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RESEARCH **Open Access**

Association Between Glycated Hemoglobin (HbA1c) Levels and Mean Platelet Volume (MPV) in Patients with Type 2 Diabetes Mellitus

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Abstract
Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia, which can trigger inflammatory responses contributing to various vascular complications. Inflammation plays a key role in the pathogenesis of DM-related complications through mechanisms involving oxidative stress and activation of NF-κB signaling, which influence platelet production and activity. Given inconsistent findings regarding the association between HbA1c and mean platelet volume (MPV) in previous studies, this study aims to investigate the relationship between HbA1c and MPV, a pro-thrombotic and inflammatory marker, in patients with type 2 diabetes mellitus. This study is an analytical observational study with a cross-sectional approach. Data were collected from the medical records of Universitas Sebelas Maret (UNS) Hospital, Indonesia, using purposive sampling. HbA1c and MPV data were obtained from patients' medical records over the past year. Statistical analysis was performed using the Shapiro–Wilk normality test and Pearson correlation test. A total of 38 samples were included in the study. The mean HbA1c level was 10.37% (range: 6.50–16.10), while the mean MPV was 9.38 fL (range: 7.30–12.50). Pearson correlation test showed a significant relationship between HbA1c and MPV ($r = 0.467$; $p = 0.003$). There is a significant positive correlation between HbA1c and MPV in patients with type 2 diabetes mellitus.

Keywords: Type 2 Diabetes Mellitus, HbA1c, MPV.

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1. INTRODUCTION

Diabetes mellitus (DM) is a metabolic disease characterized by chronic hyperglycemia resulting from impaired blood glucose regulation (Sapra & Bhandari, 2023). There are four significant types of DM, with type 2 DM accounting for more than 90% of cases globally (Batubara, 2024). According to the International Diabetes Federation (IDF, 2021), approximately 19.46 million adults in Indonesia are living with diabetes, with 1 in 10 adults affected. DM was the third leading cause of death in Indonesia in 2019 (Darmawan et al., 2024). In Surakarta City, the number of cases increased from 12,105 in 2021 to 17,191 in 2023, making DM the second most common non-communicable disease and a top public health priority in Central Java (Dinkes Surakarta, 2023). Furthermore, according to the 2023 IDF report, approximately 94% of patients with DM experience at least one complication. Chronic hyperglycemia in DM can trigger inflammatory responses that contribute to the development of both microvascular and macrovascular complications (Ma et al., 2022; Mansour et al., 2023; Zhao et al., 2024), which in turn increase DM-related mortality. However, previous studies have reported heterogeneous findings, which may be explained by differences in study design, HbA1c cut-off values, and patient characteristics. These variations highlight the need for context-specific evaluation of inflammation-related markers in clinical practice.

Inflammation contributes to complications in patients with DM through several molecular mechanisms. Hyperglycemia increases the production of reactive oxygen species (ROS), leading to tissue injury and activation of inflammatory pathways. Excessive ROS induces activation of the inhibitor of nuclear factor kappa B kinase (IKK), resulting in the release and activation of nuclear factor kappa B (NF-κB), a key regulator of immune and inflammatory responses (Hong et al., 2024). NF-κB promotes the expression of pro-inflammatory cytokines such as interleukin-6 (IL-6), interleukin-1 (IL-1), and tumor necrosis factor-α (TNF-α), which stimulate bone marrow to produce more platelets by increasing megakaryocyte ploidy, leading to the release of larger, younger platelets (Korniluk et al., 2019). These larger platelets are more reactive, resulting in an increased mean platelet volume (MPV). Larger, younger platelets are metabolically and ezymatically more active, containing higher amounts of pro-thrombotic mediators such as thromboxane A2, more dense granules, and expressing increased levels of adhesion molecules such as P-selectin (Cassano et al., 2024; Hamilos et al., 2018). Consequently, they exhibit enchanced aggregation capacity and promote endothelial dysfunction, contributing to a pro-thrombotic state. In patients with diabetes mellitus, this condition increases the risk of microvascular and macrovascular complications, particulartly cardiovascular events (Dahan et al., 2025). In addition to their role in coagulation, platelets play an essential role in immune and inflammatory responses (Chen et al., 2020).

Mean platelet volume (MPV) is an indicator of platelet size and activity and can reflect inflammatory status (Inoue et al., 2020). Chronic hyperglycemia in type 2 DM, as assessed by glycated hemoglobin (HbA1c), is closely associated with inflammation and the development of complications. Several studies, including those by Inoue et al. and Ulutas et al., have demonstrated a positive correlation between MPV and HbA1c, particularly in patients with HbA1c levels above 7% (Ulutas et al., 2014). However, other studies, such as that by Amruthavarshini & Amita, found no significant correlation between the two parameters. In Indonesia, particularly among patients with type 2 diabetes mellitus treated in referral and teaching hospitals, data regarding the relationship between HbA1c and MPV remains limited. Most existing studies have been conducted in non-Indonesian populations, making their applicability to local clinical practice uncertain. However, it remains unclear whether the relationship between HbA1c and MPV observed in other populations is applicable to patients with type 2 diabetes mellitus in Indonesian referral and teaching hospitals. This study has novelty in evaluating the relationship between HbA1c and MPV in the context of a teaching hospital in Indonesia using routinely available medical record data. Given the high burden of diabetes mellitus in Indonesia, identification of simple and low-cost inflammatory markers such

as MPV is increasingly important for early detection of the risk of diabetes mellitus complications, particularly in resource-limited healthcare settings.

Although HbA1c and MPV are both closely associated with inflammatory processes in type 2 diabetes mellitus, the relationship between these two parameters remains unclear and shows incosistent results across previous studies. This inconsistency is clinically important because it limits the reliability of MPV as a simple inflammatory marker for assessing glycemic control and predicting the risk of diabetes mellitus complications. Clarifying this relationship is therefore essential to determine the potential clinical utility of MPV, particularly in settings where access to advanced inflammatory biomarkers is limited. Therefore, this study aims to evaluate and analyze the relationship between HbA1c and MPV in patients with type 2 diabetes mellitus at UNS Hospital as a basis for the potential use of MPV as a simple inflammatory marker in clinical practice.

2. RESEARCH METHOD

This study employed an observational analytic design with a cross-sectional approach to assess the relationship between glycated hemoglobin (HbA1c) and mean platelet volume (MPV) based on a single measurement time. The study was conducted at Universitas Sebelas Maret (UNS) Hospital, Sukoharjo, Central Java, using secondary data obtained from electronic medical records. Data collection was carried out at the Medical Records Department from September to October 2025 and included hospitalized patients with Type 2 Diabetes Mellitus (T2DM) treated during 2024–2025. A total of 38 subjects were selected using purposive sampling and met the predefined inclusion and exclusion criteria. The sample size was determined based on the minimum requirement for correlation analysis, calculated using an assumed correlation coefficient of 0.4, a significance level of 0.05, and a power of 80%, as described by Sopiyudin Dahlan (2010). Inclusion criteria consisted of adult patients aged 18–65 years with a confirmed diagnosis of T2DM according to the Indonesian Society of Endocrinology (Perkeni) criteria and complete medical records containing HbA1c and MPV data. Patients with conditions that could affect platelet indices—such as hematological disorders, infectious diseases, endocrine disorders, chronic kidney disease, liver cirrhosis, pregnancy, recent blood transfusion, Type 1 diabetes mellitus, or corticosteroid therapy—were excluded to minimize confounding and improve internal validity.

The independent variable in this study was HbA1c level, expressed as a percentage (%), representing glycemic control, while the dependent variable was MPV, expressed in femtoliters (fL), serving as an inflammatory marker. HbA1c levels were measured using a chemical analyzer (TMS 30i) based on the high-performance liquid chromatography (HPLC) method, whereas MPV values were obtained from complete blood count analyses using a hematology analyzer (Mindray BC-760). Blood samples were collected in EDTA tubes and analyzed within the standard time frame to reduce pre-analytical variation. For descriptive purposes, HbA1c values were categorized using a cut-off of ≥ 7% to indicate poor glycemic control, in accordance with Perkeni guidelines (Perkeni, 2024). Statistical analysis was performed using IBM SPSS Statistics version 25. Data normality was assessed using the Shapiro–Wilk test. Pearson's correlation test was applied for normally distributed data, while Spearman's rank correlation test was used for non-normally distributed data. A p-value of ≤ 0.05 was considered statistically significant. This study was approved by the Health Research Ethics Committee of UNS Hospital (No. 237/UN27.46.4/PT.01.04/2025).

3. RESULTS AND DISCUSSION

Analysis showed a significant moderate positive correlation between HbA1c and MPV ($r = 0.467$, $p = 0.003$).

A normality test was conducted to determine whether the study variables were normally distributed. The Shapiro–Wilk test was used because the sample size was 38 (<50). Based on the Shapiro–Wilk test, the age variable was not normally distributed ($p < 0.05$), whereas HbA1c, MPV, and platelet values were normally distributed ($p > 0.05$).

To determine the relationship between HbA1c and MPV, a correlation analysis was performed. The Shapiro–Wilk normality test previously conducted showed that both HbA1c and MPV were approximately normally distributed. Therefore, the correlation between these variables was assessed using the Pearson correlation test.

Table 1. Pearson Correlation Analysis of the Relationship Between HbA1c and MPV in Patients With Type 2 Diabetes Mellitus

		MPV
HbA1c	Pearson Correlation (r)	0.467
	Sig. (2-tailed) (p)	0.003
	N	38

Table 1 presents the correlation between HbA1c and MPV in patients with type 2 diabetes mellitus. Based on a Pearson correlation test in IBM SPSS Statistics v25, the p-value for HbA1c and MPV was 0.003 ($p = 0.003$), indicating a statistically significant correlation. The Pearson correlation coefficient was 0.467 ($r = 0.467$), indicating a positive, moderate relationship between the two variables.

Table 2. Comparison of MPV Values by HbA1c Category

HbA1c Category (%)	**N (people)**	**MPV (fL), mean ± SD**
< 7	3	8.3 ± 0.66
≥ 7	35	9.5 ± 1.4

Table 2 shows the comparison of MPV values according to HbA1c categories. Patients with HbA1c ≥ 7% (n = 35) had higher mean MPV values compared to those with HbA1c < 7% (n = 3) (9.5 ± 1.4 vs 8.3 ± 0.66). These findings suggests a tendency toward increased platelet activation in patients with poorer glycemic control.

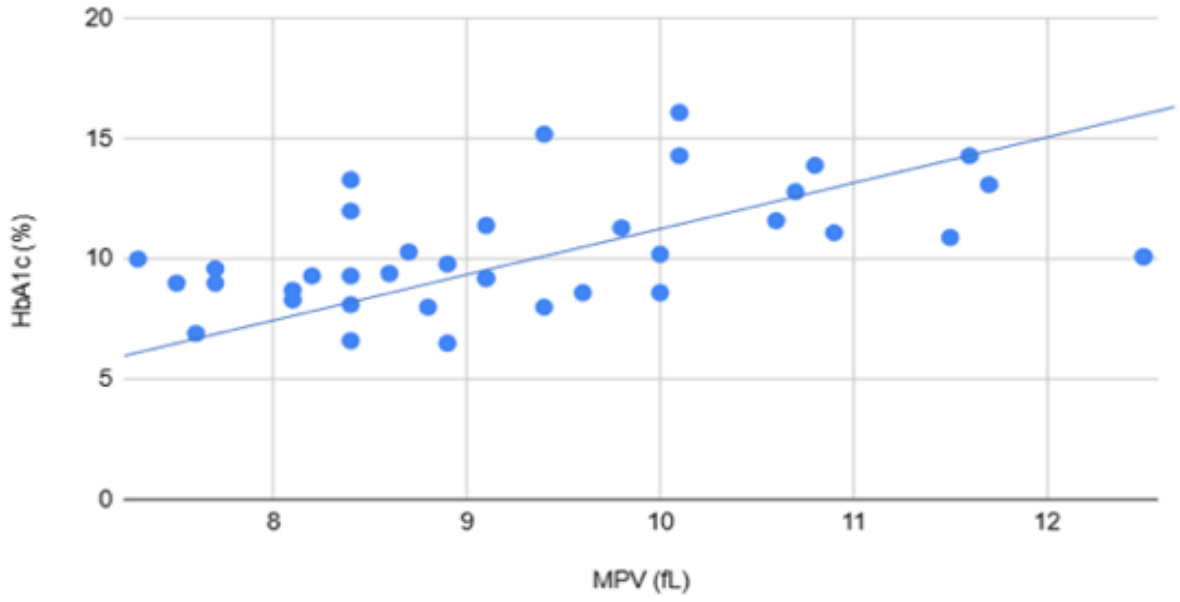

Figure 1. Characteristics of HbA1c and MPV

The graph in Figure 1 illustrates the relationship between HbA1c levels and MPV values. The visualized correlation plot shows that, although individual values vary, there is a general tendency for MPV to increase with rising HbA1c levels. This indicates a positive association between HbA1c and MPV. However, MPV variability is present across samples; therefore, not all individuals with elevated HbA1c exhibit correspondingly high MPV values. Among patients with HbA1c levels above 7%, most show increased MPV values, although these remain within the normal reference range for MPV established by UNS Hospital (7.2–11.1 fL). In this study, only four subjects demonstrated abnormal MPV values, specifically 11.5, 11.7, 11.6, and 12.5 fL

Table 3. Overall Characteristics of the Subjects

Data	Minimal	Maximal	Mean	Standard Deviation	p-value	Unit
Age	41	65	56.2632	7.44959	0.001	Years
HbA1c	6.50	16.10	10.3711	2.38394	0.095	%
MPV	7.30	12.50	9.3842	1.39604	0.056	fL
Platelet	110.00	476.00	272.8947	74.89481	0.472	$\times 10^3/\mu L$

Table 3 presents the overall characteristics of the study. The mean age of patients with type 2 DM was 56.2632 years. The mean HbA1c level was 10.4%. Based on the complete blood count results, the mean MPV value was 9.3842 fL, and the mean platelet count was 272.8947 $\times 10^3/\mu L$.

Table 4. Characteristics of Subjects by Age and Sex.

Variable	Category	Frequency (people)	Percentage (%)
Age (years)	41 – 45	6	15.8
	46 – 50	5	13.2
	51 – 55	4	10.5
	56 – 60	7	18.4
	61 – 65	16	42.1
Sex	Male	10	26.3
	Female	28	73.7
	Total	38	100.0

Table 4 summarizes the demographic characteristics of the study subjects. Of the 38 participants, 28 (73.7%) were female and 10 (26.3%) were male. The participants were aged 41–65 years, with the largest proportion in the 61–65-year age group (42.1%).

Table 5. Mean Age, HbA1c, and MPV According to Sex

Variable	Male (n = 10)	Female (n = 28)
Age (years), mean ± SD	56.60 ± 6.30	56.14 ± 7.92
HbA1c (%), mean ± SD	10.10 ± 2.01	10.50 ± 2.53
MPV (fL), mean ± SD	9.50 ±1.40	9.35

Table 5 presents the mean age, HbA1c levels, and MPV according to sex. The mean age of male patients was 56.60 ± 6.30 years, while female patients had a mean age of 56.14 ± 7.92 years. Mean HbA1c levels were slightly higher in female patients compared to male patients (10.50 ± 2.53% vs 10.10 ± 2.01%). Similarly, mean MPV values were marginally higher in male patients than ini female patients (9.50 ± 1.40 fL vs 9.35 ± 1.42 fL).

This study aimed to determine the relationship between HbA1c and MPV in patients with type 2 diabetes mellitus. A total of 38 subjects met the inclusion and exclusion criteria. Most subjects were female (73.7%) and predominantly in the older age category, particularly 61–65 years (42.1%), with a mean age ranging from adulthood to the early elderly category (56.2632 years).

The predominance of female subjects (73.7%) aligns with findings from previous epidemiological studies. According to the 2018 Indonesian National Health Survey (Riskesdas), the prevalence of diabetes mellitus among individuals of all ages is higher in females than males, with a female-to-male ratio of 1.78% to 1.21%. However, global data indicate that the prevalence of type 2 diabetes is slightly higher in males than in females, with a ratio of 10.8% to 9.8% (IDF, 2021). These differences may vary across countries due to genetic and lifestyle factors (IDF, 2021).

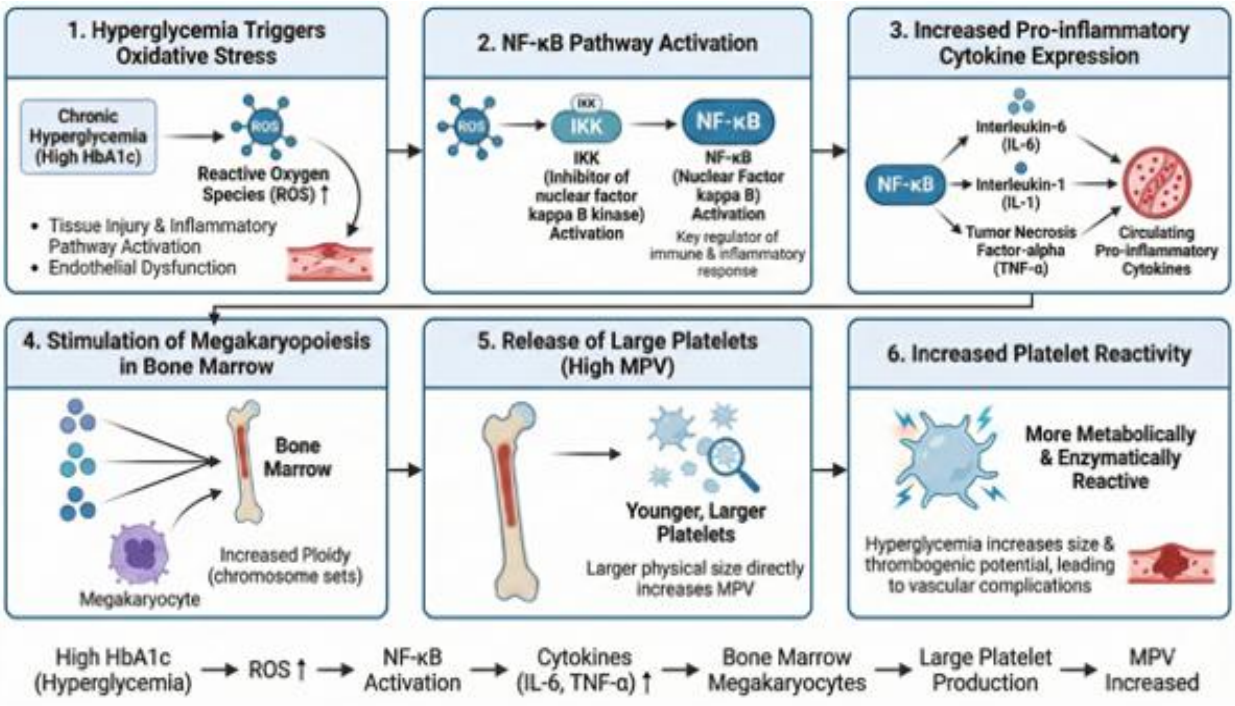

Figure 2. Pathophysiological Mechanism of Increased Mean Platelet Volume (MPV) Induced by Chronic Hyperglycemia via Oxidative Stress and Inflammatory Pathways.

Figure 2 illustrates the pathophysiological mechanism linking chronic hyperglycemia (high HbA1c) to increased Mean Platelet Volume (MPV) and thrombotic risk. The process begins with hyperglycemia triggering oxidative stress through increased Reactive Oxygen Species (ROS). This activates the NF-κB inflammatory pathway, leading to a surge in circulating pro-inflammatory cytokines such as IL-6 and TNF-α. These cytokines stimulate megakaryopoiesis in the bone marrow, causing the release of younger, larger platelets into circulation. This elevation in MPV signifies platelets that are more metabolically active and reactive, contributing to a higher thrombogenic potential and risk of vascular complications.

This study also found that the average HbA1c level was higher in female subjects than in male subjects. This may be attributed to the higher body fat percentage typically found in women, which can reduce insulin sensitivity. In addition, women generally have lower muscle mass, leading to decreased glucose utilization and, consequently, higher long-term glucose levels (Palmer & Clegg, 2015).

The mean age of the female subjects in this study was 56.1429 years, indicating that most were postmenopausal. Menopause leads to a decline in estrogen and progesterone, which contributes to increased insulin resistance (Wahab et al., 2025). A previous study also reported

that HbA1c levels are lower in premenopausal women than in postmenopausal women (Alghamdi et al., 2021). Moreover, women tend to exhibit higher sensitivity to emotional stress and are more likely to engage in stress eating, which may contribute to elevated HbA1c levels (Gonçalves et al., 2024).

Most of the study subjects were in the older age category, particularly in the 61–65-year age range (42.1%), with a mean age between adulthood and early old age (56.2632 years). This finding is consistent with national data from the 2018 Indonesian Basic Health Research (Riskesdas), which reported that the highest prevalence of diabetes mellitus by age group occurs in individuals aged 55–64 years, at 6.29%. With increasing age, pancreatic β-cells lose their ability to produce insulin to compensate for insulin resistance. In middle-aged and elderly individuals, the adaptive capacity of β-cells in response to insulin resistance is more limited than in younger adults (Lee & Halter, 2017). A study also demonstrated that insulin resistance increases with age (Koo et al., 2016). Moreover, aging is associated with reduced physical activity and loss of muscle mass (sarcopenia), which decreases glucose utilization in muscle tissue and consequently increases blood glucose levels (Lee & Halter, 2017). Aging also contributes to mitochondrial dysfunction, intramyocellular lipid accumulation, oxidative stress, and chronic inflammation, all of which further impair insulin sensitivity (Shou et al., 2020).

In this study, the mean HbA1c level among the 38 subjects was 10.3711%, which was significantly higher than the glycemic control target for patients with type 2 diabetes recommended by Perkeni (<7%). This indicates poor glycemic control in most subjects. The mean HbA1c level in this study was also higher than those reported in several previous studies, which reported average HbA1c levels of 8.29% (Kusdiantini & Istiqomah, 2024), 7.84% (Kazemiathar et al., 2024), and 7.9% (Inoue et al., 2020).

The mean MPV level in this study was 9.3842 ± 1.39604 fL, which is lower than the MPV levels reported in earlier studies on patients with type 2 diabetes, ranging from 9.629 ± 0.85 fL (Hartini et al., 2025) to 10.36 ± 0.84 fL (Mahdalena et al., 2021).

The visualization in Figure 4.1 shows a tendency for MPV values to increase with rising HbA1c levels. This finding is supported by the Shapiro–Wilk normality test and the Pearson correlation analysis, which revealed a statistically significant, moderate positive correlation between HbA1c and MPV. These results align with studies by Inoue et al. and Ulutas et al., both of which reported a positive association between MPV and HbA1c.

In this study, higher HbA1c levels were associated with higher MPV values, as demonstrated by a statistically significant moderate positive correlation ($r = 0.467$). This finding indicates that poorer glycemic control is related to increased platelet activation in patients with type 2 diabetes mellitus. However, the moderate strength of this correlation suggests that HbA1c is not the sole determinant of MPV.

The variability of MPV observed in this study further supports this interpretation. As shown in Figure 4.1, several subjects with elevated HbA1c levels still exhibited MPV values within the normal range, indicating that factors beyond glycemic control may independently influence platelet size. The increase in MPV associated with higher HbA1c levels can be explained by chronic hyperglycemia–induced oxidative stress and low-grade inflammation, which affect megakaryocyte activity and promote the release of larger, more reactive platelets (Kaur et al., 2018; Li et al., 2021).

Nevertheless, MPV is known to be influenced by various non-glycemic factors, including age, sex, genetic variation, comorbid conditions, medications, and pre-analytical and analytical factors related to blood sampling and laboratory measurement (Korniluk et al., 2019). These factors may explain why not all individuals with poor glycemic control demonstrated elevated MPV values in this study. Therefore, the present findings highlight that while HbA1c is associated with MPV, platelet activation in type 2 diabetes mellitus is a multifactorial process.

These findings highlight the potential of mean platelet volume (MPV) as an additional, non-invasive biomarker that is routinely available through complete blood count testing and may be used alongside glycated hemoglobin (HbA1c) to evaluate glycemic status and thrombosis risk in patients with type 2 diabetes mellitus. The combined use of HbA1c and MPV may be useful in identifying patients with poor glycemic control who are at increased risk of thrombosis, monitoring the effectiveness of therapy, and assessing the risk of microvascular and macrovascular complications. However, the clinical application of MPV should be approached with caution due to variability in MPV measurement standards across laboratories.

This study has several limitations that should be considered when interpreting the results. First, the cross-sectional design limits causal inference between HbA1c and MPV, as the observed association reflects a single time point rather than temporal relationships. Second, although an association between HbA1c and MPV was identified, MPV is influenced by multiple non-glycemic factors that were not fully controlled in this study, including comorbid conditions common in patients with type 2 diabetes, genetic variability, demographic characteristics, lifestyle factors, medications, and pre-analytical and analytical variables. Consequently, these unmeasured factors may have contributed to the variability in MPV and affected the strength of the observed correlation. Third, the relatively small sample size (n = 38) may have limited the statistical power of the analysis and reduced the generalizability of the findings to the broader population of patients with type 2 diabetes mellitus. Future studies employing larger sample sizes, longitudinal designs, and multivariate analyses are warranted to better elucidate the independent effect of glycemic control on MPV and to validate the present findings.

4. CONCLUSION

This study found a moderate positive correlation between HbA1c levels and mean platelet volume (MPV) among patients with type 2 diabetes mellitus treated at UNS Hospital, Indonesia. These findings indicate an associational relationship, suggesting that poorer glycemic control is linked to higher MPV values, although causality cannot be inferred due to the cross-sectional design. The observed moderate correlation highlights that glycemic control contributes to, but does not fully explain, variations in MPV among patients with type 2 diabetes. This study reinforces existing evidence that MPV is associated with glycemic control in local clinical populations, providing contextual data from an Indonesian tertiary care setting.

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