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ASSOCIATION BETWEEN HBA1C WITH PLATELET TO LYMPHOCYTE RATIO AND NEUTROPHIL TO LYMPHOCYTE RATIO IN TYPE 2 DIABETES MELLITUS

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a chronic metabolic disease in which inflammation plays a significant role in both microvascular and macrovascular complications. The Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) are simple hematological biomarkers that can reflect systemic inflammatory status and potentially correlate with HbA1c levels as an indicator of glycemic control. The aim of the research is determine the association between HbA1c levels and NLR and PLR in T2DM patients at Haji Adam Malik General Hospital, Medan.
Methods: This was a retrospective cross-sectional study using secondary data from the medical records of T2DM patients between May and July 2024. A total of 96 patients met the inclusion criteria. Data were analyzed using the Kruskal-Wallis test with a significance level of $p<0.05$.
Results: The median HbA1c of the patients was 9% (range 4.2–15.4%). Median NLR increased according to HbA1c categories: 3.91 (HbA1c <7%), 5.77 (HbA1c 7–9%), and 7.19 (HbA1c >9%) with p=0.012. Median PLR also increased across categories: 134.75, 189.00, and 233.33 with p=0.009.
Conclusion: A significant association was observed between HbA1c and both NLR and PLR. NLR and PLR can be used as additional hematological parameters to assess inflammation and glycemic control in patients with type 2 diabetes.

Keywords: T2DM, HbA1c, NLR, PLR.

ABSTRAK

Latar Belakang: Diabetes mellitus tipe 2 (T2DM) adalah penyakit metabolik kronis di mana peradangan memainkan peran penting dalam komplikasi mikrovaskular dan makrovaskular. Rasio Neutrofil-ke-Limfosit (NLR) dan Rasio Trombosit-ke-Limfosit (PLR) adalah biomarker hematologis sederhana yang dapat mencerminkan status inflamasi sistemik dan berpotensi berkorelasi dengan kadar HbA1c sebagai indikator kontrol glikemik. Tujuan penelitian ini adalah mengetahui hubungan antara kadar HbA1c dengan NLR dan PLR pada pasien T2DM di RSUD Haji Adam Malik, Medan.
Metode: Ini adalah studi cross-sectional retrospektif menggunakan data sekunder dari rekam medis pasien T2DM antara Mei dan Juli 2024. Sebanyak 96 pasien memenuhi kriteria inklusi. Data dianalisis menggunakan uji Kruskal-Wallis dengan tingkat signifikansi p<0,05.
Hasil: Median HbA1c pasien adalah 9% (kisaran 4,2–15,4%). Median NLR meningkat menurut kategori HbA1c: 3,91 (HbA1c <7%), 5,77 (HbA1c 7–9%), dan 7,19 (HbA1c >9%) dengan p=0,012. PLR median juga meningkat di seluruh kategori: 134,75, 189,00, dan 233,33 dengan p=0,009.

Kesimpulan: Hubungan yang signifikan diamati antara HbA1c dan NLR dan PLR. NLR dan PLR dapat digunakan sebagai parameter hematologis tambahan untuk menilai peradangan dan kontrol glikemik pada pasien dengan diabetes tipe 2.

Kata kunci: T2DM, HbA1c, NLR, PLR

1. Introduction

Diabetes mellitus (DM) is a major global health issue. According to the International Diabetes Federation (IDF) 2025 report, the global prevalence of diabetes among adults aged 20–79 years reached 589 million in 2024 and is projected to increase by 45% to 853 million by 2050. In Indonesia, the 2023 Indonesian Health Survey reported a DM prevalence of 1.4% in North Sumatra.[1,2] Type 2 diabetes mellitus (T2DM) is the most common form, characterized by chronic hyperglycemia due to insulin resistance and/or impaired insulin secretion. Persistent hyperglycemia promotes oxidative stress, advanced glycation end-products (AGEs) formation, and inflammatory activation, which contribute to both microvascular and macrovascular complications.[3,4]

Systemic inflammation plays a pivotal role in the pathogenesis of T2DM. Conventional inflammatory biomarkers such as C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α) are not always readily available in all clinical settings. Therefore, hematological indices, particularly the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), have been proposed as simple, inexpensive, and widely accessible indicators of systemic inflammation. [5,6] Previous studies have demonstrated significant associations between elevated NLR and PLR values and poor glycemic control as well as diabetic complications. The pathophysiological basis of increased NLR and PLR reflects an imbalance between inflammatory activation and immune regulation. Systemic inflammation promotes neutrophilia and thrombocytosis through cytokine-mediated bone marrow stimulation, while concurrently suppressing lymphocyte proliferation and survival, resulting in elevated NLR and PLR values. Beyond diabetes, these indices have been extensively investigated in other disease conditions, including cardiovascular disorders, malignancies, chronic kidney disease, autoimmune diseases, and infections, where higher NLR and PLR levels are consistently associated with greater disease severity and poorer clinical outcomes [7]. El-Sayed et al. reported that PLR and NLR values were significantly higher in patients with type 2 diabetes mellitus with both macrovascular and microvascular complications. A study conducted by Putra et al. involving 102 patients with acute coronary syndrome at Sanjiwani Gianyar Regional Hospital demonstrated that PLR and NLR were positively correlated with the occurrence of acute coronary syndrome ($p = 0.000$). Furthermore, Khairani et al. found that in patients with type 2 diabetes mellitus, an NLR value ≥ 2.11 was associated with an increased risk of peripheral arterial disease ($p = 0.007$).[8-10]

Glycated hemoglobin (HbA1c) reflects long-term glycemic control and correlates with the risk of diabetes complications.[1,12] As both inflammation and hyperglycemia are interrelated, evaluating the relationship between HbA1c and hematologic inflammatory indices may provide useful clinical insight. However, limited data are available in Indonesia, particularly in Medan. Therefore, this study aims to determine the association between HbA1c levels and NLR and PLR among patients with type 2 diabetes mellitus in Medan.

2. Method

This retrospective analytic study with a cross-sectional design was conducted at Haji Adam Malik General Hospital, Medan, North Sumatra, from May 1 to July 31, 2024. The data used in this study

were secondary data obtained from medical records of patients diagnosed with type 2 diabetes mellitus (T2DM), both inpatients and outpatients. Samples were selected using a consecutive sampling technique, including all eligible subjects who met the inclusion criteria until the required sample size was achieved. Data collected included demographic characteristics (age and sex) and laboratory results (hemoglobin, platelet, leukocyte, lymphocyte, absolute lymphocyte count, neutrophil, absolute neutrophil count, HbA1c, neutrophil-to-lymphocyte ratio, and platelet-to-lymphocyte ratio). Ethical approval for this study was obtained from the Health Research Ethics Committee, Faculty of Medicine, Universitas Sumatera Utara (approval number: DP.04.03/D.XXVIII/1321/2024). A total of 96 patients met the inclusion criteria. Statistical analyses were performed using SPSS version 27.0. The Kruskal–Wallis test was used to assess the association between HbA1c levels and NLR and PLR values in patients with T2DM. Spearman's correlation test was applied to evaluate the strength and direction of correlations between HbA1c levels and hematological parameters. A p-value < 0.05 was considered statistically significant.

3. Result

A total of 96 participants were involved in this study. The median age of the participants was 59 years, ranging from 20 to 86 years. Based on sex distribution, the majority of patients were male (52 patients; 54.17%), while 44 patients (45.83%) were female. The HbA1c levels were divided into three categories according to glycemic control. More than half of the subjects (51.04%) were classified into category 3 (HbA1c >9 %), indicating poor glycemic control and a higher risk of chronic complications. Meanwhile, 33.3% of patients were in category 2 (HbA1c 7–9%), reflecting suboptimal glycemic control, and only 15.6% of patients were in category 1 (HbA1c < 7%), which corresponds to good glycemic control as recommended by clinical guidelines. (Table 1).

Table 1. Characteristics of Participants

Characteristic	n (%)
Sex	
– Male,	52 (54.2)
– Female,	44 (45.8)
HbA1c category	
– Category 1 (<7%),	15 (15.6)
– Category 2 (7–9%),	32 (33.3)
– Category 3 (>9%),	49 (51.0)
	median (min–max)
Age (years),	52 (20–86)
Hemoglobin (g/dL),	12.1 (10.6–16.2)
Platelet ($\times 10^3/\mu L$),	280 (145–659)
Lymphocyte (%),	12.4 (2.7–43.6)
Absolute lymphocyte count ($\times 10^3/\mu L$),	1.44 (0.42–5.47)
Neutrophil (%),	78.2 (47.9–94.5)
Absolute neutrophil count ($\times 10^3/\mu L$),	9.30 (1.54–29.56)
Neutrophil-to-lymphocyte ratio (NLR),	5.61 (1.14–35.10)
Platelet-to-lymphocyte ratio (PLR),	189.6 (43.2–855.8)
HbA1c (%),	9.0 (4.2–15.4)

Note: NLR = neutrophil-to-lymphocyte ratio; PLR = platelet-to-lymphocyte ratio.

As shown in Table 2, the median values of the Platelet-to-Lymphocyte Ratio (PLR) and Neutrophil-to-Lymphocyte Ratio (NLR) tended to increase with higher HbA1c categories. In HbA1c category 1 (<7%, n = 15), the median PLR was 134.75, and the median NLR was 3.91. In category 2 (7 – 9%, n = 32), the median PLR increased to 189.00 and the median NLR to 5.77. Meanwhile, in category 3 (> 9%, n = 49), the median PLR was even higher at 233.33, and the median NLR also rose to 7.19.

Table 2. Distribution of PLR and NLR According to HbA1c Categories

HbA1c (**%**)	n	PLR, Med (min–max)	NLR, Med (min–max)
<7.0	15	134,75 (81,71-855,84)	3,91 (1,2-17,3)
7.0 - 9.0	32	189,00 (43,1-692,1)	5,77 (1,3-27,6)
>9.0	49	233,33 (63,7-608,3)	7,19 (1,14-35,1)

There was a significant association between HbA1c categories and both PLR (p = 0.009) and NLR (p = 0.012) values.

Table 3. Mean Rank and the Association between HbA1c, PLR, and NLR in T2DM

HbA1c (%)	Parameter	Mean Rank	P-value
<7.0	RPL	31,07	**0.009**
7.0 - 9.0		45,69	
>9.0		55,67	
<7.0	RNL	30,93	**0,012**
7.0 - 9.0		46,69	
>9.0		55,06	

Spearman's correlation analysis was performed to assess the relationship between HbA1c levels and various clinical parameters. The results showed significant positive correlations between HbA1c and platelet count (r = 0.275, p = 0.007) as well as HbA1c and platelet-to-lymphocyte ratio (PLR) (r = 0.283, p = 0.005). Neutrophil-to-lymphocyte ratio (NLR) showed a borderline positive correlation (r = 0.189, p = 0.065), whereas other variables, including age, hemoglobin, neutrophil count, absolute neutrophil count, lymphocyte count, and absolute lymphocyte count, showed no significant correlations with HbA1c levels.

Table 4. Correlation between HbA1c and Clinical Parameters

Variable	Correlation Coefficient (r)	p-value
Age	-0,154	0,133
Hemoglobin	0,002	0,988
Platelet	0,275	**0,007**
Neutrophil	0,055	0,592
Absolute neutrophil	0,175	0,088
Lymphocyte	-0,074	0,475
Absolute lymphocyte	-0,104	0,312
PLR	0,283	**0,005**
NLR	0,189	0,065

4. Discussion

Type 2 diabetes mellitus (T2DM) remains a major global health problem, significantly affecting patients' functional capacity and quality of life. According to the International Diabetes Federation (IDF), the global prevalence of T2DM is estimated at 10.5% (536.6 million cases) and is projected to increase to 12.2% (783.2 million cases) by 2045. In the present study involving 96 patients treated at

Haji Adam Malik General Hospital, the median age was 59 years (range 20–86), with a male predominance (54.2%). This relatively younger age distribution compared to global data may reflect earlier disease onset and more rapid disease progression among Southeast Asian populations. Previous studies have consistently shown that Southeast Asian individuals tend to develop T2DM at a younger age and lower body mass index, with greater insulin resistance and earlier beta-cell dysfunction compared to European populations, which may contribute to a higher inflammatory burden [13,14].

Chronic low-grade inflammation plays a pivotal role in the pathogenesis and progression of T2DM and its complications. Traditional inflammatory markers such as C-reactive protein, IL-1, IL-6, and TNF-α are frequently elevated in T2DM; however, their routine use is limited by cost and availability. In recent years, hematological indices such as the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have emerged as practical surrogate markers of systemic inflammation.[15] In this study, the median NLR (5.61) and PLR (189.61) were higher than those reported in several previous studies. For example, Hussain et al. and Kula et al. reported lower median NLR values in relatively stable T2DM populations. [16–18] The higher values observed in our cohort may be explained by the inclusion of patients with multiple comorbidities and advanced disease stages, which are known to amplify systemic inflammatory responses.

A progressive increase in NLR across higher HbA1c categories was observed in this study, indicating a close relationship between poor glycemic control and systemic inflammation. This finding is consistent with previous studies demonstrating a positive correlation between NLR and HbA1c levels.[16–18] Pathophysiologically, chronic hyperglycemia promotes oxidative stress, endothelial dysfunction, and activation of inflammatory signaling pathways, leading to neutrophilia and relative lymphopenia. Compared with studies conducted in outpatient or well-controlled T2DM populations, the stronger association observed in our study may reflect a higher inflammatory burden in hospitalized patients or those with more severe metabolic dysregulation.

Similarly, PLR showed a significant association with HbA1c levels. Elevated PLR reflects both increased platelet activation and reduced lymphocyte counts, suggesting an enhanced pro-inflammatory and pro-thrombotic state. Previous studies by Fabin et al. and Atak et al. also reported a positive relationship between PLR and HbA1c, supporting the role of PLR as a marker of metabolic stress and inflammation in T2DM.[19,20] Differences in absolute PLR values between studies may be influenced by variations in study populations, disease duration, comorbid cardiovascular conditions, and laboratory measurement methods.

Collectively, these findings are in line with existing evidence demonstrating that worsening glycemic control is associated with heightened systemic inflammation. Compared with prior studies, our results suggest that NLR and PLR may be particularly elevated in T2DM patients with poor glycemic control and possible comorbid conditions. Therefore, NLR and PLR may serve not only as markers of inflammation but also as adjunctive indicators of disease severity and potential complications in T2DM, especially in resource-limited clinical settings.

This study has several strengths and limitations that should be considered when interpreting the results. One of the main strengths of this study is the use of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), which are simple, inexpensive, and widely available biomarkers derived from routine complete blood counts, making them practical for clinical application, particularly in resource-limited settings. In addition, patients were stratified according to clinically relevant HbA1c categories, allowing for a meaningful comparison of inflammatory markers across different levels of glycemic control. The observed trend of increasing NLR and PLR with higher HbA1c categories further supports the biological plausibility of the association between poor

glycemic control and systemic inflammation. Moreover, this study contributes data from a Southeast Asian population, which remains underrepresented in the existing literature.

However, several limitations should be acknowledged. The cross-sectional design limits the ability to establish causal relationships between HbA1c levels and inflammatory markers. This study was conducted at a single center with a relatively small sample size, which may limit the generalizability of the findings. Potential confounding factors such as comorbid conditions, concurrent infections, and medication use were not fully controlled and may have influenced NLR and PLR values. Furthermore, conventional inflammatory biomarkers such as C-reactive protein or interleukin-6 were not measured, preventing direct comparison with established inflammatory markers. Finally, the lack of longitudinal follow-up precludes evaluation of the prognostic value of NLR and PLR for long-term clinical outcomes.

5. Conclusion

Statistical analysis revealed a significant association between HbA1c and both NLR ($p = 0.012$) and PLR ($p = 0.009$) values in patients with type 2 diabetes mellitus. Further prospective studies with larger sample sizes are warranted to confirm these findings.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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