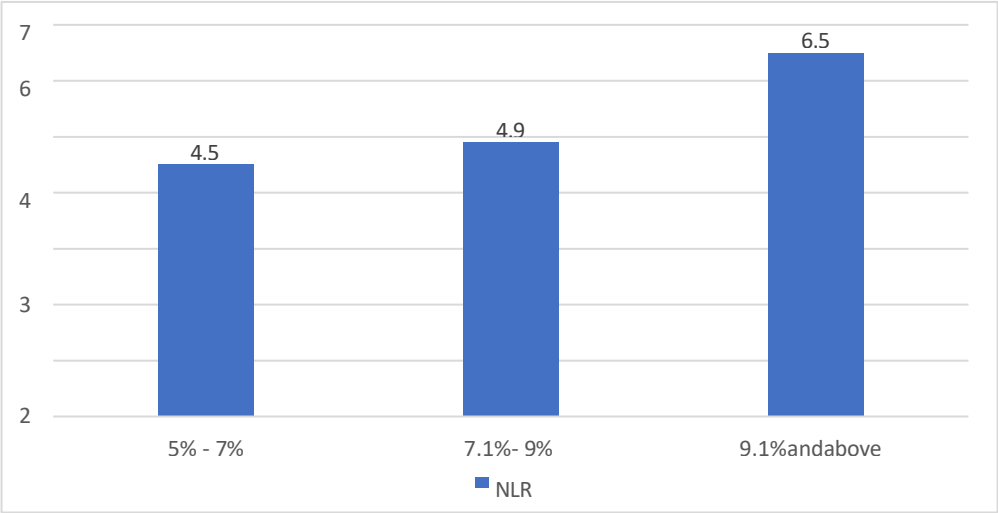


A significant association was observed between HbA1c and NLR levels. The mean NLR increased progressively from 4.5 in patients with HbA1c levels of 5–7% to 4.9 in those with HbA1c levels of 7.1–9%, reaching 6.5 among patients with HbA1c levels above 9% as depicted in table 6. This upward trend was statistically significant, indicating that higher HbA1c levels were associated with increased NLR values.

Table 6:

HbA1c(%)	NLR	
	Mean±SD	Median
5%-7%	4.5±3.2	2.8
7.1%-9%	4.9±3.1	2.9
9.1%and above	6.5±4.9	5.3
p-value	0.007	

Graph 2: AssociationbetweenHbA1clevelsandmeanNLRvalues



In our study multivariate analysis identified several independent predictors of elevated NLR. Alcohol consumption (adjusted coefficient = 1.520, p = 0.041), hypothyroidism (adjusted coefficient = 2.105, p = 0.006), age (adjusted coefficient = 1.018, p = 0.017), HbA1c (adjusted coefficient = 9.850, p < 0.001), fasting blood sugar (adjusted coefficient = 2.820, p < 0.001), and postprandial blood sugar (adjusted coefficient = 1.905, p = 0.028) showed statistically significant associations with NLR. In contrast, gender, place of residence, BMI, and hemoglobin levels were not significantly associated with NLR (p > 0.05) as shown in table 7.

Table 7: Table12.Multivariateregression(n=100)

Parameters	Adjustedcoefficient	p-value
Female	0.932	0.710
Male	1	-
Rural	0.821	0.231
Urban	1	-
Alcohol	1.520	0.041*
Hypothyroidism	2.105	0.006*
Age	1.018	0.017*
BMI	1.182	0.255
Hemoglobin	1.005	0.870
HbA1c	9.850	<0.001*
FBS	2.820	<0.001*
PPBS	1.905	0.028*

DISCUSSION

The present study was undertaken to evaluate the neutrophil–lymphocyte ratio (NLR) in patients with Type-II Diabetes Mellitus and to determine its association with glycemic parameters using a cross-sectional observational design conducted in a tertiary care setting involving 100 patients. The study aimed to explore NLR as a potential inflammatory marker reflecting metabolic control and disease burden in diabetic individuals.

In the current study, most participants belonged to the 60–69 years age group (42%), followed by 50–59 years (25%) and ≥70 years (25%), while only 8% were below 50 years of age. This distribution clearly reflects the higher prevalence of Type-II Diabetes Mellitus in older age groups, which is consistent with the well-established epidemiological trend that glucose intolerance and insulin resistance increase with advancing age. This age-related rise in diabetes burden is multifactorial, involving reduced β-cell function, increased adiposity, and chronic low-grade inflammation.

Comparable observations were reported by Verdoia et al. (2015), who noted that diabetic patients were predominantly older and carried a higher burden of cardiovascular risk factors, thereby emphasizing the role of age in both disease development and progression.[40]Further supporting this relationship, Duman et al. (2019) demonstrated a significant positive correlation between NLR and age (r = 0.26, p = 0.008), suggesting that systemic inflammatory activity increases progressively with aging in diabetic individuals.[45] This supports the present study's observation that a larger proportion of elderly patients may exhibit heightened inflammatory markers such as NLR.

Regarding gender distribution, the present study showed near-equal involvement of males (52%) and females (48%), with only a slight male predominance. This finding suggests that Type-II Diabetes Mellitus affects both sexes almost equally in the studied population. Similar observations were reported by Chen et al. (2024), who found no significant interaction between sex and NLR in diabetic patients, indicating that inflammatory markers such as NLR are not substantially influenced by gender differences.[44] Likewise, Huang et al. (2015) demonstrated that elevated NLR remained independently associated with diabetic complications irrespective of sex, further reinforcing its role as a universal inflammatory marker across genders.[39]

The present study showed that vital parameters, including pulse rate, blood pressure, respiratory rate, and temperature, remained largely within normal physiological limits, indicating that most patients were hemodynamically stable at the time of assessment. The mean systolic blood pressure (122.10 ± 18.20 mmHg) and

diastolic blood pressure (80.15 ± 8.45 mmHg) suggested that blood pressure was either well-controlled or mildly elevated in a subset of patients.

These findings are indirectly supported by Huang et al. (2015), who identified systolic blood pressure as an independent predictor of diabetic nephropathy along with NLR, highlighting the interplay between hemodynamic stress and inflammation in diabetic complications.[39]

Similarly, Wan et al. (2020) reported that higher NLR quartiles were associated with increased prevalence of cardiovascular disease, indicating that inflammatory status is closely linked with cardiovascular risk factors such as blood pressure in diabetic populations.[46] Although the present study did not directly analyze these associations, existing literature strongly suggests a shared pathophysiological link between inflammation and cardiovascular parameters in diabetes.

In the present study, hematological analysis revealed a mean neutrophil percentage of 71.20 ± 11.20%, lymphocyte percentage of 21.10 ± 9.80%, and mean NLR of 4.85 ± 2.80, indicating a state of relative neutrophilia and lymphocytopenia. This pattern reflects an activated innate immune response along with suppression of adaptive immunity, consistent with chronic inflammatory stress seen in Type-II Diabetes Mellitus.

These findings are consistent with previous literature. Shiny et al. (2014) reported significantly higher NLR levels in diabetic patients compared to individuals with impaired and normal glucose tolerance, suggesting a stepwise increase in inflammation with worsening glycemic status.[37] Similarly, Duman et al. (2019) observed elevated NLR in diabetic individuals (median 2.44) compared to healthy controls (1.5), reinforcing the association between diabetes and systemic inflammation.[45]

Notably, the mean NLR in the present study (4.85 ± 2.80) was higher than that reported in many earlier studies. This may indicate a comparatively higher inflammatory burden in the studied population. Supporting this interpretation, Hussain et al. (2017) reported that poorly controlled diabetic patients exhibited significantly higher NLR values (4.3 ± 2.8) compared to well-controlled individuals (2.0 ± 0.5), which closely aligns with the present findings.[42]Additionally, Lou et al. (2015) demonstrated that increased insulin resistance was significantly associated with elevated NLR, further emphasizing the close relationship between metabolic dysfunction and systemic inflammation.[41]

The present study demonstrated poor glycemic control among participants, with mean HbA1c of 8.92 ± 1.95%, fasting blood sugar (FBS) of 118.20 ± 20.40 mg/dl, and random blood sugar (RBS) of 205.30 ± 50.20 mg/dl. These values indicate inadequate glycemic regulation in the study population, reflecting suboptimal long-term and short-term glucose control.

These findings are in agreement with Sefil et al. (2014), who reported that patients with HbA1c levels above 7% had significantly increased neutrophil counts and NLR, suggesting a direct association between poor glycemic control and systemic inflammation.[36] Similarly, Hussain et al. (2017) observed that NLR increased progressively with worsening glycemic status, being highest in patients with HbA1c ≥ 9%.[42] Furthermore, Shiny et al. (2014) reported a significant positive correlation between NLR and HbA1c ($r = 0.411$), as well as fasting plasma glucose, indicating that hyperglycemia contributes directly to inflammatory activation.[37]

Renal function parameters in the present study showed mean serum urea (31.50 ± 10.80 mg/dl) and creatinine (0.89 ± 0.18 mg/dl), suggesting that most participants had preserved renal function at the time of assessment. However, extensive literature suggests that elevated NLR is strongly associated with diabetic nephropathy and early renal damage.

Huang et al. (2015) demonstrated that NLR was significantly higher in patients with diabetic nephropathy and that each unit increase in NLR increased the risk of nephropathy by more than two-fold (OR 2.088).[39] Similarly, Khandare et al. (2017) reported significantly elevated NLR in patients with nephropathy compared to those without renal involvement.[47] Abdallah et al. (2018) further confirmed that NLR levels increase progressively with worsening albuminuria, indicating its potential role as an early marker of renal injury.[48] Although renal complications were not specifically categorized in the present study, elevated NLR values may indicate a future risk of renal involvement.

Electrolyte and liver function parameters, including sodium (138.10 ± 3.95 mEq/L), potassium (4.22 ± 0.55 mEq/L), chloride, bilirubin, and albumin (3.52 ± 0.42 g/dL), were largely within normal limits. While these parameters were not directly correlated with NLR, systemic inflammation in diabetes is known to affect multiple organ systems.

Wan et al. (2020) highlighted that elevated NLR reflects broader metabolic and vascular dysfunction, extending beyond glycemic abnormalities to multisystem involvement, including hepatic and cardiovascular systems.[46] This emphasizes the systemic nature of inflammation in Type-II Diabetes Mellitus.

In terms of NLR distribution, 43% of patients had NLR <3, 16% had NLR between 3–5, and 41% had NLR >5, indicating that a substantial proportion of patients exhibited elevated inflammatory status. This suggests that nearly half of the diabetic population demonstrated significant systemic inflammation.

These findings are consistent with Shiny et al. (2014), who reported a progressive increase in NLR with worsening glucose tolerance.[37] Similarly, Mertoglu et al. (2017) observed that both prediabetic and diabetic individuals had significantly higher NLR compared to normoglycemic controls, indicating that inflammation begins early in the disease process.[49]Yilmaz et al. (2015) further demonstrated that NLR >3.12 could predict diabetes development, supporting its role as a potential predictive biomarker.[50]

Studies on diabetic complications also reinforce these findings. Khandare et al. (2017) reported higher NLR in nephropathy patients,[47] Wang et al. (2020) observed elevated NLR in diabetic retinopathy,[43].These findings collectively suggest that NLR is not only a marker of diabetes but also reflects its complication burden.

The present study demonstrated a statistically significant positive correlation between NLR and glycemic parameters, including HbA1c ($r = 0.44$, $p < 0.001$), fasting blood sugar ($r = 0.36$, $p < 0.001$), and random blood sugar ($r = 0.30$, $p = 0.003$). These findings indicate that worsening glycemic control is directly associated with increased systemic inflammation.

These results are consistent with Shiny et al. (2014), who reported significant correlations between NLR and HbA1c, fasting glucose, and insulin resistance[37] Duman et al. (2019) also demonstrated a strong correlation between NLR and HbA1c ($r = 0.49$), reinforcing the relationship between inflammation and glycemic status.[45] Hussain et al. (2017) further observed increasing NLR across worsening glycemic categories, confirming a dose–response relationship.[42]

Lou et al. (2015) also reported a positive association between NLR and insulin resistance,[41] while Chen et al. (2024) identified NLR as an independent risk factor for Type-II Diabetes Mellitus.[24] These findings suggest that inflammatory processes play a central role in both the development and progression of diabetes.

Studies on complications further support this association. Huang et al. (2015) identified HbA1c and NLR as predictors of nephropathy,[39] while Wan et al. (2020) reported increased cardiovascular and renal complications in patients with elevated NLR.[46] This highlights the broader clinical significance of NLR beyond glycemic assessment.

Multivariate regression analysis in the present study identified HbA1c, fasting blood sugar, postprandial blood sugar, age, alcohol consumption, and hypothyroidism as significant predictors of NLR. These findings indicate that NLR is influenced by multiple metabolic, hormonal, and lifestyle factors, highlighting its multifactorial nature.

The strong association between HbA1c and NLR is supported by Hussain et al. (2017), who identified NLR as an independent marker of poor glycemic control.[42] Duman et al. (2019) also confirmed its strong correlation with HbA1c and fasting glucose.[45] Lou et al. (2015) further demonstrated its association with insulin resistance, [41] while Chen et al. (2024) confirmed its independent predictive role for Type-II Diabetes Mellitus.[24]

Age-related association observed in this study is consistent with Duman et al. (2019), [45] Verdoia et al. (2015),[40] and Wan et al. (2020),[47] all of whom reported increasing NLR with age and cardiovascular risk burden. Huang et al. (2015) also identified NLR as an independent predictor of diabetic nephropathy, reinforcing its prognostic relevance.[39]

Overall, the present study demonstrates that NLR is significantly elevated in Type-II Diabetes Mellitus and shows strong positive correlations with glycemic indices. These findings align with existing literature and support the role of NLR as a simple, cost-effective, and clinically useful inflammatory biomarker.

Incorporation of NLR into routine diabetic evaluation may enhance early risk stratification, improve monitoring of disease progression, and aid in identifying patients at risk of complications.

CONCLUSION

The present study demonstrated that neutrophil-to-lymphocyte ratio (NLR) is significantly elevated in patients with Type 2 Diabetes Mellitus and shows a strong positive correlation with glycemic indices, including HbA1c, fasting blood sugar, and random blood sugar, indicating that NLR reflects the underlying inflammatory burden associated with poor glycemic control. A considerable proportion of patients exhibited raised NLR values, supporting the presence of chronic systemic inflammation in diabetes. NLR was also influenced by metabolic factors and showed independent association with glycemic parameters, reinforcing the role of inflammation in the pathophysiology and progression of Type 2 Diabetes Mellitus. Given its simplicity, low cost, and wide availability, NLR may serve as a useful adjunct marker in routine diabetic evaluation to identify patients at higher risk of poor glycemic control and complications, although larger studies are needed to establish standardized cut-off values and prognostic utility.

SUMMARY

This hospital-based observational cross-sectional study was conducted in the Department of General Medicine at a tertiary care center from 2025 to 2026. A total of 100 patients diagnosed with Type 2 Diabetes Mellitus according to American Diabetes Association criteria were enrolled from outpatient and inpatient departments after obtaining informed consent.

Detailed demographic and clinical data were recorded using a structured proforma. Blood samples were analyzed for complete blood count, and neutrophil-to-lymphocyte ratio (NLR) was calculated from differential leukocyte counts. Glycemic parameters, including HbA1c (measured by high-performance liquid chromatography), fasting blood sugar, and random blood sugar (measured using automated analyzers), were assessed. Additional biochemical parameters including renal function tests, liver function tests, and electrolytes were also evaluated.

REFERENCES

1 LeRoith D. β-cell dysfunction and insulinresistancein type2 diabetes: role of metabolic and genetic abnormalities. The American journal of medicine. 2002 Oct 28;113(6):3-11.

2 Theofilis P, Sagris M, Oikonomou E, Antonopoulos AS, Siasos G, Tsioufis C, Tousoulis D. Inflammatory

mechanisms contributing to endothelial dysfunction. Biomedicines. 2021 Jul 6;9(7):781.
3 Cerf ME. Beta cell dysfunction and insulin resistance. Frontiers in endocrinology. 2013 Mar 27;4:37.
4 Rudic RD, Sessa WC. Nitric oxide in endothelial dysfunction and vascular remodeling: clinical correlates and experimental links. The American Journal of Human Genetics. 1999 Mar 1;64(3):673-7.
5 Singh A, Kukreti R, Saso L, Kukreti S. Mechanistic insight into oxidative stresstriggeredsignaling pathways and type 2 diabetes. Molecules. 2022 Jan 30;27(3):950.
6 Oguntibeju OO. Type 2 diabetes mellitus, oxidative stress and inflammation:examining the links. International journal ofphysiology, pathophysiology and pharmacology.2019Jun15;11(3):45.
7 Ponugoti B, Dong G, Graves DT. Role of forkhead transcriptionfactors in diabetes-induced oxidative stress. Journal of Diabetes Research. 2012;2012(1):939751.
8 Chen L, Chen R,Wang H, Liang F. Mechanisms linking inflammation to insulin resistance. International journal of endocrinology. 2015;2015(1):508409.
9 Ratter-Rieck JM, Maalmi H, Trenkamp S, Zaharia OP, Rathmann W, Schloot NC, Straßburger K, Szendroedi J, Herder C, Roden M, GDS Group:. Leukocyte counts and T-cell frequencies differ between novel subgroups of diabetes and are associated with metabolic parameters and biomarkers of inflammation. Diabetes.2021Nov1;70(11):2652-62.
10 Vilariño RJ, Paragano RA. Endothelial dysfunction in normal and abnormal glucose metabolism. Series Editor. 2008:17.
11 Zarbock A, Polanowska-Grabowska RK, Ley K. Platelet-neutrophil-interactions: linking he most asisandin flammation. Bloodreviews.2007 Mar 1;21(2):99-111.
12 Jackson DG. Leucocyte trafficking via the lymphatic vasculature—mechanisms and consequences. Frontiers in immunology. 2019 Mar 14;10:471.
13 Luc K, Schramm-Luc A, Guzik TJ, Mikolajczyk TP. **Oxidative stress and inflammatory markers in prediabetes and diabetes.***Journal of Physiology and Pharmacology.* 2019;70(6):809–824.
14 ThimmappaPY,VasishtaS,GaneshK,NairAS,JoshiMB.Neutrophil (dys) function due to altered immuno-metabolic axis in type 2diabetes: implications in combating infections. Human Cell. 2023 Jul;36(4):1265-82.
15 Winterbourn CC, Kettle AJ, Hampton MB. Reactive oxygen species and neutrophil function. Annual review of biochemistry. 2016 Jun 2;85:765-92.
16 Jafar N, Edriss H, Nugent K. **The effect of short-term hyperglycemia on the innate immune system.***The American Journal of the Medical Sciences.* 2016;351(2):201–211.
17 Wang Q, Doerschuk CM. The signaling pathways induced by neutrophilendothelial cell adhesion. Antioxidants & redox signaling. 2002 Feb;4(1):39- 47.
18 DaryaborG,AtashzarMR,KabelitzD,MeriS,KalantarK.Theeffects of type 2 diabetes mellitus on organ metabolism and the immune system. Frontiers in immunology. 2020 Jul 22;11:1582.
19 Zhou T, Hu Z, Yang S, Sun L, Yu Z, Wang G. Role of adaptive and innate immunity in type 2 diabetes mellitus. Journal of diabetes research. 2018;2018(1):7457269.
20 Chakraborty S, Khamaru P, Bhattacharyya A. Regulation of immune cell metabolism in health and disease: Special focus on T and B cell subsets. Cell biology international. 2022 Nov;46(11):1729-46.
21 Angeli V, Randolph GJ. Inflammation, lymphatic function, and dendritic cell migration. Lymphatic research and biology. 2006 Mar 1;4(4):217-28.
22 Ts alamandris S, Antonopoulos AS, Oikonomou E, Papamikroulis GA, Vogiatzi G, Papaioannou S, et al. *The role of inflammation in diabetes: current concepts and future perspectives.* European Cardiology Review. 2019;14(1):50–59.
23 Islam MM, Satici MO, Eroglu SE. Unraveling the clinical significance and prognostic value of the neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, systemic immune-inflammation index, systemic inflammationresponseindex,anddeltaneutrophilindex:Anextensive literature review. Turkish journal of emergency medicine. 2024 Jan 1;24(1):8-19.
24 Pongratz G, Straub RH. Chronic effects of the sympathetic nervous system in inflammatory models. Neuroimmunomodulation. 2023 May 18;30(1):113-34.
25 Lipke K, Kubis-Kubiak A, Piwowar A. Molecular mechanism of lipotoxicityas an interesting aspect in the development of pathological states—current view of knowledge. Cells. 2022 Mar 1;11(5):844.
26 Maestroni GJ.Adrenergicmodulationofhematopoiesis.Journalof Neuroimmune Pharmacology. 2020 Mar;15(1):82-92.
27 Chrousos GP. The stress response and immune function: clinical implications. AnnNYAcadSci. 2000;917(8):38-67.
28 Donath MY, Shoelson SE. Type 2 diabetes as an inflammatory disease. *Nature Reviews Immunology.* 2011 Feb;11(2):98–107
29 Newsholme P, Keane KN, Carlessi R, Cruzat V. Oxidative stress pathways in pancreatic β-cells and insulin-sensitive cells and tissues: importance to cell metabolism, function, and dysfunction. *American Journal of Physiology-Cell Physiology.* 2019;317(3):C420–C433.
30 Abell SK, De Courten B, Boyle JA,Teede HJ. Inflammatoryand other biomarkers: role in pathophysiology and prediction of gestational diabetes mellitus. Int J Mol Sci. 2015;16(6):13442-73.
31. WangJ,ZhouD,LiX.Theassociationbetweenneutrophil-to-lymphocyte ratio and diabetic depression in US

adults with diabetes: findings from the 2009-2016 National Health and Nutrition Examination Survey (NHANES). Biomed Res Int. 2020;2020(1):8297628.
32. Ulandari R, Kurniawan LB, Nurahmi N, Muhadi D. Analysis of NLR in type 2 diabetes mellitus with and without diabetic foot ulcer.Indones J Clin Pathol Med Lab. 2023;29(2):185-8
33. Wang SY, Shen TT, Xi BL, Shen Z, Zhang X. Vitamin D affects the neutrophilto-lymphocyte ratioin patients with type2diabetesmellitus. J Diabetes Investig. 2021;12(2):254-65.
34. Liu S, Zheng H, Zhu X, Mao F, Zhang S, Shi H, et al. Neutrophil-to-lymphocyte ratio is associated with diabetic peripheral neuropathy in type 2 diabetes patients. Diabetes Res Clin Pract. 2017;130:90-7.
35. Li X, Wang L, Liu M, Zhou H, Xu H.Association between neutrophil-tolymphocyte ratio and diabetic kidney disease in type 2 diabetes mellitus patients: a cross-sectional study. Front Endocrinol. 2024;14:1285509.
36.SefilF, UlutasKT, DokuyucuR, SumbulAT, YengilE, YagizAE, etal. Investigation of neutrophilly mphocyteratio and blood glucose
regulation in patients with type 2 diabetes mellitus. J Int Med Res. 2014;42(2):581-8.
37. Shiny A, Bibin YS, Shanthirani CS, Regin BS, Anjana RM, Bala subramanyamM, etal. Association of neutrophil-lymphocyteratio with glucose intolerance: an indicator of systemic inflammation in patients with type 2 diabetes. Diabetes Technol Ther. 2014;16(8):524-30.
38. Kahraman C, Yümün G, Kahraman NK, Namdar ND, Cosgun S. Neutrophil-tolymphocyte ratio in diabetes mellitus patients with and without diabetic foot ulcer. Eur J Med Sci. 2014;1(1):8-13.
39. Huang W, Huang J, Liu Q, Lin F, He Z, Zeng Z, et al. Neutrophil–lymphocyte ratio is areliablepredictivemarker forearly-stage diabetic nephropathy. Clin Endocrinol (Oxf). 2015;82(2):229-33.
40. Verdoia M, SchafferA, Barbieri L, Aimaretti G, Marino P, Sinigaglia F, et al. Impact of diabetes on neutrophil-to-lymphocyte ratio and its relationship to coronary artery disease. Diabetes Metab. 2015;41(4):304-11.
41. Lou M, Luo P, Tang R, Peng Y, Yu S, Huang W, et al. Relationship between neutrophil-lymphocyte ratio and insulin resistance in newly diagnosed type 2 diabetes mellitus patients. BMC EndocrDisord. 2015;15:1-6.
42. Hussain M, Babar MZ,Akhtar L, Hussain MS. Neutrophil lymphocyte ratio(NLR): a well assessment tool of glycemic control in type 2 diabetic patients. Pak J Med Sci. 2017;33(6):1366.
43. WangJR,ChenZ,YangK,YangHJ,TaoWY,LiYP,etal.Association between neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and diabetic retinopathy among diabetic patients without a related family history. DiabetolMetab Syndr. 2020;12:1-0.
44. Chen HL, Wu C, Cao L, Wang R, Zhang TY, He Z. The association between the neutrophil-to-lymphocyte ratio and type 2 diabetes mellitus:across-sectionalstudy.BMCEndocrDisord.2024;24(1):107.
45. Duman TT, Aktas G, Atak BM, Kocak MZ, Erkus E, Savli H. Neutrophil to lymphocyte ratio as an indicative of diabetic controllevel in type 2 diabetes mellitus. Afr Health Sci. 2019;19(1):1602-6.
46. Wan H,WangY, Fang S, ChenY, ZhangW, Xia F, et al.Associations between the neutrophil-to-lymphocyte ratio and diabetic complications in adults with diabetes: a cross-sectional study. J Diabetes Res. 2020;2020(1):6219545.
47. Khandare SA, Chittawar S, Nahar N, DubeyTN, Qureshi Z. Study of neutrophil-lymphocyte ratio as novel marker for diabetic nephropathy in type 2 diabetes.IndianJEndocrinolMetab.2017;21(3):387-92
48. Abdallah AI, Abdelaziz AA, El-Sayed ES, Emran TM. Study of neutrophil lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR) as a predictor inflammatory marker for diabetic nephropathy in type 2 diabetic patients. Egypt J Hosp Med. 2018;72(7):4800-7.