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CORRELATION OF NEUTROPHIL LYMPHOCYTE RATIO WITH HbA1C IN DIABETIC ULCERS

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Abstract

Background: Patients diagnosed with diabetes are susceptible to complications, including diabetic ulcers. HbA1C is one of the key parameters used to evaluate glycemic control At the same time, the neutrophil-to-lymphocyte ratio (NLR) is a test used to detect inflammatory processes in patients with diabetes mellitus who develop diabetic ulcers.

Objective: This research analyzes the relationship between the neutrophil-to-lymphocyte ratio (NLR) and HbA1C levels in patients with diabetes mellitus and diabetic foot ulcers.

Methods: The research has a cross-sectional design. Data were collected retrospectively using non-probability sampling through a purposive sampling method from January 2024 to January 2025. Data were obtained from 83 individuals diagnosed with diabetes mellitus, including those with diabetic ulcer.

Results: The highest NLR value was 26.47 and the lowest was 1.14. The highest HbA1C value was 51.0, while the lowest was 5.40. Spearman's statistical test indicated no significant correlation between NLR and HbA1C in patients with diabetes mellitus and diabetic foot ulcers ($p = 0.534 > 0.05$).

Conclusions: There is no correlation between the neutrophil-to-lymphocyte ratio (NLR) and HbA1C levels in patients with diabetes mellitus and diabetic foot ulcers.

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INTRODUCTION

The International Diabetes Federation (IDF) estimates that 10.5% of adults aged 20 to 79 are currently living with diabetes, with over 90% of these cases identified as type 2 diabetes. Indonesia ranks as the fifth-highest country in terms of diabetes prevalence, recording an estimated 19.5 million cases in 2021(1). In 2021, the prevalence of diabetes mellitus among individuals aged 15 and above in West Nusa Tenggara (NTB) Province reached 63,488 cases. This figure reflects a rising trend in diabetes cases from 2019 to 2021, with West Lombok Regency ranking fourth in terms of the highest number of diabetes mellitus cases (2). Medical records from H. Moh. Ruslan Regional General Hospital in Mataram City reported 617 outpatient cases of diabetes mellitus with diabetic foot ulcers in 2024.

Diabetes Mellitus (DM) is a metabolic condition marked by chronic elevations in blood glucose levels. This persistent hyperglycemia results from either insufficient insulin production or abnormalities in insulin action (3). HbA1C testing is one method used to monitor blood glucose levels throughout 1 to 3 months, depending on the lifespan of red blood cells (4). An HbA1C level greater than 6.5% indicates that the patient has uncontrolled diabetes mellitus (5). Patients with long-standing diabetes mellitus (DM) are at increased risk of developing various complications (6). Diabetic neuropathy is one of the most common complications associated with diabetes mellitus and plays a critical role in the formation of diabetic foot ulcers among affected individuals (7). Diabetic foot ulcers are a type of inflammatory complication that can result in tissue and organ loss due to infection (8). Infections caused by inflammation are associated with an increased number of neutrophils in the blood. Therefore, the neutrophil-to-lymphocyte ratio (NLR) is often used to predict the severity of inflammation (9).

The neutrophil-to-lymphocyte ratio (NLR), obtained from a differential leukocyte count, is calculated by dividing the neutrophil count by the lymphocyte count (10). In individuals with diabetes mellitus, NLR is regarded as a potential indicator for assessing the level of systemic inflammation (11). Considering the explanation above, the researcher is interested in conducting a study titled "Analysis of the Relationship Between Neutrophil-to-Lymphocyte Ratio (NLR) and HbA1C Levels in Diabetes Mellitus Patients With Diabetic Foot Ulcers."

MATERIALS AND METHODS

This research employed an analytical observational approach with a cross-sectional study design. The study population includes all DM patients with diabetic foot ulcer complications at H. Moh. Ruslan Regional General Hospital in Mataram City from January 2024 to January 2025.

The sampling technique is retrospective, and the data were collected using a non-probability purposive sampling method. The selection of samples was carried out according to predefined inclusion and exclusion criteria.

a. Inclusion Criteria
    1) DM patients with diabetic foot ulcer complications that worsen the patient's condition.
    2) Patients aged over 18 years.

b. Exclusion Criteria
   1) Patients without complete laboratory data regarding full blood count and HbA1C results.
   2) Patients undergoing chemotherapy may affect NLR values.
   3) Patients with comorbidities such as malignancies (cancer) or autoimmune diseases.

RESULTS AND DISCUSSIONS

Based on the collected research data, a total of 83 patient records were obtained. These data were then processed to generate information on respondent distribution, frequency, and percentage for each variable. The following table presents the distribution of respondents, along with the frequency and percentage for each variable.

Table 1. Distribution of DM Patients with Diabetic Foot Ulcers

	F	%	Mean	±SD	Min	Maks
Sex						
Male	36	43%				
Female	47	57%				
Age						
>18	1	1%				
26-45	10	12%				
>45	72	87%				
NLR			6,17	5,71	1,14	26,47
HbA1C			9,35	5,14	5,40	51,0

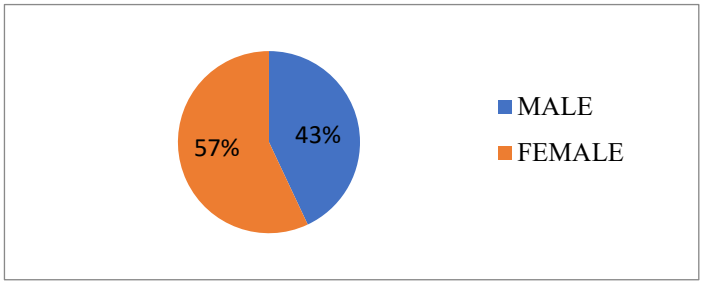


Figure 1. Pie chart illustrating the percentage distribution of gender among patients with diabetes mellitus and diabetic foot ulcers.

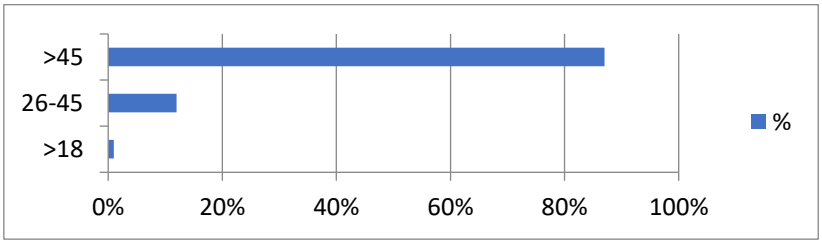


Figure 2. Bar chart illustrating the percentage distribution of age among patients with diabetes mellitus and diabetic foot ulcers.

As shown in Table 1 and Figure 1, the majority of diabetes mellitus (DM) patients with diabetic foot ulcers were female, accounting for 57% (n = 47) of the total, while male patients represented 43% (n = 36). Pregnancy increases insulin resistance in women, raising their risk diabetes compared to men (12). Furthermore, the age distribution indicates that 87% of the cases were found in patients aged over 45 years, suggesting a significantly higher prevalence of diabetic foot ulcers in this age group compared to those under 45.

Table 2. Frequency and Percentage Distribution of NLR in DM Patients with Diabetic Foot Ulcers

NLR		
Category	**Frequency**	**Percentage (%)**
Abnormal	45	54.2
Normal	38	45.8
Total	**83**	**100.0**

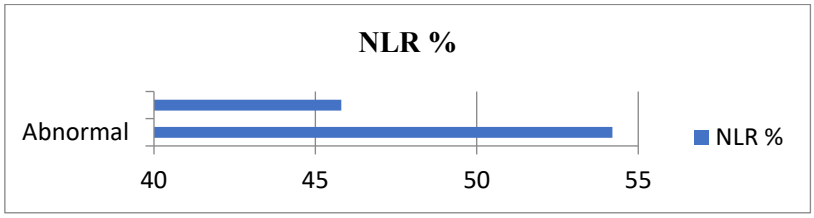


Figure 3. Percentage Distribution of NLR in DM Patients with Diabetic Foot Ulcers

Table 2 and Figure 3 demonstrates that the neutrophil-to-lymphocyte ratio (NLR) was predominantly within the abnormal category, observed in 45 patients (54.2%), compared to 38 patients (45.8%) in the normal category. This finding suggests a systemic inflammatory response among the majority of patients, likely triggered by the underlying diabetic foot ulcers. Elevated NLR levels have been associated with ongoing inflammation, supporting the role of NLR as an inflammatory marker in diabetic complications (13).

Table 3. Distribution Frequency and Percentage HbA1C in DM Patients with Diabetic Foot Ulcers

HbA1C		
Category	**Frequency**	**Percentage (%)**
Abnormal	62	74.7
Normal	21	25.3
Total	**83**	**100.0**

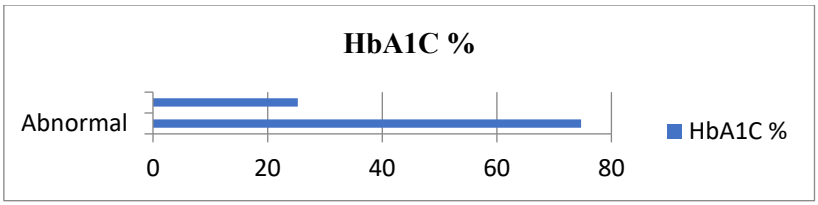


Figure 4. Percentage Distribution of HbA1C in DM Patients With Diabetic Foot Ulcers

As shown in Table 3 and Figure 4, the frequency distribution of HbA1C levels reveals that 62 patients (74.7%) exhibited abnormal HbA1C values, while only 21 patients (25.3%) had values within the normal range. These findings indicate that the majority of DM patients with diabetic foot ulcers had suboptimal glycemic control, which may contribute to the development or worsening of ulcerative complications (14).

Table 4. Cross Tabulation of NLR and HbA1C Levels in DM Patients with Diabetic Foot Ulcers

NLR dan HbA1C Crosstabulation				
		HbA1C		
		Normal	Abnormal	**Total**
NLR	Normal	9	29	38
	Abnormal	12	33	45
Total		**21**	**62**	**83**

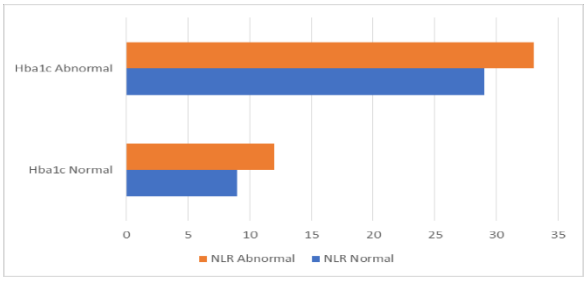


Figure 5. Cross Tabulation of NLR and HbA1C Levels in DM Patients with Diabetic Foot Ulcers

Table 4 and Figure 5 presents the results of a cross-tabulation analysis examining the relationship between the neutrophil-to-lymphocyte ratio (NLR) and HbA1C levels in diabetes mellitus patients with diabetic foot ulcers. Among the thirty-eight patients with a normal NLR, nine patients had normal HbA1C levels, while twenty-nine patients had abnormal HbA1C levels. In contrast, among the fourty-five patients with an abnormal NLR,

twelve patients had normal HbA1C levels, and thirty-three patients had abnormal HbA1C levels.

Table 5. Normality Test of NLR and HbA1C Data in DM Patients with Diabetic Foot Ulcers

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	Df	Sig.	Statistic	Df	Sig.
NLR	.214	83	.000	.774	83	.000
HbA1C	.221	83	.000	.452	83	.000

a. Lilliefors Significance Correction

Based on the research data, a total of 83 patient records were analyzed. Therefore, the Kolmogorov–Smirnov test was used to assess data normality. Referring to the results of the normality test, a p-value of 0.000 ($p \leq 0.05$) was obtained, indicating that the data were not normally distributed. The following are the normality plots, provided due to the sample size being greater than 20.

Table 6. Spearman's Rank Correlation Test

Correlations

			HbA1C	NLR
Spearman's rho	HbA1C	Correlation Coefficient	1.000	.069
		Sig. (2-tailed)	.	.534
		N	83	83
	NLR	Correlation Coefficient	.069	1.000
		Sig. (2-tailed)	.534	.
		N	83	83

Based on Spearman's rank correlation analysis, the obtained p-value was 0.534. Since this value is greater than the standard level of significance ($p > 0.05$), the null hypothesis is accepted while the alternative hypothesis is rejected. These findings indicate that there is no statistically significant correlation between the neutrophil-to-lymphocyte ratio (NLR) and HbA1C levels in patients with diabetes mellitus and diabetic foot ulcers.

The results of this study indicate that in patients with diabetes mellitus (DM) complicated by diabetic foot ulcers, there is an impact on neutrophil and lymphocyte counts (15).As shown in the frequency and percentage distribution of NLR in Table 2, a larger proportion of patients with diabetic foot ulcers exhibited elevated NLR values. One contributing factor is the inflammatory response (16). Chronic inflammation leads to a persistent inflammatory process, promoting neutrophil migration to the inflamed tissue. As a result, the phagocytic cells responsible for clearing dying neutrophils fail to function properly, while lymphocyte levels decline, reflecting increased apoptosis (17).

These findings are consistent with a study by Chen et al. (2024), titled "*The Association Between the Neutrophil-to-Lymphocyte Ratio and Type 2 Diabetes Mellitus: A Cross-Sectional Study.*" The study reported that individuals with type 2 diabetes mellitus (T2DM) had significantly higher NLR levels compared to non-diabetic individuals (13).

Furthermore, Table 3 presents the frequency and percentage distribution of HbA1C levels, showing that most patients had abnormal values. This suggests that the majority of DM patients with diabetic foot ulcers experienced poor glycemic control, which increases the risk of diabetic foot complications (18). This study aligns with the findings of Teddy and Eka Silvia (2019), who reported that out of 50 samples, 39 patients (78%) had elevated HbA1C levels and 24 patients (48%) experienced diabetic foot ulcers (19). One of the contributing factors is the elevated blood glucose level, which can impair blood flow and consequently hinder the delivery of nutrients necessary for ulcer healing (20). In addition, excessive glucose levels can disrupt the biochemical homeostasis of cells, thereby increasing the risk of chronic complications (21). These chronic complications may eventually lead to the development of diabetic foot ulcers (22).

Statistical analysis using the Kolmogorov–Smirnov normality test revealed a significance value of 0.000 for both HbA1C and NLR, indicating that the data did not follow a normal distribution. As a result, Spearman's rank correlation test was employed as a non-parametric alternative. The analysis produced a p-value of 0.534, which exceeds the 0.05 significance threshold. Thus, it was concluded that there is no statistically significant association between the neutrophil-to-lymphocyte ratio (NLR) and HbA1C levels in patients with diabetes mellitus and diabetic foot ulcers.

The result of the Spearman correlation test yielded a p-value of 0.534. Given that this value exceeds the 0.05 significance level, it can be concluded that there is no significant relationship between the neutrophil-to-lymphocyte ratio (NLR) and HbA1C levels in diabetes mellitus patients with diabetic foot ulcers.

These findings are consistent with those of Ni Made Ersi Dwitami Barsua et al. (2025), who conducted a study titled "*Correlation of HbA1C with Neutrophil-Lymphocyte Ratio and Monocyte-Lymphocyte Ratio as Markers of Inflammation in Type 2 Diabetes Mellitus Patients at Sanjiwani Hospital From 2021 to 2023.*" Their study also reported no significant positive correlation between the variables ($r = 0.195$, $p = 0.098$) (23).

This may be due to the fact that in patients with diabetic foot ulcers, the level of inflammation can vary greatly depending on the degree of ulcer infection, the use of antibiotics, and wound care management—all of which can influence NLR and HbA1C values (24). Additionally, sample size and sample quality may also play a role, as limited or inconsistent samples can yield correlations that are not statistically meaningful (25).

CLINICAL IMPLICATION

Based on the findings of this study, the highest neutrophil-to-lymphocyte ratio (NLR) observed in diabetes mellitus (DM) patients with diabetic foot ulcers was 26.47, while the lowest was 1.14. In terms of HbA1C levels, the highest recorded value was 51.0 and the lowest was 5.40. The Spearman's rank correlation analysis produced a p-value of 0.534 ($p > 0.05$), indicating no statistically significant association between NLR and HbA1C levels in this group of patients. These findings imply that while NLR serves as a marker of systemic

inflammation, it does not appear to have a direct correlation with glycemic control in individuals with diabetic foot ulcers.

LIMITATIONS

This study has several limitations. First, the cross-sectional design only captures associations at a single point in time, which limits the ability to infer any causal relationship between the neutrophil-to-lymphocyte ratio (NLR) and HbA1C levels. Second, the relatively small sample size may reduce statistical power and increase the risk of type II error, potentially obscuring clinically relevant associations. Third, the potential confounding factors, including the use of anti-inflammatory medications, acute infections, and diabetes duration, were not controlled, which could have impacted the results.

CONCLUSIONS

The neutrophil-to-lymphocyte ratio (NLR) in patients ranged from 1.14 to 26.47, while HbA1C levels varied between 5.40 and 51.0. Spearman's correlation analysis demonstrated no statistically significant association between NLR and HbA1C levels in patients with diabetes mellitus and diabetic foot ulcers ($p = 0.534$; $p > 0.05$). These findings indicate that there is no correlation between the neutrophil-to-lymphocyte ratio and HbA1C levels in this patient population.

CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

AUTOR CONTRIBUTIONS

N.N.D.P.M.W. was responsible for the conceptual design of the study, data collection, and drafting of the manuscript. E.R. contributed to data analysis, and interpretation of results. F.F. supervised the research process, provided critical revisions, manuscript editing and approved the final version of the manuscript. All authors have read and agreed to the published version of the manuscript. We are deeply grateful to our families for their unwavering support, encouragement, and prayers throughout the research process.

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activities, including data collection, data analysis, and manuscript preparation, were independently undertaken by the researcher.

DECLARATION OF ARTIFICIAL INTELLIGENCE USE

Artificial Intelligence (AI) tools, specifically ChatGPT version GPT-4.5, were employed in this study solely to support the manuscript preparation process, including language refinement, assistance with references, organization of the writing structure, and other editorial suggestions. The application of AI was carried out in a limited manner and under the full supervision of the researcher. Responsibility for the overall content of the study, including the analysis, interpretation of data, research outcomes, and conclusions, remains entirely with the researcher. Furthermore, all information generated or assisted by AI was critically evaluated and verified to ensure its accuracy and compliance with established academic principles and research ethics.

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