

Association Between Complete Blood Count Parameters and Glycemic Control in Type 2 Diabetes Mellitus: A Descriptive Cross-Sectional Study

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ABSTRACT

Objective: This study investigated the association between HbA1c levels and hematological parameters in patients with type 2 diabetes mellitus to determine their potential as markers of glycemic regulation.

Methods: This retrospective cross-sectional study included 498 patients with Type 2 diabetes mellitus attending the Endocrinology Outpatient Clinic of Selçuk University Faculty of Medicine between January 2023 and December 2024, along with 500 healthy adults as controls. Demographic data (age and sex) and laboratory results were retrospectively analyzed.

Results: HbA1c levels showed positive correlations with age ($r = 0.558$, $p < 0.001$), WBC ($r = 0.237$, $p < 0.001$), RDW ($r = 0.128$, $p < 0.001$), and NLR ($r = 0.068$, $p = 0.040$). An inverse association was detected between HbA1c levels and MCV ($r = -0.238$, $p < 0.001$). There were no statistically meaningful associations identified between HbA1c levels and MPV, PLT, or Hgb ($p > 0.05$). Among individuals with type 2 diabetes, WBC, RDW and NLR were notably elevated, whereas MCV was significantly reduced in comparison to the control group ($p < 0.05$).

Conclusion: The observed associations between HbA1c and selected hematological parameters indicate that complete blood count—given its affordability and accessibility—may serve as a supportive tool for the assessment of glycemic status in patients with Type 2 diabetes mellitus. Parameters such as MCV, RDW, and NLR could act as potential biomarkers for glycemic control and early complication detection. However, these findings require validation through large-scale, multicenter, prospective studies.

Keywords: glycemic control, HbA1c, hematological parameters, MCV, NLR, RDW, Type 2 diabetes mellitus

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic condition defined by persistent hyperglycemia resulting from inadequate insulin production, resistance to insulin action, or a combination of these mechanisms. Globally, approximately 422 million people have diabetes, and the increasing number of cases has become a global public health problem [1]. In 2019, there were 463 million individuals with diabetes worldwide, and this number has reached 588.7 million (11.1%) by 2024. Estimates from the International Diabetes Federation (IDF) suggest that the global diabetic population may rise to approximately 853 million by the year 2050 [2-4]. In Türkiye, according to the Türkiye Diabetes Program 2023–2027 and Turkish Statistical Institute (TUIK) 2022 data, the prevalence of Type 2 diabetes mellitus (T2DM) among individuals aged 18 years and older is reported to range between approximately 11.4% and 14.5% [5, 6].

T2DM affects not only glucose metabolism but also the hematological system. Although glycated hemoglobin (HbA1c) is routinely used to evaluate long-term glycemic control in individuals with diabetes, it may not sufficiently reflect the wider systemic disturbances associated with the condition. Exploring the association between HbA1c levels and specific hematological indices may offer deeper insights into the systemic manifestations of the disease. A range of hematological parameters—including white blood cell (WBC) count, hemoglobin (Hgb), mean corpuscular volume (MCV), mean platelet volume (MPV),

red cell distribution width (RDW), neutrophil-to-lymphocyte ratio (NLR), hematocrit (Hct), and platelet count (PLT)—may be influenced by the chronic inflammation and oxidative stress associated with diabetes mellitus [7, 8].

These hematological parameters may serve as useful indicators for the early detection of complications associated with diabetes. Given that these parameters can be easily and inexpensively obtained through routine laboratory tests, they are considered valuable tools for assessing glycemic control and personalizing patient monitoring in primary healthcare services [8, 9].

The present study investigated the relationship between glycated hemoglobin (HbA1c) and routine hematological markers that could indicate underlying systemic inflammation or metabolic imbalance. However, there is still limited evidence on how commonly used hematological indices correlate with HbA1c levels and reflect systemic inflammation or glycemic dysregulation in patients with type 2 diabetes mellitus. This study aims to fill this gap by evaluating the relationship between HbA1c and routine hematologic parameters to identify potential biomarkers for glycemic control.

MATERIAL AND METHODS

Study Design

A retrospective, observational study with a cross-sectional design was carried out at the Endocrinology Outpatient Clinic of Selcuk University Faculty of Medicine between January 1, 2023, and December 31, 2024. Medical records of patients who presented during this period and met the inclusion criteria were systematically reviewed. As all eligible patients presenting during the study period were retrospectively analyzed, no prior sample size calculation was conducted, and no specific patient subgroup was selected.

Study Group (Participants)

The study sample included 498 adults (aged 18 and above) with a confirmed diagnosis of type 2 diabetes mellitus (T2DM), along with 500 individuals without diabetes whose HbA1c values were within the normal reference interval, serving as the control group. A total of 998 individuals were enrolled in the study. Since this was a retrospective review of all eligible cases during a two-year period, no formal sample size calculation was performed. However, the large sample size was deemed sufficient for statistical analysis. The inclusion and exclusion criteria were applied, resulting in 998 total participants (498 T2DM patients

Main Points

- Significant associations were identified between HbA1c levels and several hematological parameters, including WBC, RDW, MCV, and NLR.
- Complete blood count parameters, which are easily accessible and cost-effective, may serve as supportive tools for monitoring glycemic control and detecting early complications in patients with type 2 diabetes mellitus.
- These findings underscore the potential utility of routine hematological indices in primary care follow-up of diabetic patients.
- The integration of hematological parameters into routine diabetic screening may enhance early diagnosis and personalized treatment strategies.

and 500 healthy controls). A flow diagram summarizing this process is illustrated in Figure 1.

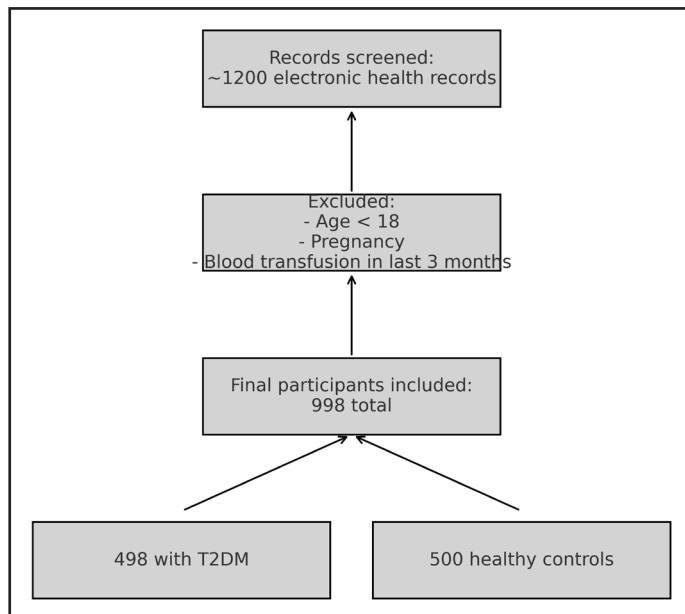


Figure 1. Flow diagram of participant inclusion and exclusion process in the study. T2DM: Type 2 diabetes mellitus.

Inclusion Criteria

Patient Group: Patients diagnosed with T2DM with HbA1c levels $\geq 6.5\%$.

Control Group: Individuals without a T2DM diagnosis and with HbA1c levels within the normal reference range.

Exclusion Criteria

- Individuals aged <18 years
- Pregnant women
- Those with a history of blood transfusion in the preceding three months

Data Collection

The age, sex, and laboratory data (WBC, Hgb, MCV, MPV, RDW, NLR, Hct, PLT, and HbA1c) of the included patients were retrospectively obtained from electronic health records.

Laboratory Analysis

Blood samples were processed at the Central Laboratory of Selçuk University Faculty of Medicine. Complete blood count (CBC) parameters—including WBC, Hgb, MCV, MPV, RDW-CV (%), Hct, and PLT—were obtained using an automated hematology analyzer (Beckman Coulter LH 780, USA). Biochemical analyses were performed using a Roche Cobas 8000 modular

analyzer (Roche Diagnostics, Germany). HbA1c levels were measured using the high-performance liquid chromatography (HPLC) method. The neutrophil-to-lymphocyte ratio (NLR) was manually calculated using an online tool (MDCalc, <https://www.mdcalc.com>) by dividing the absolute neutrophil count by the absolute lymphocyte count.

Statistical Analysis

Data were analyzed with the aid of IBM SPSS Statistics software (v22.0, IBM Corporation, Armonk, NY, USA). A p-value less than 0.05 was regarded as statistically significant. Categorical data were presented as counts and proportions, whereas continuous variables were expressed as mean \pm standard deviation. The independent samples t-test was applied for normally distributed variables. The Kruskal–Wallis and Mann–Whitney U tests were applied for the analysis of data that did not follow a normal distribution. Correlations between variables were analyzed using Spearman’s rank correlation coefficient. Due to the retrospective design of the study, no predefined sample size estimation was conducted; nonetheless, the large number of included cases is deemed statistically sufficient.

Ethical Approval

Approval for the study was granted by the Ethics Committee of Selçuk University Faculty of Medicine before the initiation of data analysis (Date: December 17, 2024; Decision No: 2024/643). The study’s objectives and methodology were verified to comply with the ethical guidelines established by the institutional review board, in line with the principles outlined in the Declaration of Helsinki and its later revisions. The ethics committee exempted the study from the need for informed consent due to its retrospective nature.

RESULTS

Demographic Characteristics

The study cohort comprised 498 adults diagnosed with type 2 diabetes mellitus (T2DM) and 500 healthy controls (Table 1). Diabetic participants had a higher mean age (56.94 ± 11.18 years) compared to controls (39.76 ± 14.14 years), and the difference was statistically significant ($p < 0.001$). In terms of sex distribution, 38.6% ($n=192$) of the T2DM patients were male and 61.4% ($n=306$) were female, compared to 30.8% ($n=154$) males and 69.2% ($n=346$) females in the control group. Female predominance was observed in both cohorts, and a statistically significant variation in gender distribution was noted between the groups ($p=0.01$). The mean HbA1c level of

male participants (7.2 ± 1.5) was significantly higher than that of female participants (6.8 ± 1.3) ($p=0.005$). HbA1c levels were markedly higher in the diabetic group compared to the control group (7.56 ± 1.73 vs. 5.43 ± 0.35 ; $p<0.001$).

Comparison of Hematological Parameters

Patients with diabetes exhibited elevated WBC, RDW, and NLR values relative to the control group, with statistically significant differences. In contrast, MCV was significantly reduced among individuals with T2DM (Table 1). No statistically significant variation was detected in other hematological parameters, such as Hgb, Hct, PLT, and MPV, between the two groups. ($p>0.05$; Table 1).

Relationship Between Glycemic Control (HbA1c) and Hematological Parameters

The correlations between HbA1c and other parameters are summarized in Table 2. A moderate positive correlation between age and HbA1c levels reached statistical significance ($r=0.558$, $p<0.001$). Additionally, a weak positive correlation was identified between NLR and HbA1c, whereas a weak inverse relationship was noted between MCV and HbA1c ($r=0.068$, $p=0.040$; $r=-0.238$, $p<0.001$). In addition, low positive correlations were detected between HbA1c and both WBC and RDW ($r=0.237$, $p<0.001$; $r=0.128$, $p<0.001$) (Figure 2). On the other hand, HbA1c levels did not exhibit any statistically significant correlation with Hgb, PLT, or MPV ($r=0.025$, $p=0.456$; $r=0.017$, $p=0.616$; $r=-0.061$, $p=0.068$).

Table 1. Comparison of Blood Parameters Between Diabetes Mellitus and Control Groups

Parameters Mean \pm SD (n=498)		T2DM	Control	p-value
		Mean \pm SD (n=500)		
Age (years)		56.94 \pm 11.18	39.76 \pm 14.14	<0.001
Sex, n (%)	Male	192 (38.6)	154 (30.8)	0.010
	Female	306 (61.4)	346 (69.2)	
WBC (109/L)		8.04 \pm 2.24	7.24 \pm 1.90	<0.001
Hgb (g/dL)		14.01 \pm 1.77	13.94 \pm 1.57	0.433
Hct (%)		42.80 \pm 4.70	42.54 \pm 4.27	0.206
PLT (109/L)		277.9 \pm 76.95	282.85 \pm 69.83	0.202
MCV (fL)		85.26 \pm 5.91	86.85 \pm 7.701	<0.001
RDW (fL)		14.18 \pm 1.59	13.96 \pm 1.68	0.013
MPV (fL)		10.63 \pm 1.07	10.72 \pm 1.09	0.120
HBA1C (%)		7.56 \pm 1.73	5.43 \pm 0.35	<0.001
NLR		2.08 \pm 1.02	1.93 \pm 0.86	0.040

Table 2. Correlation analysis between HbA1c and laboratory parameters

Parameters	HbA1c	
	R	p-value
Age (years)	0.558	<0.001
WBC (109/L)	0.237	<0.001
Hgb (g/dL)	0.025	0.456
Hct (%)	0.057	0.086
PLT (109/L)	0.017	0.616
MCV (fL)	-0.238	<0.001
RDW (fL)	0.128	<0.001
MPV (fL)	-0.061	0.068
NLR	0.068	0.040

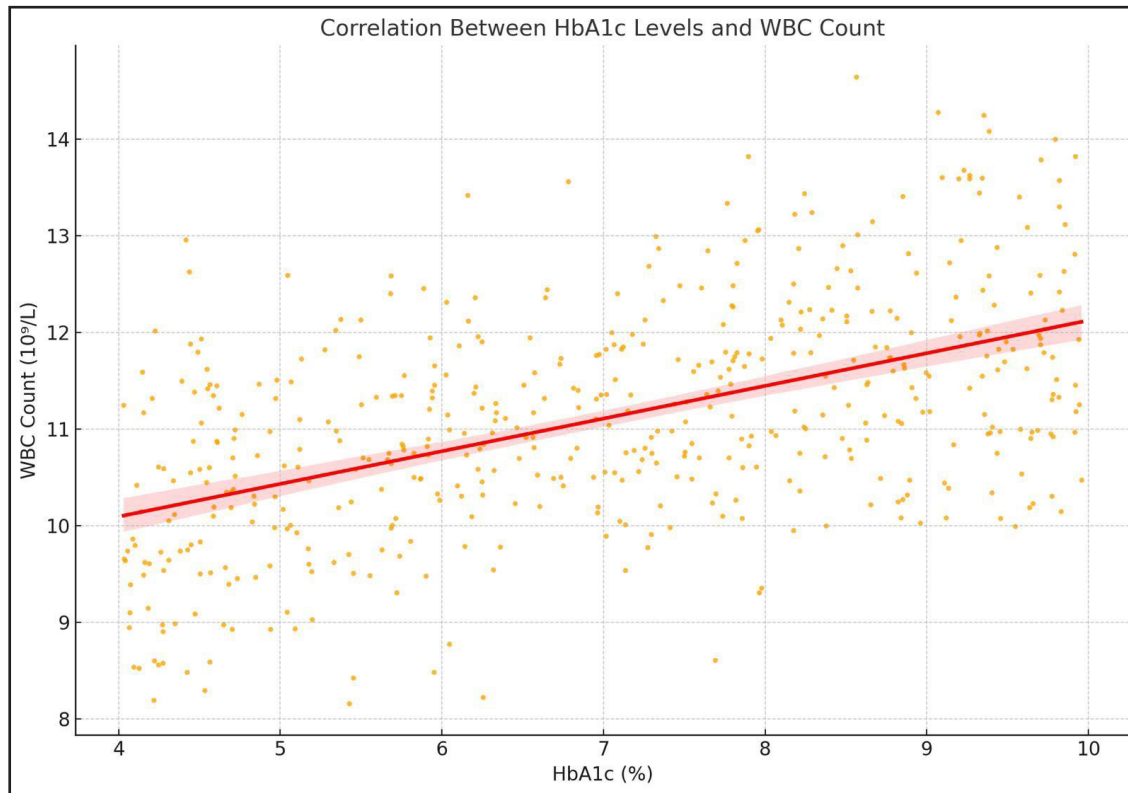


Figure 2. Scatter plot graph representing the correlation between WBC and HbA1c of the patients. WBC: White blood cell count; HbA1c: Glycated hemoglobin.

DISCUSSION

Our findings demonstrated a statistically significant moderate positive correlation between age and HbA1c levels. In the study population, men showed elevated mean HbA1c levels relative to women. In the literature, HbA1c has been reported to increase with age and to be higher in men, possibly due to hormonal and physiological factors, including menstruation and menopause [10, 11]. For instance, a study on Taiwanese adults reported similar findings in non-diabetic individuals. These factors, along with differences in lifestyle and genetics, may explain the observed gender differences. However, age- and sex-specific effects remain complex, and our study's non-homogeneous distribution may have influenced HbA1c levels as a potential confounding factor. Establishing age- and sex-specific reference ranges could improve diagnostic accuracy and patient follow-up [11, 12].

Some studies have reported a positive correlation between HbA1c levels and MPV, which could be associated with increased platelet activation in diabetic individuals [13-16]. However, no correlation was found between HbA1c and MPV in our study. Although this finding may seem inconsistent with

previous studies, it suggests that the ability of hematological parameters to reflect glycemic control may vary depending on individual differences, comorbidities, and treatments. It may be inferred that parameters such as MPV may not be sufficient alone for diagnosis or follow-up and should be evaluated together with other biomarkers. Moreover, the limited sample size and non-homogeneous study population may also explain this discrepancy.

Previous research has demonstrated a significant association between HbA1c levels and MCV [17, 18]. In alignment with previous reports, this investigation demonstrated a significant inverse correlation linking HbA1c and MCV. The relationship between HbA1c and MCV may be attributed to the adverse effects of diabetes on erythrocyte structure and production.

RDW serves as a dependable marker of anisocytosis and is frequently applied in differentiating microcytic from normocytic anemias. Studies in the literature have reported significant correlations between HbA1c and RDW [19, 20]. This analysis identified a weak positive association between RDW and HbA1c levels. Poor glycemic control in diabetes has been linked to

modifications in hemoglobin properties and disturbances within the intracellular milieu of erythrocytes. Emerging evidence suggests that the persistent inflammatory state linked to diabetes may impair erythropoiesis, reduce erythrocyte survival, and consequently elevate RDW levels [21].

NLR is a frequently used, non-invasive, and cost-effective parameter for evaluating systemic inflammation. Neutrophils increase during the initial inflammatory response, while lymphocytes may decrease under chronic stress and inflammatory conditions. Therefore, NLR rises as inflammation progresses. Several studies have demonstrated a link connecting the NLR with T2DM [22-24]. Our findings also revealed a weak positive association between the NLR and HbA1c levels. This is in line with the results of a 2023 systematic review and meta-analysis, and a 2024 study from Turkey, both of which showed a statistically significant positive association between elevated NLR values and poor glycemic control in patients with T2DM [23, 25]. These findings support the hypothesis that systemic inflammation, as reflected by NLR, plays a crucial role in the pathogenesis of insulin resistance and chronic hyperglycemia [23].

Studies have shown a positive correlation between HbA1c and WBC in patients with T2DM [26]. Several studies have indicated a link between increased WBC count and reduced insulin sensitivity [26, 27]. In a study conducted in Korea in 2018, it was suggested that hyperglycemia increases the production of pro-inflammatory molecules, thereby elevating neutrophil counts and triggering the inflammatory response. Additionally, it was emphasized that chronic inflammation may increase insulin resistance and consequently elevate HbA1c levels [28]. The results suggest that WBC may serve as a surrogate indicator for monitoring glycemic status. The present study revealed a weak positive association between WBC count and HbA1c levels. This finding suggests that as glycemic control deteriorates, low-grade inflammation increases, which is reflected in hematological parameters.

Similarly, a study performed in India in 2021 also found that elevated WBC counts were associated with poor glycemic control, and suggested WBC as a potential marker for diabetes management [24].

In summary, our results are largely in agreement with previous literature, particularly in identifying low-grade inflammation

and erythrocyte abnormalities as important contributors to glycemic control. These findings highlight the potential role of hematologic indices such as NLR, RDW, and WBC as complementary tools in diabetes monitoring. However, given the modest correlation strength and the influence of various confounders, these markers should be interpreted alongside established clinical and biochemical parameters. Further large-scale and prospective studies are needed to validate these observations and assess their clinical applicability.

Limitations

Due to the retrospective design of the study, analyses were conducted post hoc, and a significant difference in age distribution was observed between the diabetic and control groups. The average age of individuals in the diabetic group was 56.94 ± 11.18 years, notably higher than the 39.76 ± 14.14 years observed in the control group, and this age difference reached statistical significance. Given that age can influence various hematological parameters, this imbalance may pose a limitation in fully interpreting the study outcomes. Similarly, the gender distribution was not homogeneous between the groups; considering the significantly higher HbA1c levels found in male participants compared to female participants in this study, it may be difficult to evaluate the isolated effect of gender on HbA1c levels. In addition, due to the retrospective study design, data regarding key anthropometric measures—namely stature, body weight, and body mass index—were unavailable. Given that the study was conducted at a single center, the extent to which the findings can be generalized is limited. Therefore, confirmation through multi-center investigations involving larger cohorts is warranted. This study relies on retrospective electronic health records, and as such, potential sources of bias, including selection and information bias, may exist. Efforts were made to include all eligible individuals during the study period to reduce selection bias. Because the study setting was limited to one tertiary care facility, caution should be exercised when extrapolating the findings to other demographic or clinical groups. The lack of body mass index (BMI), lifestyle, and treatment data may have influenced the associations between glycemic control and hematological parameters.

CONCLUSIONS

This study revealed significant associations between HbA1c and several hematologic indices, including NLR, RDW, WBC, MCV, and age. Elevated HbA1c levels tended to coincide with higher values of these parameters, except for MCV, which showed a

notable decline. These findings highlight the potential utility of CBC parameters in evaluating glycemic control and predicting diabetes-related complications during routine clinical follow-up. Particularly in primary care settings, the assessment of readily available and cost-effective CBC parameters may offer a practical means of supporting the clinical monitoring of individuals with T2DM. These results may aid in the timely recognition of diabetes-associated complications. Nonetheless, additional prospective research is warranted to validate these observations.

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Conflict of interest: The authors declare that they have no conflicts of interest.

Informed Consent: Not applicable due to the retrospective nature of the study.

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