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ORIGINAL RESEARCH

The Association Between HbA1c Levels And Hematological Biomarkers in Adults with Type 2 Diabetes Mellitus: A Retrospective Study

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Background: Type 2 Diabetes Mellitus (T2DM) is associated with chronic hyperglycemia that contributes to oxidative stress and alterations in hemostatic and hematological pathways, potentially leading to measurable changes in routine blood parameters. These biomarkers may provide early indications of metabolic or vascular complications. This study investigates the association between glycated hemoglobin (HbA1c) levels and hematological and hemostatic abnormalities in Saudi adults with T2DM.

Methods: This retrospective study analyzed laboratory records of 651 adult patients categorized into four glycemic groups based on HbA1c levels: normal (<5.7%), prediabetes (5.7–6.4%), controlled diabetes (6.5–7.9%), and uncontrolled diabetes (≥8.0%). Hemostatic parameters and red and white blood cell indices were compared across groups. Multiple regression analysis was performed to evaluate associations between demographic and clinical characteristics and hematological outcomes.

Results: Statistically significant differences in platelet counts were observed between the prediabetes group and both the controlled and uncontrolled diabetes groups. Red and white blood cell counts were significantly higher in the controlled and uncontrolled groups than in the normal and prediabetes groups. Regression analysis further identified sex, age, and comorbidity as key predictors of several hematological markers.

Conclusion: This study demonstrates significant hematological variations across HbA1c-defined glycemic groups, indicating that worsening glycemic control is associated with measurable changes in platelet counts and red and white blood cell parameters. These findings suggest that routine hematological profiles may serve as supportive indicators for identifying patients at increased risk of glycemic deterioration or hematologic complications, offering potential value in early clinical assessment and monitoring of T2DM.

Keywords: type 2 diabetes mellitus, HbA1c, hemostasis, hematological parameters, Saudi patients

Introduction

Diabetes Mellitus (DM) affects over 537 million adults worldwide, with this number projected to rise to 783 million by 2045, highlighting the growing global burden of this condition.[1] Type 2 Diabetes Mellitus (T2DM), accounting for 90% of global diabetes cases, is a growing public health crisis linked to significant morbidity and mortality.[1,2] In Saudi Arabia, the prevalence of T2DM has risen significantly over the past two decades reaching a pooled prevalence of 16.4% between 2000 and 2020, ranking seventh globally and second in the Middle East.[3,4] The high prevalence may be attributed to genetic predisposition and the continued high prevalence of consanguinity among the Saudi population.[5]

T2DM is associated with significant alterations in hemostasis, contributing to an increased risk of thrombotic events, which account for approximately 80% of deaths in T2DM patients.[6] The dysfunction in hemostasis observed in T2DM is attributed to several mechanisms, including endothelial dysfunction, activation of coagulation factors, and heightened platelet reactivity.[7,8] Additionally, insulin resistance contributes to increased activity of fibrinolytic inhibitors, such as plasminogen activator inhibitor-1 (PAI-1), along with elevated fibrinogen levels and various coagulation factors.[9] Due to

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the elevated thrombotic risk in individuals with diabetes, further research is warranted to evaluate the role of routine coagulation profiling as a core component of diabetes management.

In patients with T2DM, chronic hyperglycemia alters blood cell production, function, and lifespan, impacting various hematological parameters.[10] Metabolic disturbances and systemic inflammation in T2DM influence white blood cells (WBCs), red blood cells (RBCs), and platelets. Among these hematological changes, the gradual glycosylation and sustained elevation of HbA1c levels play a central role in modifying RBC structure and function.[11] These changes alter hemoglobin structure, increase RBC viscosity, and cause osmotic imbalances.[12] Given the association between elevated Glycated hemoglobin or Hemoglobin A1c (HbA1c) and microvascular complications, changes in RBC deformability and hemorheological properties suggest that these parameters could be valuable markers for monitoring diabetes progression.[13]

Although prior studies have described hematologic and hemostatic alterations in individuals with Type 2 Diabetes Mellitus, few have examined these parameters across clearly defined HbA1c-based glycemic stages, and data from Saudi populations remain particularly limited despite the region's high disease burden. Because chronic hyperglycemia can influence erythropoiesis, red blood cell morphology, and coagulation physiology through glycation-related and oxidative mechanisms, evaluating routine hematologic markers across glycemic categories may yield meaningful clinical insights. Accordingly, this study aims to examine hematological and coagulation parameters across HbA1c-defined glycemic groups in a large Saudi cohort. We hypothesized that progressive deterioration in glycemic control, as reflected by increasing HbA1c levels, is associated with measurable alterations in hematologic and coagulation profiles.

Materials and Methods

Study Design

This retrospective observational study was conducted at King Khalid University Hospital (KKUH) in Riyadh, Saudi Arabia, and included patient records from January to July 2024. It focused on Saudi patients admitted with T2DM and diagnosed during this period. The study focused on Saudi patients who were admitted and diagnosed within the study period, from the beginning of January 2024 to the end of July 2024. Exclusion Criteria include non-Saudi patients, duplicate records, and patient records with missing or unavailable HbA1c. Pediatric patients were also excluded, as the study focused on adult patients with T2DM.

A total of 1262 T2DM patient records were initially reviewed, illustrated in Figure 1. After applying the exclusion criteria, the final sample comprised 651 T2DM adult patients, who were categorized into four groups based on HbA1c

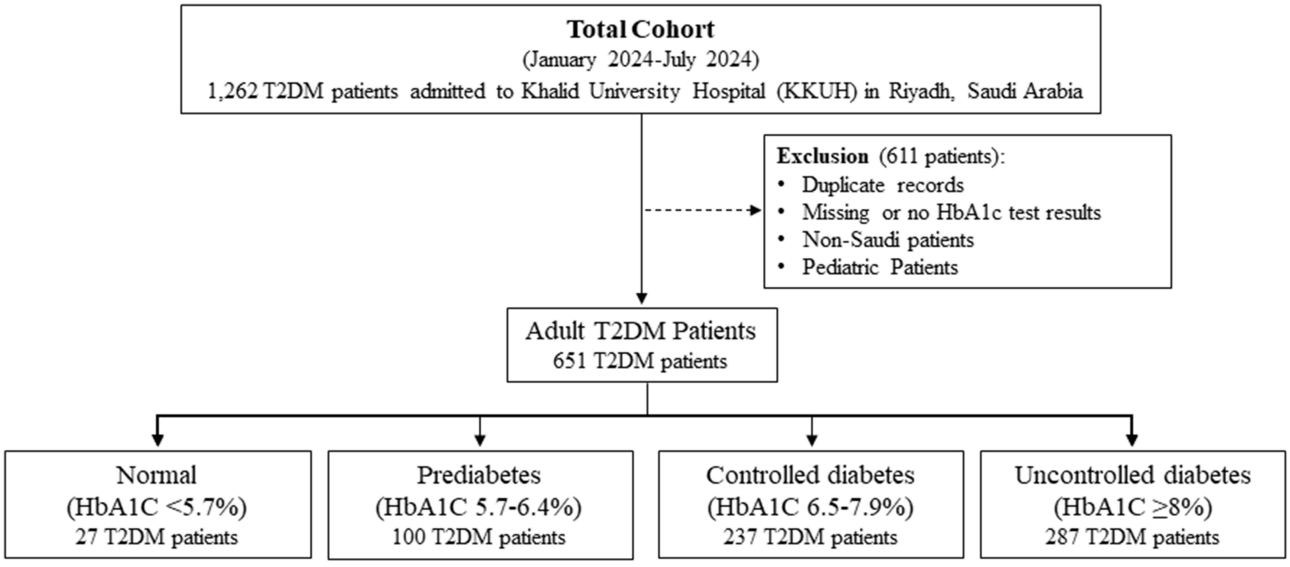

Figure 1 Flowchart of the Study Population.

levels according to the American Diabetes Association (ADA)[14] The normal group, with HbA1c levels below 5.7%, included 27 individuals. The prediabetes group, with HbA1c levels between 5.7% and 6.4%, consisted of 100 patients. The controlled diabetes group, defined by HbA1c levels ranging from 6.5% to 7.9%, included 237 individuals. The uncontrolled diabetes group, characterized by HbA1c levels of 8% or higher, comprising 287 patients. Ethical approval for this study was obtained from the Institutional Review Board (IRB) of the College of Medicine at King Saud University (Approval No. E-24-8824; Approval Date: 22 May 2024).

Variables and Data Collection

HbA1c was analyzed using high-performance liquid chromatography (HPLC) on the Bio-Rad D-100 system. Hemostasis parameters include prothrombin time (PT), activated partial thromboplastin time (APTT), and International Normalized Ratio (INR), which were assessed using the STAR Max® automated coagulation analyzer. The study also examined hematological parameters such as platelet count, mean platelet volume (MPV), RBC count, hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and red cell distribution width (RDW). In addition, white blood cell count parameters included total white blood cell (WBC) count, neutrophil (NEU) count, eosinophil (EOS) count, basophil (BASO) count, monocyte (MONO) count, and lymphocyte (LYM) count. Complete blood counts (CBC) were performed using the Sysmex XN-9100 automated hematology analyzer. To account for other factors that might influence the results, the study collected additional variables on demographics, such as sex, age, fasting glucose, body mass index (BMI), height, weight, smoking status, marital status, and insulin resistance. Health conditions, including cardiovascular disease, neuropathy, nephropathy, and musculoskeletal disorders, were recorded along with medication use, particularly antidiabetic treatments such as metformin. Comorbidities and insulin resistance were identified based on documented physician diagnoses recorded in the electronic medical record.

Statistical Analysis

Statistical analysis was performed using SPSS software (version 26) for data processing and hypothesis testing, while graphical presentations were generated using GraphPad Prism (version 10.4.1). Categorical variables were presented as frequencies (N) and percentages (%), while continuous variables were reported as medians and interquartile ranges (IQR). To assess the distribution of continuous variables, the Shapiro–Wilk test was performed. To compare differences across the four study groups, one-way ANOVA was employed for data that followed a normal distribution, while the Kruskal–Wallis test was used as a non-parametric alternative for data that did not meet the assumption of normality. Subsequently, correlation analyses were conducted to examine associations between the independent variables (demographic and clinical characteristics) and the dependent variables (hemostatic and hematological parameters), with particular attention to those that showed statistically significant results ($p < 0.05$). The choice of correlation test was based on the nature of the variables: Pearson's product-moment correlation was used when both variables were continuous, Spearman's rank-order correlation was applied when at least one variable was ordinal, and point-biserial correlation was employed for associations involving one continuous and one dichotomous variable. Variables with a p-value less than 0.2 in the initial correlation analysis were included in the multiple regression model to assess their potential relevance in predicting the outcome.[15]

Results

Demographic and Clinical Characteristics of the Study Population

The demographic and clinical characteristics of the study participants were summarized in Table 1. Among the total sample, 296 patients (45.5%) were male, and 355 (54.5%) were female. The majority of patients were aged above 60 years, with 59.9% in the controlled diabetes group and 56.1% in the uncontrolled diabetes group. The fasting glucose levels varied across the groups, with a median (IQR) of 5.6 (5.4–5.9) mmol/L in the normal group, 6.6 (6.1–7.2) mmol/L in the prediabetes group, 8.4 (7.3–9.4) mmol/L in the controlled diabetes group, and 9.3 (8.4–11.8) mmol/L in the

Table 1 Characteristics of Patients Included in the Study

Variables	Groups			
	Normal (27 Patients)	**Prediabetes (100 Patients)**	**Controlled Diabetes (237 Patients)**	**Uncontrolled Diabetes (287 Patients)**
Sex, N (%)				
Male	11 (40.7)	48 (48.0)	116 (48.9)	121 (42.2)
Female	16 (59.3)	52 (52.0)	121 (51.1)	166 (57.8)
Age (years), N (%)				
18-30	0 (0)	0 (0)	3 (1.3)	10 (3.5)
31-40	3 (11.1)	1 (1.0)	8 (3.4)	3 (1.0)
41-50	3 (11.1)	13 (13.0)	31 (13.1)	39 (13.6)
51-60	8 (29.6)	26 (26.0)	53 (22.4)	74 (25.8)
>60	13 (48.1)	60 (60.0)	142 (59.9)	161 (56.1)
Glucose fasting (mmol/L), median (IQR)	5.6 (5.4–5.9)	6.6 (6.1–7.2)	8.4 (7.3–9.4)	9.3 (8.4–11.8)
BMI, median (IQR)	32.9 (25.9–38.8)	29.0 (25.8–31.8)	30.4 (26.4–34.4)	30.3 (26.6–33.5)
Hight (cm), median (IQR)	159.0 (153.0–166.4)	161.0 (156.0–169.1)	162.0 (153.0–170.0)	160.0 (154.0–168.0)
Weight (kg), median (IQR)	86.0 (77.0–91.9)	77.0 (63.2–86.8)	79.0 (67.1–90.0)	78.0 (68.0–87.3)
Smoking Status, N (%)				
Smoker	0 (0.0)	1 (1.0)	3 (1.3)	0 (0.0)
Non-smoker	27 (100.0)	99 (99.0)	234 (98.7)	287 (100.0)
Marital Status, N (%)				
Married	21 (80.8)	79 (79.0)	178 (75.1)	224 (78.0)
Single	6 (19.2)	21 (21.0)	59 (24.9)	63 (22.0)
Comorbidity, N (%)				
Cardiovascular Comorbidities	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.7)
Neuropathy	1 (3.7)	4 (4.0)	5 (2.1)	5 (1.7)
Nephropathy	0 (0.0)	1 (1.0)	1 (0.4)	0 (0.0)
Musculoskeletal	0 (0.0)	0 (0.0)	0 (0)	1 (0.3)
No comorbidity	26 (96.3)	95 (95.0)	229 (96.6)	279 (97.2)
Insulin resistant, N (%)				
No	25 (92.6)	100 (100.0)	235 (99.2)	285 (99.3)
Yes	2 (7.4)	0 (0.0)	2 (0.8)	2 (0.7)
Taking metformin, N (%)				
No	26 (96.3)	93 (93.0)	223 (94.1)	275 (95.8)
Yes	1 (3.7)	7 (7.0)	14 (5.9)	12 (4.2)

Abbreviations: N, frequencies; %, percentages; IQR, interquartile range.

uncontrolled diabetes group. The use of metformin was particularly prevalent in the controlled and uncontrolled diabetes groups, where 94.1% and 95.8% of patients, respectively, reported not taking the medication.

Comparison of Hemostatic Parameters Across Study Groups

According to Figure 2, no statistically significant differences were found in APTT (p-value > 0.05), while PT and INR were considered marginally significant (p-value = 0.064 and p-value = 0.052, respectively). In contrast, the uncontrolled diabetes group showed a significantly higher platelet counts (289.0 × 10^3/μL, IQR: 237.0–353.5, p-value < 0.05) and the controlled diabetes group (291.5 × 10^3/μL, IQR: 227.0–352.7, p-value < 0.05) compared to the prediabetes group (236.0 × 10^3/μL, IQR: 203.5–272.0).

Correlation between demographic variables and coagulation parameters is presented in Supplementary Table 1. A multiple regression analysis was conducted to assess the relationship between platelet count and four predictor variables: sex, age, BMI, and comorbidity. Among the predictors, sex (p-value < 0.001) and age (p-value < 0.05) were statistically significant predictors of platelet count (Table 2).

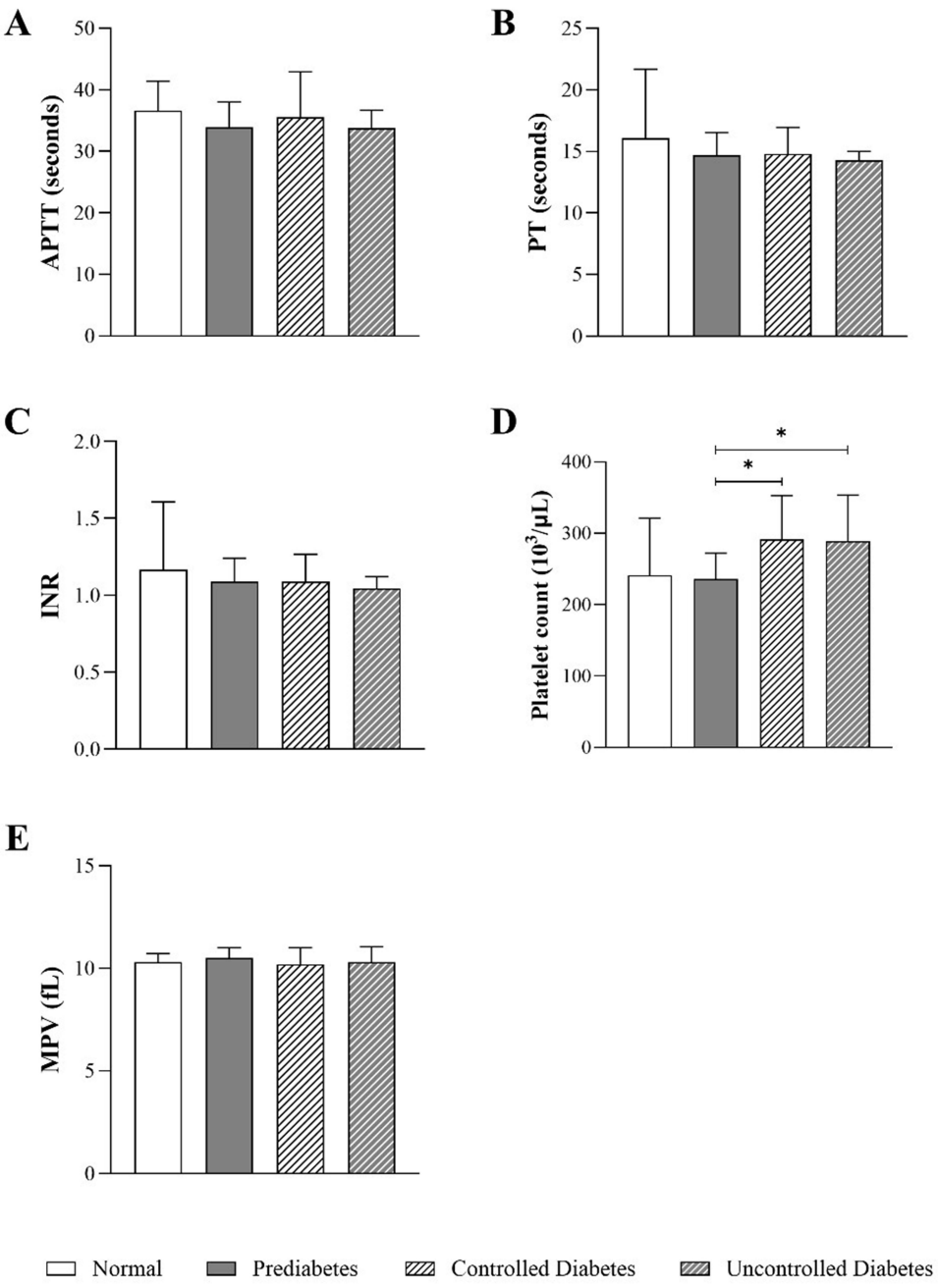

Figure 2 Comparison of hemostatic parameters among study groups categorized by HbA1c levels. (**A**) Activated Partial Thromboplastin Time (APTT), (**B**) Prothrombin Time (PT), (**C**) International Normalized Ratio (INR), (**D**) Platelet count, and (**E**) Mean Platelet Volume (MPV). *Denotes a significant difference (*p < 0.05).

Comparison of RBC Parameters Among Study Groups

Statistical analyses using one-way ANOVA revealed significant differences in RBC, hemoglobin, and hematocrit levels across the four study groups (p-value < 0.001, p-value < 0.05, and p-value < 0.01, respectively) (Figure 3). RBC count was significantly higher in both the controlled (4.60×10^{12}/L, IQR: 4–5) and uncontrolled diabetes groups (4.80×10^{12}/µL, IQR: 4.30–5.10) compared to the normal group (3.55×10^{12}/L, IQR: 2.95–4.60; p-value < 0.05). Similarly, hemoglobin levels were significantly higher in the uncontrolled diabetes group (131 g/L, IQR: 118–142) compared to the prediabetes group (116 g/L, IQR: 102.5–128, p-value < 0.05). Hematocrit levels were also significantly higher in the uncontrolled diabetes group (40.90%, IQR: 36.05–42.55) compared to the prediabetes group (34.80%, IQR: 29.85–40.35, p-value < 0.01). MCV was significantly lower in the uncontrolled diabetes group (85.00 fL, IQR: 81.00–88.30) compared

Table 2 Multiple Regression Analysis for Variables Predicting Platelet Count

Variable	Regression Coefficient (B)	p-value	R^2
Sex	53.35	<0.001	0.132
Age	24.06	0.010	
BMI	0.683	0.297	
Comorbidity	20.72	0.235	

to the prediabetes group (87.70 fL, IQR: 83.13–91.28, p-value < 0.001) and the normal group (89.80 fL, IQR: 86.20–91.62, p-value< 0.001). MCH levels were significantly lower in the uncontrolled diabetes group (27.60 pg, IQR: 26.00–29.30) compared to both the prediabetes group (28.75 pg, IQR: 27.63–29.90, p-value < 0.001) and the normal group (29.35 pg, IQR: 28.00–30.30, p-value < 0.01).

Correlation between demographic variables and RBC parameters is presented in Supplementary Table 2. A multiple regression analysis (Table 3) was conducted to examine the relationship between RBC count and five predictor variables: sex, age, comorbidity, insulin resistance, and metformin use. Among the predictors, sex (p-value < 0.01), age (p-value < 0.05), and comorbidity (p-value < 0.001) were statistically significant predictors of RBC count. For hemoglobin level, sex (p-value < 0.001), age (p-value < 0.01), and comorbidity (p-value < 0.01) were statistically significant predictors. Sex (p-value < 0.001), age (p-value < 0.05), and comorbidity (p-value < 0.01) were statistically significant predictors of hematocrit. For MCV, age (p-value < 0.01) was found to be a statistically significant predictor. Among the predictors for the MCH model, sex (p-value < 0.001) was found to be a statistically significant predictor of MCH level.

Comparison of WBC Count and Its Differential Components Among Study Groups

Figure 4 showed that WBC counts were significantly higher in the uncontrolled diabetes group (7.94 × 10^9/L, IQR: 6.442–9.7475) and the controlled diabetes group (8.02 × 10^9/L, IQR: 6.435–10.1425) compared with the normal group (5.85 × 10^9/L, IQR: 5.145–8.780; both p-value < 0.01). Furthermore, both the uncontrolled and controlled diabetes groups exhibited significantly higher WBC counts compared with the prediabetes group (6.96 × 10^9/L, IQR: 5.82–8.74; p-value < 0.05 and p-value < 0.01, respectively). Similarly, neutrophil counts were significantly higher in the controlled diabetes group (54.30 × 10^9/L, IQR: 46.50–64.80) compared to the normal group (41.70 × 10^9/L, IQR: 36.80–64.80, p-value < 0.05), as well as compared to the prediabetes group (53.70 × 10^9/L, IQR: 42.40–61.40, p-value < 0.05). Regarding basophil count, levels were significantly higher in the uncontrolled diabetes group (0.60 × 10^9/L, IQR: 0.50–0.825) compared to the controlled diabetes group (0.50 × 10^9/L, IQR: 0.40–0.80, p-value < 0.01). For monocyte count, levels were significantly higher in the controlled diabetes group (8.20 × 10^9/L, IQR: 6.30–10.00) compared to the normal group (7.90 × 10^9/L, IQR: 6.10–10.475, p-value < 0.05). Additionally, monocyte counts were significantly higher in the uncontrolled (8.00 × 10^9/L, IQR: 6.375–9.20) and controlled diabetes groups compared with the prediabetes group (7.40 × 10^9/L, IQR: 6.50–9.05; p-value < 0.01 and p-value < 0.001, respectively).

Correlation between demographic variables and WBC parameters is presented in Supplementary Table 3. Among the two predictors for neutrophil count, sex (p-value < 0.05) was found to be a statistically significant predictor of neutrophil count (Table 4). Specifically, females had a slightly higher mean (M = 4.60, SD = 2.53) than males (M = 4.44, SD = 2.47). For basophil and lymphocytes, there were no significant associations.

Discussion

T2DM is a complex metabolic disorder associated with hemostatic and hematological abnormalities that contribute to an increased risk of thrombotic and cardiovascular complications. Although many studies have examined the metabolic and vascular consequences of poor glycemic control, the specific relationship between HbA1c levels and coagulation or hematological biomarkers remains insufficiently explored, particularly within Middle Eastern populations. The current study sought to address these research gaps by analyzing hemostatic and hematological parameters across four HbA1c-

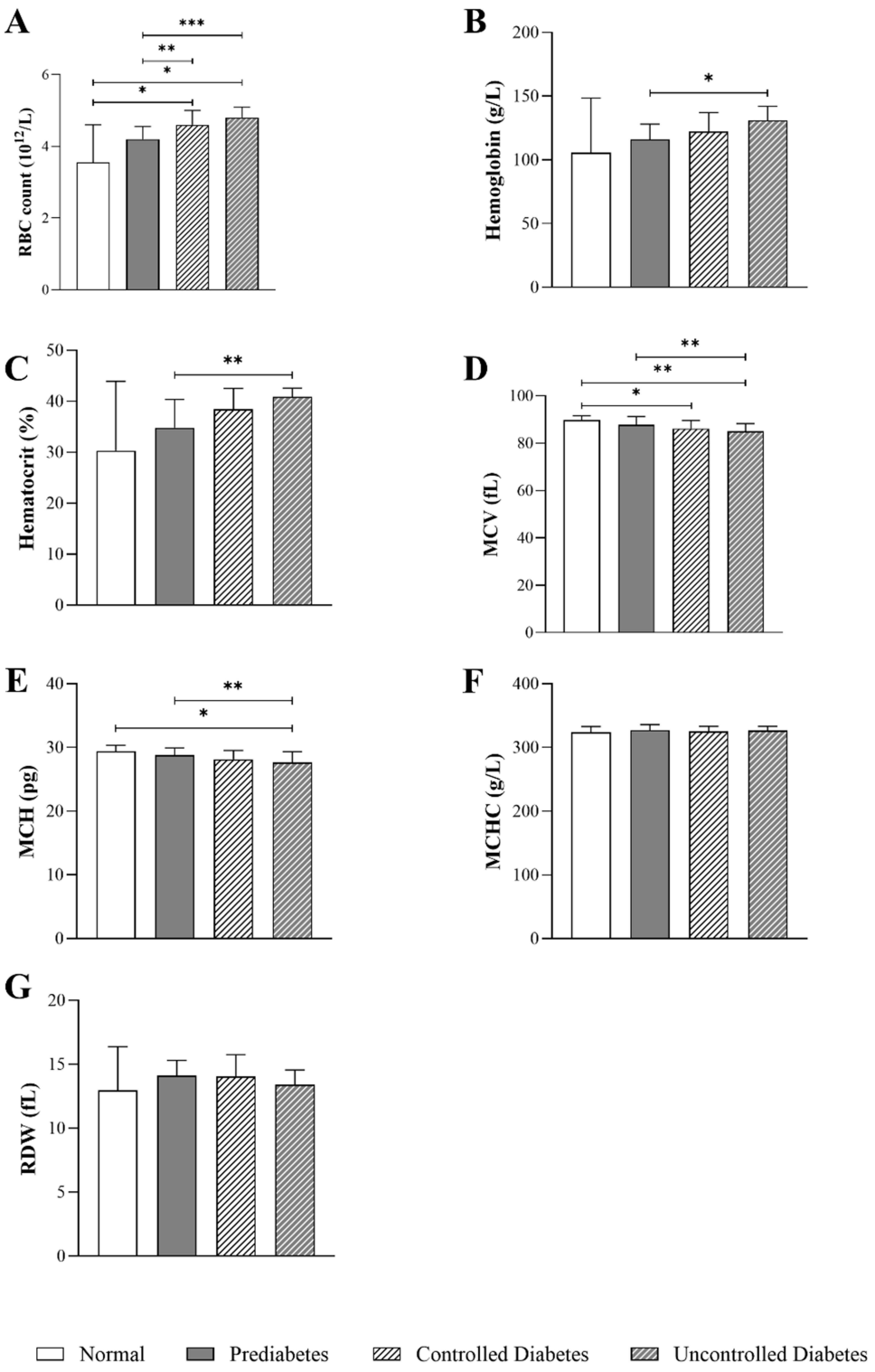

Figure 3 Comparison of RBC parameters among study. (**A**) Red blood cell (RBC) count, (**B**) Hemoglobin, (**C**) Hematocrit, (**D**) Mean Corpuscular Volume (MCV), (**E**) Mean Corpuscular Hemoglobin (MCH), (**F**) Mean Corpuscular Hemoglobin Concentration (MCHC), and (**G**) Red cell distribution width (RDW). * denotes a significant difference (*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$).

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Table 3 Multiple Regression Analysis for Variables Predicting RBC Parameters

	Variable	Regression Coefficient (B)	p-value	R^2
RBC	Sex	0.329	0.002	0.156
	Age	0.152	0.016	
	Comorbidity	0.525	<0.001	
	Insulin Resistant	0.137	0.746	
	Taking Metformin	0.220	0.197	
Hemoglobin	Sex	15.125	<0.001	0.203
	Age	4.661	0.008	
	Comorbidity	12.637	0.002	
	Insulin Resistant	6.189	0.600	
	Taking Metformin	4.054	0.395	
Hematocrit	Sex	3.633	<0.001	0.177
	Age	1.269	0.014	
	Comorbidity	3.764	0.002	
	Insulin Resistant	0.442	0.899	
	Taking Metformin	1.655	0.238	
MCV	Age	0.958	0.007	0.039
	BMI	0.078	0.059	
	Weight	0.002	0.936	
	Taking Metformin	2.175	0.057	
MCH	Sex	0.954	<0.001	0.069
	Age	0.223	0.159	
	BMI	0.020	0.276	
	Weight	0.011	0.243	
	Marital Status	0.308	0.349	
	Taking Metformin	0.561	0.236	

defined glycemic groups in Saudi patients with T2DM. In addition, this study examined the influence of demographic and clinical factors such as sex, age, BMI, and comorbidities on the evaluated parameters.

The significant differences in platelet counts observed between the prediabetes group and the controlled and uncontrolled diabetes groups suggest that platelet counts may be more sensitive to glycemic alterations than other coagulation parameters. A range of interrelated pathophysiological mechanisms may drive these differences. In individuals with uncontrolled diabetes, chronic hyperglycemia promotes oxidative stress, which enhances the externalization of phosphatidylserine on platelet membranes, thereby increasing thrombin generation and contributing to microthrombus formation.[16,17] Insulin resistance, a key feature of type 2 diabetes, further exacerbates this prothrombotic environment by impairing cyclic adenosine monophosphate (cAMP) signaling, which normally suppresses intraplatelet calcium release and platelet aggregation, thereby facilitating increased platelet activation and turnover.[16] Together, these mechanisms may explain the altered platelet dynamics observed even among patients with relatively controlled glycemia.

In contrast to the significant differences in platelet count, other hemostatic parameters, APTT, PT, INR, and MPV, did not show statistically significant variation across glycemic groups. Although PT and APTT are commonly used in clinical practice, their effectiveness in evaluating thrombotic risk in individuals with T2DM is limited. Despite the growing body of scientific research identifying hemostatic abnormalities in patients with T2DM, including elevated levels of fibrinogen, D-dimer, coagulation factors, and impaired fibrinolysis, these findings have not been translated into routine clinical practice. International clinical guidelines do not recommend routine ordering of hemostatic profiles or coagulation assays to manage thrombotic risk in diabetic patients.[18,19] These guidelines prioritize glycemic control, lipid management, blood

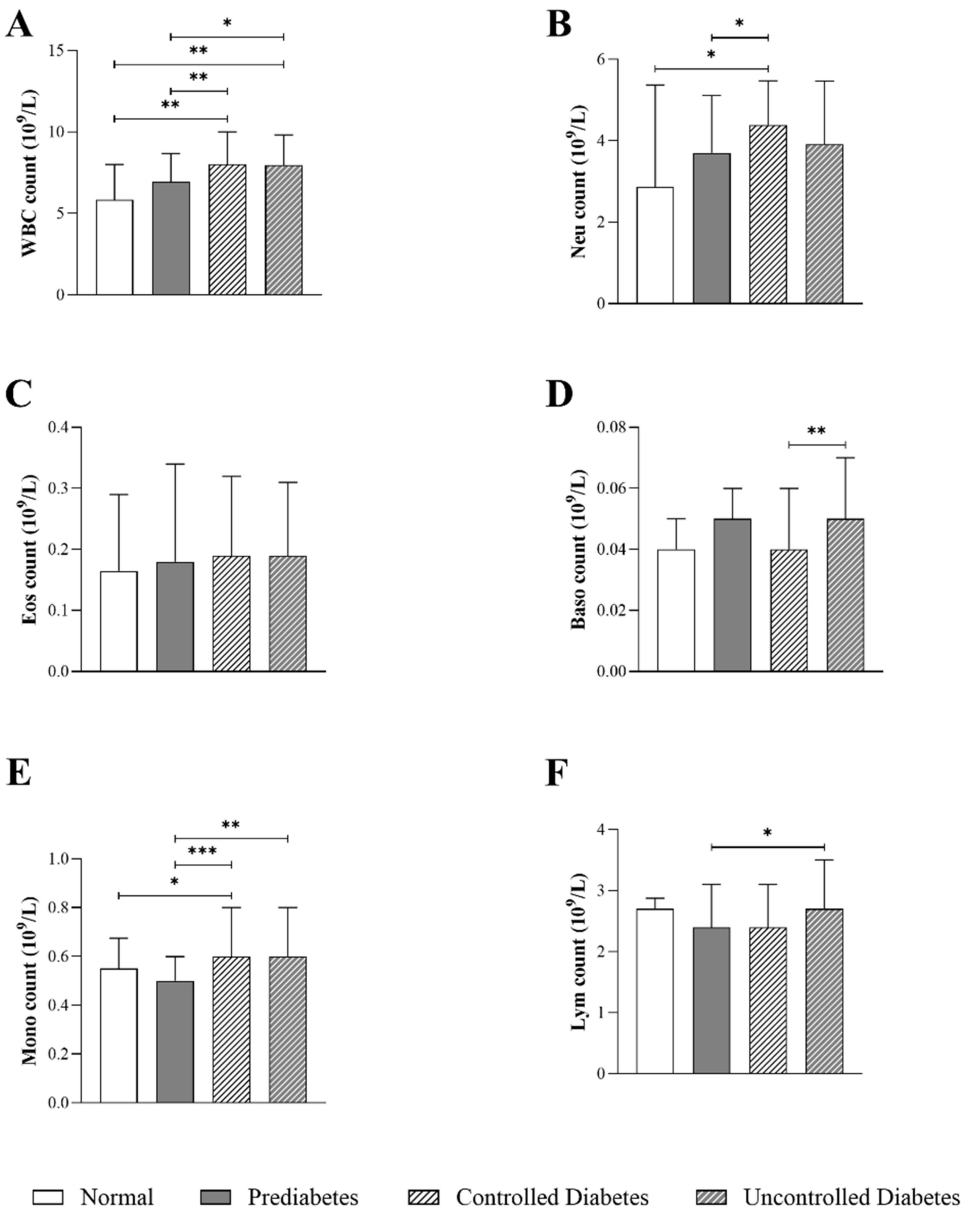

Figure 4 Comparison of white blood cell count and its differential components among study groups. (**A**) Total white blood cell (WBC) count, (**B**) Neutrophil (NEU) count, (**C**) Eosinophil (EOS) count, (**D**) Basophil (BASO) count, (**E**) Monocyte (MONO) count, and (**F**) Lymphocyte (LYM) count. * denotes a significant difference (*p < 0.05, **p < 0.01, ***p < 0.001).

pressure regulation, and cardiovascular risk reduction through evidence-based pharmacological interventions, while excluding hemostatic markers due to insufficient clinical trial evidence. Conversely, numerous studies have demonstrated that T2DM is a prothrombotic condition associated with elevated fibrinogen, D-dimer, PAI-1, and other coagulation factor abnormalities, suggesting a state of hypercoagulability and impaired fibrinolysis.[8,20]

In the current study, significant differences in RBC count, hemoglobin, and hematocrit levels were observed across glycemic groups, with the highest values found in the uncontrolled diabetes group. These results align with previous studies suggesting that hematological alterations are common in individuals with T2DM, where advancing age and comorbid conditions serve as key contributors to anemia and diminished erythrocyte indices.[21] Moreover, notable sex-related differences were observed, with female patients showing lower RBC parameters, likely influenced by hormonal changes, dietary habits, and healthcare access. This observation supports existing research suggesting that menstruation and menopause can affect hematological profiles.[22] Differences across populations may reflect variations in hormonal

Table 4 Multiple Regression Analysis for Variables Predicting WBC Parameters

	Variable	Regression Coefficient (B)	p-value	R^2
Neutrophil	Sex	0.616	0.015	0.016
	Age	0.082	0.512	
Basophil	Glucose Fasting	0.002	0.184	0.152
	BMI	0.001	0.429	
	Weight	0.000	0.401	
Lymphocyte	BMI	0.015	0.082	0.015
	Height	0.002	0.419	
	Marital Status	0.308	0.349	
	Taking Metformin	0.561	0.236	

and nutritional contexts, underscoring the importance of considering such factors when evaluating RBC measures in female T2DM patients.[23–25] In addition to these findings, the study identified a positive correlation between age and both MCV and MCH, and a negative correlation between these parameters and BMI. This pattern may indicate age-related macrocytic changes and the inhibitory effects of obesity on micronutrient absorption, particularly iron and vitamin B12.[26]

Moreover, the current study found statistically significant differences in WBC, neutrophil, basophil, monocyte, and lymphocyte counts across glycemic groups. This pattern reinforces the well-established concept that low-grade systemic inflammation is a hallmark of T2DM, particularly in patients with poor glycemic control. These results are further supported by Farooqui et al (2019), who observed that elevated WBC and neutrophil levels were closely associated with insulin resistance and chronic hyperglycemia.[13] Additionally, a recent study by Ari et al investigated the association of inflammatory markers and HbA1c levels, concluding that the using the neutrophil-lymphocyte ratio (NLR) and the systemic immune-inflammation index (SII) as affordable and easily accessible inflammatory markers is a promising approach for predicting diabetes in individuals with HbA1c levels above 6.5 or below 6.[27] Indeed, elevated immune cell counts have been proposed as early markers of vascular inflammation and predictors of complications such as atherosclerosis and nephropathy.[28]

In addition, the observed elevations in WBC, monocyte, and lymphocyte counts in the uncontrolled diabetes group compared to the prediabetes group align with previous findings documented increased inflammatory profiles in individuals with T2DM.[29] It is widely believed that chronic hyperglycemia drives immune cell activation and pro-inflammatory cytokine production, thereby contributing to disease progression. Interestingly, no significant differences in eosinophil counts were identified between groups in the present study. This finding differs from a Saudi Arabian analysis, which reported elevated eosinophil levels in patients with T2DM compared to healthy controls.[30] The discrepancy may be due to differences in sample characteristics, glycemic control status, or analytical methods. These variations suggest that the role of eosinophils in T2DM-related inflammation may vary across populations or disease stages and may not be consistently detectable in all clinical settings. Taken together, these hematological patterns, especially WBC alterations, highlight the inflammatory burden associated with hyperglycemia and support routine hematological profiling as a potential tool for early detection of metabolic complications in diabetic patients.

Despite the valuable insights provided by this study on the associations between glycemic control and hematological and hemostatic alterations among Saudi patients with T2DM, several limitations should be acknowledged, as they may influence the interpretation and generalizability of the findings. The retrospective design limited causal inference, as data were collected from existing medical records, making it difficult to establish temporal relationships between HbA1c levels and the observed hematological or hemostatic changes. Another limitation is the absence of a formal power analysis. While the total sample size was adequate for exploratory analyses, the smallest HbA1c subgroup (n = 27) may have restricted statistical power and limited the generalizability of findings within that category. Moreover, a key limitation of this study was the omission of important coagulation biomarkers such as D-dimer, fibrinogen, and

coagulation factors, which are not routinely included in the clinical evaluation of diabetic patients and therefore were absent from the medical records reviewed. These sensitive biomarkers and global coagulation assays provide a more comprehensive assessment of the hypercoagulable state associated with T2DM than conventional tests like PT and APTT. Furthermore, several potentially important variables, such as nutritional status, iron and vitamin B12 levels, inflammatory markers, medication adherence, and the use of specific medications (eg, antiplatelets, anticoagulants), were not available in the dataset. The absence of these factors may have introduced residual confounding, complicating the interpretation of abnormalities in RBC, WBC, and coagulation parameters.

Conclusions

In conclusion, this study highlighted important hematological alterations associated with glycemic control and provided preliminary evidence of hemostatic changes that warrant further investigation. The findings revealed significant alterations in hemostatic and hematological parameters across HbA1c-defined glycemic groups. Notably, platelet count and several red and white blood cell parameters demonstrated meaningful variation with worsening glycemic control, underscoring their potential as critical early warning indicators of vascular and inflammatory complications in T2DM. Among hemostatic markers, platelet count emerged as a particularly sensitive biomarker, even in individuals with apparently controlled blood glucose levels. These insights powerfully support the notion that a comprehensive assessment of the hematological profile can facilitate timely interventions, potentially preventing the onset of serious diabetic complications. These insights offer a foundation for future research and hold potential for improving early risk stratification and targeted interventions in diabetes care, particularly within the Saudi context. Future prospective studies incorporating dynamic Coagulation biomarkers and inflammatory indices could validate the predictive utility of hematologic parameters in diabetic vascular complications.

Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board (IRB) Sub-Committee for Health Sciences Colleges Research on Human Subjects at King Saud University – College of Medicine, Riyadh, Saudi Arabia (Approval No. E-24-8824; Approval Date: 22 May 2024).

Data Sharing Statement

Data are available upon request to the corresponding author.

Informed Consent Statement

Patient consent was waived by the Institutional Review Board due to the retrospective nature of the study and the use of anonymized clinical data.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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