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Original Article

Association between Neutrophil-to-Lymphocyte Ratio and Glycemic Control in Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is associated with chronic low-grade inflammation that contributes to poor glycemic control and the development of diabetic complications. The neutrophil-to-lymphocyte ratio (NLR), derived from a routine complete blood count, has emerged as a simple and inexpensive marker of systemic inflammation. However, evidence regarding its relationship with glycemic control in Bangladeshi patients remains limited. Aim of the study: To evaluate the association between the neutrophil-to-lymphocyte ratio and glycemic control in patients with type 2 diabetes mellitus and to determine the diagnostic performance of NLR in identifying poor glycemic control. **Methods & Materials**: This hospital-based cross-sectional analytical study included 260 adult patients with T2DM. Clinical, anthropometric, and laboratory data were collected using a structured questionnaire and hospital records. Glycemic control was classified according to HbA1c levels as good (<7.0%) or poor (≥7.0%). NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. Comparisons between groups were performed using the independent samples t-test and Chi-square test. Pearson's correlation analysis and receiver operating characteristic (ROC) curve analysis were conducted to evaluate the relationship and diagnostic performance of NLR. **Result**: The mean age of the participants was 56.8±9.4 years, and 56.5% were male. The mean NLR was 2.42±0.91. Patients with poor glycemic control had significantly higher neutrophil percentages and NLR values (2.70±0.87 vs. 1.89±0.46, p<0.001), while lymphocyte percentages were significantly lower (p<0.001). A significant association was observed between NLR categories and glycemic control (χ^2=20.87, p<0.001). NLR demonstrated moderate positive correlations with fasting blood glucose (r=0.49), postprandial blood glucose (r=0.45), and HbA1c (r=0.58) (all p<0.001). ROC analysis identified an optimal NLR cutoff value of 2.25 for predicting poor glycemic control, with an AUC of 0.82 (95% CI: 0.74–0.89), sensitivity of 79.5%, specificity of 73.8%, and overall diagnostic accuracy of 77.5%. **Conclusion**: Elevated NLR was significantly associated with poor glycemic control and higher HbA1c levels in patients with T2DM. Given its simplicity, low cost, and availability from routine blood testing, NLR may serve as a useful adjunctive inflammatory marker for identifying patients at risk of poor glycemic control, particularly in resource-limited healthcare settings. Further prospective multicenter studies are warranted to validate its prognostic utility.

Keywords: *Type 2 diabetes mellitus; Neutrophil-to-lymphocyte ratio; Glycemic control; HbA1c*

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from insulin resistance and progressive impairment of pancreatic β-cell function. The neutrophil-to-lymphocyte ratio (NLR), calculated from a routine complete blood count, has emerged as a simple and inexpensive indicator of systemic inflammation and is being investigated as a potential marker of glycemic control [1-3]. The global diabetes prevalence in 2021 was estimated to be 10.5% (536.6 million people) in 20- 79-year-old adults, and this number is projected to increase substantially over the coming decades, making diabetes one of the leading causes of morbidity and mortality worldwide [4]. In Bangladesh, the number of adults aged 20-79 years with diabetes is approximately 13.1 million adults were estimated to have diabetes, and the prevalence is 12.5%, reflecting a rapidly growing public health challenge driven by urbanization, unhealthy lifestyles, obesity, and population ageing [5]. Persistent hyperglycemia induces oxidative stress and activates inflammatory pathways, resulting in the release of cytokines such as interleukin-6 and tumor necrosis factor-α. These inflammatory mediators stimulate neutrophil production while reducing lymphocyte activity, leading to an elevated NLR. Since inflammation plays a central role in insulin resistance and endothelial dysfunction, NLR may reflect both metabolic imbalance and the inflammatory burden associated with poor glycemic control. Consequently, patients with higher HbA1c levels frequently demonstrate increased NLR values, suggesting that this ratio may complement conventional biochemical markers in evaluating disease status. In recent years, T2DM has also been associated with chronic low-grade inflammation, which contributes to disease progression and the development of vascular complications [6-8]. Poor glycemic control contributes to both microvascular and macrovascular complications, including diabetic nephropathy, retinopathy, neuropathy, and cardiovascular disease. Early identification of patients with increased inflammatory activity may therefore improve risk assessment and encourage timely therapeutic intervention. Individuals with poorly controlled T2DM have significantly higher NLR values than those with adequate glycemic control, highlighting the potential clinical relevance of NLR [9,10]. The neutrophil-to-lymphocyte ratio (NLR) is an inexpensive, readily available, and easily calculated inflammatory biomarker derived from a routine complete blood count, without requiring additional laboratory investigations, making it a practical tool for clinical assessment, particularly in resource-limited settings [11]. These characteristics make it particularly valuable in resource-limited healthcare settings. However, NLR is a non-specific inflammatory marker and may be influenced by infections, autoimmune disorders, malignancies, medications, and other inflammatory conditions, limiting its diagnostic specificity when used alone [12]. Nevertheless, previous studies have

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reported inconsistent cut-off values, varied study populations, and predominantly cross-sectional designs, limiting the generalizability of their findings. Furthermore, studies of South Asian populations, particularly Bangladesh, remain relatively limited [13]. Therefore, further investigation is needed to clarify the association between NLR and glycemic control among patients with T2DM in different clinical settings. The study aimed to evaluate the association between neutrophil-to-lymphocyte ratio and glycemic control in patients with Type 2 diabetes mellitus and to determine whether NLR can serve as a practical inflammatory marker for assessing glycemic status.

METHODS & MATERIALS

This hospital-based cross-sectional analytical study was conducted in the Department of Pathology, Gazi medical College Hospital, Khulna, Bangladesh, from January 2023 to December 2025. A total of 260 patients were enrolled using consecutive sampling after obtaining written informed consent.

Inclusion Criteria:

- Patients aged 18 years or older.
- Diagnosed with type 2 diabetes mellitus according to the American Diabetes Association (ADA) criteria.

Exclusion Criteria:

- Type 1 diabetes mellitus or gestational diabetes.
- Acute or chronic infections.
- Autoimmune or inflammatory diseases.
- Hematological disorders.
- Malignancy.
- Chronic liver disease.
- Current corticosteroid or immunosuppressive therapy.
- Recent surgery or trauma (within the previous 3 months).
- Pregnancy.

Ethical Considerations

Ethical approval for the study was obtained from the Institutional Review Board (IRB) of the participating institution before commencement of the study. Written informed consent was obtained from all participants after explaining the purpose of the study. Confidentiality of participant information was maintained throughout the study, and all procedures were conducted in accordance with the ethical principles of the Declaration of Helsinki.

Data Collection

Data were collected using a pretested structured data collection form. Socio-demographic information, including age, sex, residence, body mass index (BMI), and comorbidities, was obtained through face-to-face interviews and review of patients' medical records. Clinical information, including duration of diabetes, blood pressure, and relevant medical history, was also recorded. Height and weight were measured using standard procedures, and BMI was calculated as weight in kilograms divided by the square of height in meters (kg/m^2).

Following an overnight fast of 8–10 hours, approximately 5 mL of venous blood was collected from each participant under aseptic conditions. Fasting blood glucose (FBG), postprandial blood glucose (PPBG), and glycated hemoglobin (HbA1c) levels were measured using standard laboratory methods in the hospital's clinical laboratory. A complete blood count (CBC) was performed using an automated hematology analyzer to determine hemoglobin concentration, total white blood cell count, differential leukocyte count, and platelet count. The neutrophil-to-lymphocyte ratio (NLR) was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. For categorical analysis, NLR values were classified as low (<2.0), intermediate (2.0–2.99), and high (≥3.0).

Glycemic control was assessed using HbA1c levels according to the American Diabetes Association criteria. Participants with HbA1c levels below 7.0% were categorized as having good glycemic control, whereas those with HbA1c levels of 7.0% or higher were considered to have poor glycemic control. The primary outcome of the study was the association between NLR and glycemic control. Secondary outcomes included comparison of hematological parameters between good and poor glycemic control groups, assessment of the correlation between NLR and glycemic indices (FBG, PPBG, and HbA1c), and evaluation of the diagnostic performance of NLR in identifying poor glycemic control using receiver operating characteristic (ROC) curve analysis.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) software version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables were presented as frequencies and percentages. Comparisons between two groups were performed using the independent samples Student's t-test for continuous variables and the Chi-square test for categorical variables. Pearson's correlation coefficient (r) was used to assess the relationship between NLR and glycemic parameters (FBG, PPBG, and HbA1c). ROC curve analysis was performed to determine the optimal NLR cutoff value for predicting poor glycemic control. The area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy were calculated. A two-tailed p-value <0.05 was considered statistically significant.

RESULT

The study included 260 patients with type 2 diabetes mellitus, with a mean age of 56.8 ± 9.4 years. The largest proportion of participants belonged to the 55–64 years age group (36.54%). Males constituted 56.54% of the study population, and 59.23% of participants were from urban areas. The mean BMI was 27.2 ± 3.8 kg/m^2, with 45.00% of participants being overweight and 22.31% being obese. Hypertension was the most common comorbidity (55.00%), followed by dyslipidemia (40.77%), ischemic heart disease (14.23%), and chronic kidney disease (9.23%) (*Table I*).

Table I
Socio-demographic characteristics of the study participants (*n*=260).

Variables	Frequency (n)	Percentage (%)
Age (years)		
<45	39	15.00
45–54	78	30.00
55–64	95	36.54
≥65	48	18.46
Mean ± SD	56.8 ± 9.4	
Gender		
Male	147	56.54
Female	113	43.46
Residence		
Urban	154	59.23

Rural	106	40.77
BMI (kg/m²)		
Normal (18.5–24.9)	85	32.69
Overweight (25.0–29.9)	117	45.00
Obese (≥30)	58	22.31
Mean BMI ± SD	27.2 ± 3.8	
Comorbidities		
Hypertension	143	55.00
Dyslipidemia	106	40.77
Ischemic heart disease	37	14.23
Chronic kidney disease	24	9.23

The participants had a mean diabetes duration of 8.6 ± 5.2 years, with mean fasting and postprandial blood glucose levels of 164.9 ± 54.8 mg/dL and 236.4 ± 71.2 mg/dL, respectively. The mean HbA1c was 8.31 ± 1.74%, while the average blood pressure was 132.8 ± 16.4/81.7 ± 9.6 mmHg (*Table II*).

Table II
Clinical characteristics of the study participants (*n*=260).

Variables	Mean ± SD
Duration of diabetes (years)	8.6 ± 5.2
Systolic BP (mmHg)	132.8 ± 16.4
Diastolic BP (mmHg)	81.7 ± 9.6
Fasting blood glucose (mg/dL)	164.9 ± 54.8
Postprandial blood glucose (mg/dL)	236.4 ± 71.2
HbA1c (%)	8.31 ± 1.74

The average hemoglobin concentration was 12.7 ± 1.6 g/dL. Participants had a mean total WBC count of 8.14 ± 2.21 ×10³/µL and a mean platelet count of 257.3 ± 62.7 ×10³/µL. The mean neutrophil, lymphocyte, and monocyte percentages were 63.8 ± 8.9%, 28.4 ± 6.8%, and 5.6 ± 1.8%, respectively, with a mean NLR of 2.42 ± 0.91 (*Table III*).

Table III
Hematological parameters of the study participants.

Parameters	Mean ± SD
Hemoglobin (g/dL)	12.7 ± 1.6
Total WBC (×10³/µL)	8.14 ± 2.21
Neutrophil (%)	63.8 ± 8.9
Lymphocyte (%)	28.4 ± 6.8
Monocyte (%)	5.6 ± 1.8
Platelet count (×10³/µL)	257.3 ± 62.7
Neutrophil-to-Lymphocyte Ratio (NLR)	2.42 ± 0.91

Patients with poor glycemic control had significantly higher mean neutrophil percentages (66.1 ± 8.3% vs. 59.6 ± 6.5%) and NLR (2.70 ± 0.87 vs. 1.89 ± 0.46), whereas the mean lymphocyte percentage was significantly lower (26.5 ± 6.4% vs. 31.8 ± 5.7%) compared with those with good glycemic control (all $p < 0.001$) (*Table IV*).

Table IV
Comparison of NLR between good and poor glycemic control (*n*=260).

Parameters	Good control (n=91), Mean ± SD	Poor control (n=169), Mean ± SD	p-value
Neutrophil (%)	59.6 ± 6.5	66.1 ± 8.3	<0.001
Lymphocyte (%)	31.8 ± 5.7	26.5 ± 6.4	<0.001
NLR	1.89 ± 0.46	2.70 ± 0.87	<0.001

A significant association was observed between NLR category and glycemic control ($\chi^2 = 20.87$, $p < 0.001$). Patients with good glycemic control were predominantly in the low NLR category (59.34%). Those with poor glycemic control were more frequently classified as having intermediate (42.01%) and high NLR (38.46%) (*Table V*).

Table V
Association between NLR category and glycemic control (*n*=260).

NLR Category	Good Glycemic Control (n=91)		Poor Glycemic Control (n=169)		χ^2	p-value
	n	%	n	%		
Low (<2.0)	54	59.34	33	19.53	20.87	<0.001
Intermediate (2.0–2.99)	30	32.97	71	42.01		
High (≥3.0)	7	7.69	65	38.46		

NLR demonstrated significant positive correlations with fasting blood glucose (r = 0.49), postprandial blood glucose (r = 0.45), and HbA1c (r = 0.58) (all p < 0.001) (*Table VI*).

Table VI
Correlation between NLR and glycemic parameters.

Variables	Pearson's r	p-value
Fasting blood glucose	0.49	<0.001
Postprandial blood glucose	0.45	<0.001
HbA1c	0.58	<0.001

Receiver operating characteristic (ROC) analysis identified an optimal NLR cutoff of 2.25 for predicting poor glycemic control, yielding an AUC of 0.82 (95% CI: 0.74–0.89), with 79.5% sensitivity, 73.8% specificity, 84.9% positive predictive value, 65.2% negative predictive value, and an overall diagnostic accuracy of 77.5% (*Table VII*).

Table VII
Diagnostic performance of NLR for identifying poor glycemic control.

Parameter	Value (95% CI)
Optimal NLR cutoff	2.25
Area under ROC curve (AUC)	0.82 (0.74–0.89)
Sensitivity (%)	79.5
Specificity (%)	73.8
Positive predictive value (%)	84.9
Negative predictive value (%)	65.2
Overall diagnostic accuracy (%)	77.5

DISCUSSION

The present study found that the mean age of the study participants was 56.8 ± 9.4 years, with more than half of the participants (55.0%) being aged 55 years or older. Similar age distributions have been reported in study evaluating inflammatory biomarkers among patients with T2DM, where the participants were between 45 and 65 years of age [14]. Male participants constituted 56.5% of the study population, slightly exceeding the proportion of female participants in our study. Selvaraju et al. also reported 55% of male participants in their study investigating NLR in T2DM [15]. Approximately 59.2% of the participants resided in urban areas. Rapid urbanization has been consistently associated with increasing diabetes prevalence due to sedentary lifestyles that support the findings of other study from Asia [16]. In the present study, 45.0% of participants were overweight and 22.3% were obese, with a mean BMI of 27.2 ± 3.8 kg/m². The relatively high prevalence of overweight and obesity in the present study is therefore consistent with the observed inflammatory profile among patients with poor glycemic control [17]. In our study, hypertension was the most common comorbidity, affecting 55.0% of participants, followed by dyslipidemia (40.8%), ischemic heart disease (14.2%), and chronic kidney disease (9.2%). These findings are expected because hypertension and dyslipidemia frequently coexist with T2DM as components of the metabolic syndrome [18]. The mean duration of diabetes among the participants was 8.6 ± 5.2 years, indicating that most patients had longstanding disease. Previous study has demonstrated that longer disease duration is associated with higher HbA1c levels and increased inflammatory markers, including NLR, supporting the findings of the present study [17]. In this study, the mean systolic and diastolic blood pressures were 132.8 ± 16.4 mmHg and 81.7 ± 9.6 mmHg, respectively. Similar blood pressure profiles have been reported in studies by Verdoia et al. and Kahraman et al., where hypertensive diabetic patients exhibited higher inflammatory indices than normotensive individuals [19,20]. The mean fasting blood glucose (164.9 ± 54.8 mg/dL) and postprandial blood glucose (236.4 ± 71.2 mg/dL) observed in this study indicate inadequate glycemic control in a substantial proportion of participants. Comparable glycemic profiles have been documented by Lou et al. and Shiny et al., all of whom reported that patients with higher blood glucose levels exhibited significantly elevated inflammatory markers, particularly NLR [21,22]. The mean HbA1c level in the present study was 8.31 ± 1.74%, which exceeds the generally recommended target of <7.0% for most adults with T2DM and indicates poor long-term glycemic control. Likewise, Lou et al. observed a positive correlation between HbA1c and NLR in Chinese patients with T2DM [21]. We found that the mean hemoglobin concentration, total WBC count, neutrophil percentage, lymphocyte percentage, monocyte percentage, and platelet count were 12.7 ± 1.6 g/dL, 8.14 ± 2.21 ×10³/µL, 63.8 ± 8.9%, 28.4 ± 6.8%, 5.6 ± 1.8%, and 257.3 ± 62.7 × 10³/µL, respectively. The hematological profile of the present study demonstrated generally normal hematological indices with evidence of mild systemic inflammation, as reflected by the mean NLR of 2.42 ± 0.91. Shiny et al. reported significantly higher NLR values in diabetic patients than in healthy controls and demonstrated that NLR increased progressively with worsening glycemic control [22]. Kahraman et al. further demonstrated that higher NLR was associated with diabetic nephropathy and albuminuria, highlighting the usefulness of NLR as a marker of inflammatory diabetic complications [20]. The principal finding of the present study was that patients with poor glycemic control exhibited a significantly higher inflammatory profile than those with good glycemic control. Patients with poor glycemic control had significantly higher neutrophil percentages (66.1 ± 8.3% vs. 59.6 ± 6.5%, p < 0.001) and significantly lower lymphocyte percentages (26.5 ± 6.4% vs. 31.8 ± 5.7%, p < 0.001), resulting in a markedly elevated NLR (2.70 ± 0.87 vs. 1.89 ± 0.46, p < 0.001). The findings of the present study are further supported by the systematic review conducted by Adane et al., which analyzed data from multiple observational studies and concluded that patients with poor glycemic control consistently exhibited significantly higher NLR than those with adequate glycemic control [17]. The categorical analysis of NLR demonstrated a highly significant association between NLR category and glycemic control (χ^2 = 20.87, p < 0.001). More than half of the patients with good glycemic control (59.3%) belonged to the low NLR category (<2.0), whereas only 19.5% of patients with poor glycemic control were classified within this category. In contrast, the proportion of patients with high NLR (≥3.0) was substantially greater among those with poor glycemic control

(38.5%) compared with those with good glycemic control (7.7%). These findings indicate that increasing NLR is strongly associated with deteriorating glycemic status and support the utility of NLR as a marker of chronic inflammation in T2DM. According to this study, NLR showed a moderate positive correlation with fasting blood glucose (FBG) ($r = 0.49$, $p < 0.001$) and postprandial blood glucose (PPBG) ($r = 0.45$, $p < 0.001$), while the strongest correlation was observed with HbA1c ($r = 0.58$, $p < 0.001$). Since HbA1c reflects average glycemic exposure over the preceding two to three months, this finding suggests that chronic rather than transient hyperglycemia is more closely associated with persistent inflammatory activation. Duman et al. demonstrated a significant association between HbA1c and NLR [23]. The ROC curve analysis demonstrated good diagnostic performance of NLR for identifying poor glycemic control. The optimal NLR cutoff value was 2.25, yielding an AUC of 0.82 (95% CI: 0.74–0.89), with a sensitivity of 79.5%, specificity of 73.8%, positive predictive value of 84.9%, negative predictive value of 65.2%, and an overall diagnostic accuracy of 77.5%. Our findings are comparable to the studies of Mohammed et al and Wang et al. [24,25].

LIMITATIONS

- NLR and glycemic parameters were measured only once, preventing evaluation of longitudinal changes in inflammatory status and glycemic control over time.
- Although patients with known infections, autoimmune diseases, malignancies, and other inflammatory conditions were excluded, the influence of unrecognized subclinical inflammation or other confounding factors affecting leukocyte counts cannot be completely ruled out.
- The proposed NLR cutoff value for predicting poor glycemic control was derived from the study population only and was not validated in an independent cohort.

CONCLUSION & RECOMMENDATIONS

The present study demonstrated a significant association between elevated neutrophil-to-lymphocyte ratio and poor glycemic control among patients with type 2 diabetes mellitus. Patients with higher HbA1c levels exhibited significantly increased NLR values, and NLR showed moderate positive correlations with fasting blood glucose, postprandial blood glucose, and HbA1c. Furthermore, ROC analysis indicated that NLR possesses acceptable diagnostic accuracy for identifying poor glycemic control. As an inexpensive, readily available, and easily calculated inflammatory marker derived from a routine complete blood count, NLR may complement conventional glycemic assessment in routine clinical practice, particularly in resource-constrained settings. Nevertheless, it should not replace established glycemic markers such as HbA1c. Large-scale multicenter prospective studies are recommended to validate the optimal cutoff value and determine the prognostic role of NLR in predicting long-term diabetic complications and clinical outcomes.

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CONFLICT OF INTEREST

None declared

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee.

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