ORIGINAL RESEARCH

Comparative Analysis of Red Blood Cells, White Blood Cells, Platelet Count, and Indices in Type 2 Diabetes Mellitus Patients and Normal Controls: Association and Clinical Implications

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Background: Diabetes mellitus (DM) is a major health burden affecting 537 million adults worldwide, characterized by chronic metabolic disorder and various complications. This case control study aimed to assess the impact of type 2 diabetes mellitus (T2DM), including hyperglycemia levels, on hematological parameters and complete blood count (CBC) derived parameters.

Methods: A total of 250 known diabetic patients from the Jazan Diabetic Center, Saudi Arabia, between January 2021 and December 2022, along with 175 healthy adult controls were recruited from Jazan Hospital's blood donation center. Demographic characteristics, medical histories, and relevant factors such as gender, age, BMI, treatment, disease duration, and comorbidities were collected with informed consent.

Results: The results of the red blood cell (RBC) count, RBC indices, and mean platelet volume showed significant differences between patients and controls, while the white cell (WBC) and platelet count were comparable between the two groups. CBC-derived parameters, especially neutrophil/lymphocyte ratio (NLR), and platelet/neutrophil ratio (PNR) exhibited significant differences.

Conclusion: CBC and derived parameters serve as inexpensive tools for T2DM patients monitoring, indicating early blood cell alterations and potential development of anemia. Further studies are needed to explore their role in predicting T2DM pathogenesis and progression, aiming to reduce severe complications, mortality and morbidity.

Keywords: diabetes mellitus, complete blood count, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, platelet/neutrophil ratio, mean platelet volume/platelet count, disease complication

Introduction

Diabetes mellitus (DM) is one of the most prevalent disease, affecting 537 million adults worldwide. It is a significant health and financial burden on all countries, costing more than 966 billion US dollars in health expenses. In 2021, it caused 6.7 million deaths globally.[1] The most common type of diabetes in adults is type 2 DM (T2DM). It is a chronic metabolic disorder characterized by insufficient insulin production or insulin resistance, both of which lead to chronic elevations in blood glucose levels (hyperglycemia). Chronic hyperglycemia induces many physiological and pathological processes, including oxidative stress, which affects the glycation of lipids and proteins in the cells, lipid metabolism, inflammatory response, cell replication, cell growth, and immunological and hematological parameters, which are clearly observed in poorly controlled diabetic patients.[2] The increased oxidative stress induces hematological alteration, which affects the function, structure, and metabolism of red blood cells (RBCs), white blood cells (WBCs), and platelets.[3]

Additionally, chronic hyperglycemia causes vascular damage, leading to micro- and macrovascular consequences, such as diabetic microangiopathy, retinopathy, neuropathy, nephropathy, and cardiovascular diseases. Alteration of hematological parameters and indices can be utilized as a reliable indicator of blood changes caused by hyperglycemia as well as a predictor of DM complications.[3] The clinical consequences caused by diabetes are responsible for significant morbidity and mortality. However, controlling hyperglycemia is the most preventative method to delay/stop the development of T2DM complications. T2DM should be monitored with glycated hemoglobin (HbA1C) to achieve the optimal goal. Controlled T2DM is observed by achieving an HbA1C of 6.5–7% (hence, T2DM should be carefully monitored to achieve the ideal HbA1C range of 6.5–7%). Increased HbA1C levels in DM patients are associated with worse outcomes.[4]

Complete blood count (CBC) is a simple, routinely requested test in all healthcare facilities. CBC report includes RBC count, RBC indices, WBC count, WBC differential count, platelet count and platelet indices. The effect of DM on hematological parameters has been investigated with controversial findings.[5–9] The current study aimed to assess the effect of DM, including hyperglycemia levels, on the hematological parameters, ie, CBC and CBC-derived parameters (including neutrophil/lymphocyte ratio (NLR), platelets/lymphocyte ratio (PLR), platelet/neutrophil ratio (PNR), and mean platelet volume (MPV)/platelet count (MPR)). In addition, the association of HbA1C and demographic characteristics, CBC parameters, and CBC-derived parameters were also investigated in this study.

Materials and Methods
Study Design
The current study was a case-control study of 250 known adult diabetic patients visiting the Jazan Diabetic Center for follow-up, and 175 known adult healthy controls were recruited. This study was conducted between January 2021 and December 2022. The control group were healthy blood donors recruited from the blood donation center at Jazan Hospital, Saudi Arabia. The demographic characteristics and medical histories of the patients and controls, including gender, age, height, weight, calculated body mass index (BMI), treatment, duration of the disease, and comorbidities, were collected.

Blood specimen collection and laboratory analysis.

A venous blood sample of three mL was collected by a well trained and experienced nurse from diabetic patients and healthy controls using vacutainer tubes containing ethylenediaminetetraacetic acid (EDTA) for CBC analysis and HbA1C measurement.

Operational Definitions
Complete Blood Count
The CBC was performed using Sysmex XN–1000 Hematology Analyzer (Kobe, Japan).

Glycated Hemoglobin (HbA1C) Measurement
Glycated hemoglobin was measured using DxC 7000 AU Chemistry analyzer (Beckman Coulter, USA).

Complete Blood Count–Derived Parameters
The parameters derived from CBC were the neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), platelet/neutrophil ratio (PNR), and mean platelet volume/platelet count (MPR). These parameters were calculated as described previously.[10–12]

Classification of HbA1C Based on the Level with CBC Parameters
The study parameters were sub-analyzed based on the levels of HbA1C >9.0%, HbA1C 7.0–9.0%, and HbA1C <7.0%.[13]

Ethical Consideration
The current study was approved by the Jazan Health Ethics Committee (Reference No: 2038) and conducted in accordance with the Declaration of Helsinki.

Statistical Analysis

GraphPad Prism version 8.0 (GraphPad Software Inc., San Diego, CA, USA) was applied for statistical analysis. The data in the current study are presented as mean ± standard deviation (SD) unless otherwise stated. The unpaired *t*-test was used for the analysis of normally distributed data and Mann-Whitney was used for the analysis of non-normally distributed data. A one-way ANOVA was used to evaluate the association pattern between the studied parameters. Pearson correlation test and Multivariate analyses were performed for the association of baseline variables and comorbidities. Statistical significance was considered when P < 0.05.

Results

Demographic and Clinical Characteristics

Two hundred fifty adult T2DM patients (patient group) and 175 healthy controls (control group) were evaluated (Table 1). The mean age of the patients was 53±12 years, and for controls, it was 32.4±7.2 years; the differences were statistically significant (P<0.0001). The mean duration of diabetes incidence in the patient group was 12±7.4 years. The BMI in the patients was higher compared to the controls (29.7±11.7 vs 27.6±6.8; P=0.0504). HbA1C was significantly higher in the patients compared to controls (9.2%±2.2 vs 5.3%±0.7; P<0.0001).

Comorbidities Among the Patient Group

The comorbidities among T2DM were present in 132 patients (52.8%) with chronic disease, whereas 118 patients (47.2%) had no history of chronic diseases (Table 2). Hypertension (HTN) was the most common comorbidity observed in 121 of the patients (48.2%), followed by chronic kidney disease (CKD) and HTN (1.6%), cardiovascular disease (CVD) and HTN (1.2%), followed by CVD, CKD, hypothyroidism, Hepatitis B, and HTN with 0.4% for each condition.

Comparison of Hematological Parameters

Red Blood Cell Count and Red Blood Cell Indices

The results of the RBC count and RBC indices showed significant differences between patients and controls (P<0.01; Table 3). Red blood cells (RBCs), hemoglobin (Hb), hematocrit (HCT), mean cell volume (MCV), mean cell hemoglobin (MCH), and red blood cell distribution width (RDW) were significantly lower in the diabetic patients compared to controls, whereas mean cell hemoglobin concentration (MCHC) was higher in T2DM patients compared to controls.

White Blood Cells

The total count of WBCs and absolute lymphocyte count were comparable in the patient and control groups (P>0.05; Table 3). The absolute neutrophil count was significantly higher in patients compared to controls (3.7±1.5 vs 2.9±1.3; P<0.0001), whereas the absolute monocyte count was significantly lower in patients compared to controls (0.2±0.1 vs 0.6±0.2; P<0.0001).

Table 1 Demographic Characteristics of the Study Participants (Patients with Type 2 Diabetes Mellitus n=250 and Healthy Controls n=175)

Parameters	T2DM (n=250)	Control (n=175)	*P* value
	Mean±SD	Mean±SD	
Age (years)	53±12	32.4±7.2	<0.0001
Duration (years)	12±7.4	NA	NA
BMI (kg/m^2)	29.7±11.7	27.6±6.8	0.0504
HbA1C (%)	9.2±2.2	5.3±0.7	<0.0001

Abbreviations: NA, not applicable; T2DM, type 2 diabetes mellitus; BMI, body mass index; HbA1C, glycosylated hemoglobin A.

Table 2 Prevalence and Patterns of Comorbid Clinical Conditions in the Patient Group with Type 2 Diabetes Mellitus (n=250)

Comorbidity	Number	Percentage (%)
No chronic disease	118	47.2
Hypertension	121	48.4
CKD+Hypertension	4	1.6
CVD+Hypertension	3	1.2
CVD	1	0.4
Hypothyroidism	1	0.4
CKD	1	0.4
Hepatitis B + Hypertension	1	0.4
Total	250	100

Abbreviations: CKD, chronic kidney disease; CVD, cardiovascular disease.

Table 3 Complete Blood Count and Complete Blood Count-Calculated Parameters in Patient and Control Groups

Parameters	T2DM (n=250)	Control (n=175)	P value
	Mean±SD	Mean±SD	
WBC (10^9/L)	6.8±2	6.6±1.8	0.3157
ANC (10^9/L)	3.7±1.5	2.9±1.3	<0.0001
ALC (10^9/L)	2.8±0.9	2.8±0.8	1.00
AMC (10^9/L)	0.2±0.1	0.6±0.2	<0.0001
RBC (×10^{12}/L)	5.1±0.7	5.5±0.5	<0.0001
Hgb (g/dl)	13.1±2.0	14.8±1.2	<0.0001
HCT (%)	36.5 ±7.0	45.3±3.1	<0.0001
MCV (fl)	73±10	83±6.3	<0.0001
MCH (pg)	26±3.5	27±2.9	0.0025
MCHC (g/dl)	36.3±5.2	32.7±1.7	<0.0001
RDW (%)	10.7±2.2	13.5±1.5	<0.0001
Platelet (10^9/L)	290±72	286±67	0.5821
MPV (fl)	7.8±1	10.7±0.9	<0.0001
PCT (%)	0.4±0.3	0.3±0.1	0.6557
PDW (fl)	13.6±3.2	12.8±2.2	0.0050
P-LCR (%)	33.9±7.9	30.6±7.3	<0.0001
MPR	3.8±0.8	3.9±1.1	0.9417

(Continued)

Table 3 (Continued).

Parameters	T2DM (n=250)	Control (n=175)	P value
	Mean±SD	Mean±SD	
NLR	1.4±0.7	1.2±0.6	<0.0001
PNR	89±38.9	115±52	<0.0001
PLR	114±44	111±33	0.4728

Abbreviations: WBC, white blood cells; RBC, red blood cells; Hgb, hemoglobin; HCT, hematocrit; MCV, mean cell volume; MCH, mean cell hemoglobin; MCHC, mean cell hemoglobin concentration; RDW, red blood cell distribution width; MPV, mean platelet volume; ANC, absolute neutrophil count; ALC, absolute lymphocyte count, AMC, absolute monocyte count; MPV, mean platelet volume; PDW, platelet distribution width; P-LCR, platelet large cell ratio, PCT, plateletcrit; NLR, neutrophil/lymphocyte ratio, PLR, platelet/lymphocyte ratio, PNR, platelet/neutrophil ratio, MPR, mean platelet volume/platelet count.

Platelet Count and Indices

Platelet count and plateletcrit (PCT) were comparable in patients and controls (P>0.05; Table 3). Mean platelet volume (MPV) and platelet distribution width (PDW) were significantly lower in patients compared to controls (P<0.01), whereas P-LCR was significantly higher in patients compared to controls (P<0.0001).

Complete Blood Count-Calculated Parameters

NLR and PNR showed statistically significant differences in the patient group compared to the control group (Table 3). The NLR was slightly higher in the patient compared to controls (1.4±0.7 vs 1.2±0.6; P<0.0001). MPR and PLR were comparable among the study groups (P>0.05; Table 3).

Comparison of Hematological Parameters Among Diabetic Patients Based on the HbA1C Levels

Clinical characteristics, hematological data, and CBC-derived parameters were further categorized based on the HbA1C levels into three groups: group 1 HbA1C; < 7.0%, group 2 HbA1C; 7.0–9.0%, and group 3 HbA1C; >9.0% (Table 4). The age difference between the groups was statistically significant. The duration of the disease and HbA1C levels increased significantly from group 1 to group 3 (P<0.04). BMI was higher in group 2 compared to group 1 but lower in group 3 compared to group 2 (P>0.05). Total WBC count was slightly reduced with increasing HbA1C concentration (P>0.05) and a comparable count of neutrophils and monocytes. The RBC count, Hb, RDW, HCT, and RBC indices were compared in all three groups (P>0.05). Platelet count showed a slight increase in group 3 (HbA1C>9.0), whereas MPV, PCT, PDW, and P-LCR were comparable in the three groups. MPR and NLR were comparable in the three groups, whereas PLR and PNR were increased in group 3 (P>0.050).

Correlation of Hematological Parameters with HbA1C Levels and Duration of Diabetes

No positive or negative correlation were found between HbA1C vs all parameters including BMI, WBC, Hct, Hgb, platelet count, all platelet indices, NLR, MPR, PNR, PLR (Table 5). However, a strong significant positive correlation was found between HbA1C and duration of the disease (r=0.1774, R= squared 0.03147; P<0.01) and a strong significant negative correlation was found between RBC count and duration of the disease (r=−0.1473, R= squared 0.02170; P<0.05) (Table 5).

Discussion

The current study found a significant effect of T2DM on CBC parameters, including RBC count, Hb and RBC indices, neutrophils, monocytes, MCHC, and MPV compared to healthy controls. Statistically significant lower values of RBCs, Hb, HCT, MCV, and MCH were observed in T2DM patients compared to healthy controls. Low counts of RBC among diabetic patients have been attributed to the effects of chronic hyperglycemia. Hyperglycemia increases reactive oxygen

Table 4 Categorization of Diabetics Based on the HbA1C Levels (n = 250)

Parameters	HbA1C			P value
	Group 1 <7.0% n=28	Group 2 7.0–9.0% n=92	Group 3 >9.0% n=101	
Age (years)	51.5±12.6	53.9±11.3	53±12.5	0.4297
HbA1C (%)	6.5±0.4	8.0±0.6	11.0±1.8	<0.0001
Duration of the disease (years)	9.8±6.1	10.8±6.5	13.6±8.2	0.0131
BMI (kg/m^2)	27.3±3.9	31.6±16.6	28.6±6.4	0.1095
WBC(10^9/L)	7.0±2.1	6.9±2.0	6.6±1.9	0.6657
ANC (10^9/L)	3.9±1.8	3.7±1.4	3.7±1.6	0.1025
ALC (10^9^3/L)	2.9±0.6	2.9±1.0	2.7±0.8	0.1301
AMC (10^9/L)	0.2±0.2	0.2±0.1	0.2±0.2	0.9178
RBC (10^{12}/L)	5.0±0.6	5.1±0.8	5.1±0.7	0.0515
Hgb (g/dL)	13.3±1.6	13.1±2.3	12.9±1.9	0.6977
HCT(%)	37.7±6.4	36.8±7.5	35.9±6.6	0.4098
MCV(fL)	75.3±9.2	74.1±9.7	71.8±10.2	0.1042
MCH (pg)	26.6±2.6	26.3±3.5	25.8±3.6	0.5017
MCHC(g/dL)	35.6±4.5	36.3±5.7	36.6±5.0	0.7159
RDW-SD(fL)	22.6±3.0	22.5±3.5	21.9±3.4	0.3593
RDW-CV(%)	10.2±2.0	10.7±2.2	10.9±2.1	0.3042
Platelet (10^9/L)	279±60	285±76	298±70	0.3017
MPV (fl)	13.7±2.3	13.4±3.2	13.8±3.4	0.1804
PCT (%)	0.2±0.0	0.2±0.1	0.2±0.1	0.1031
PDW (fl)	7.9±0.8	7.8±0.9	13.8±3.4	0.5895
P-LCR (%)	33.9±8.4	33.3±7.8	34.2±8.1	0.6774
MPR	2.8±0.9	2.9±0.8	2.9±0.8	0.8172
PNR	84±37	85±37	94±42	0.1002
PLR	100±39	110±47	120±43	0.0974
NLR	1.3±0.6	1.4±0.7	1.5±0.7	0.2170

Abbreviations: WBC, white blood cells; RBC, red blood cells; Hgb, hemoglobin; HCT, hematocrit; MCV, mean cell volume; MCH, mean cell hemoglobin; MCHC, mean cell hemoglobin concentration; RDW, red blood cell distribution width; MPV, mean platelet volume; ANC, absolute neutrophil count; ALC, absolute lymphocyte count, AMC, absolute monocyte count; MPV, mean platelet volume; PDW, platelet distribution width; P-LCR, platelet large cell ratio, PCT, plateletcrit; NLR, neutrophil/lymphocyte ratio, PLR, platelet/lymphocyte ratio, PNR, platelet/neutrophil ratio, MPR, mean platelet volume/platelet count.

species production,[5,14] which ultimately affects RBC deformability and lifespan.[6] The changes in RBC in DM affect microcirculation and therefore contribute to microangiopathy 6. In contrast, other studies have reported higher RBC, Hb, and HCT counts in DM, which may be due to insulin resistance.[7,8]

RBC count is considered an independent risk for microvascular complications. This independent risk increases when the RBC count decreases.[15] Despite the RBC count, which is within the normal range, Hb, HCT, MCV, and MCH were

Table 5 Correlation Between Duration of the Disease and the Levels of (i) HbA1C, (ii) Complete Blood Count Parameters and (iii) CBC-Derived Parameters in the Patient Group

Parameter	r	R Squared	P
Duration (years) and BMI (kg/m^2)	0.05919	0.003505	0.3992
Duration (years) and HbA1C (%)	0.1774	0.03147	0.0095
Duration (years) and WBC (10^9/L)	0.05868	0.003443	0.3976
Duration (years) and ANC (10^9/L)	0.05811	0.003377	0.4022
Duration (years) and ALC (10^9/L)	0.01026	0.0001052	0. 8825
Duration (years) and AMC (10^9/L)	0.07743	0.005995	0.2640
Duration (years) and RBC (10^{12}/L)	−0.1473	0.02170	0.0329
Duration (years) and Hgb (g/dl)	−0.09981	0.009962	0.1495
Duration (years) and HCT (%)	−0.1320	0.01741	0.0562
Duration (years) and MCV (fl)	−0.02008	0.0004032	0.7767
Duration (years) and MCH (pg)	0.07112	0.005058	0.3050
Duration (years) and MCHC (%)	0.07728	0.005973	0.2649
Duration (years) and RDW (%)	0.06044	0.003654	0.3835
Duration (years) and Platelet (10^9/L)	−0.02157	0.0004653	0.7560
Duration (years) and PCT (%)	0.1039	0.01079	0.1335
Duration (years) and PDW (fl)	0.01503	0.0002259	0.8286
Duration (years) and MPV (fl)	−0.04210	0.001773	0.5440
Duration (years) and P-LCR (%)	−0.03616	0.001308	0.6023
Duration (years) and NLR	0.03662	0.001341	0.5977
Duration (years) and PLR	−0.03798	0.001442	0.5842
Duration (years) and PNR	−0.1252	0.01567	0.0703
Duration (years) and MPR	−0.0260	0.0006766	0.7078

Abbreviations: WBC, white blood cells; RBC, red blood cells; Hgb, hemoglobin; HCT, hematocrit; MCV, mean cell volume; MCH, mean cell hemoglobin; MCHC, mean cell hemoglobin concentration; RDW, red blood cell distribution width; ANC, absolute neutrophil count; ALC, absolute lymphocyte count; AMC, absolute monocyte count; MPV, mean platelet volume; PDW, platelet distribution width; P-LCR, platelet large cell ratio, PCT, plateletcrit; NLR, neutrophil/lymphocyte ratio, PLR, platelet/lymphocyte ratio, PNR, platelet/neutrophil ratio, MPR, mean platelet volume/platelet count.

low in diabetic patients, indicating the presence of microcytic hypochromic anemia. These findings are in agreement with previous reports[5,9] and in contrast to others.[7,8] Ezenwaka et al have reported a high prevalence of anemia among T2DM Caribbean diabetic patients as compared to non-diabetic controls.[5] In addition, the count of RBCs, Hb levels, and other parameters were divided according to the level of HbA1C. The levels of Hb, HCT, MCV, and MCHC were further reduced from group 1 to group 3 (Table 4). In group 1 compared to group 3, the mean values of Hb were 13.3±1.6 compared to 12.9±1.9, HCT was 37.7±6.4 compared to 35.9±6.6, MCV was 75.3±9.2 compared to 71.8±10.2, and MCH was 75.3±9.2 compared to 25.8±3.6; however, the differences were statistically non-significant (P>0.05). Furthermore, the current study reports no correlation between HbA1C and RBC count, Hb, HCT, MCV, MCH, and MCHC (P>0.05).

Similar to RBC count, low Hb is also an independent risk for microvascular complications, which can be used to predict renal outcomes.[15–17] The cause of the anemia in the current study should be investigated and treated to improve the quality of life in anemic diabetic patients.[17] However, it is known that acquired and inherited anemia are highly prevalent in Saudi Arabia, particularly in the Jazan region.[18,19] Anemia among diabetic patients has been reported to be associated with cardiovascular complications.[20] On the other hand, the MCHC was significantly higher in our patient group despite the low values of the RBC, Hb, HCT, MCV, and MCH. Significantly high values of MCHC have been reported in diabetic patients compared to healthy controls.[7,9] As Jazan is an endemic region for both acquired, mainly nutritional, and inherited anemias, and this could be the possible explanation for similarities with some studies and discrepancies with others. In addition, socio-demographic characteristics and the study population differ from study to study.

Indeed, the disease has been shown to affect the deformability of the RBCs, which participate in the development of inflammation and microvascular complications. Furthermore, red blood cell distribution width (RDW) has been proposed to reflect the deterioration in glucose regulation in T2DM. The current RDW was significantly lower than that of healthy controls. The mean value of RDW in the patient group was 10.5%, which is below the normal values of RDW-CV (normal values: 11.5% to 14.5%). This finding contrasts with other studies reported in DM patients. The RDW is an indicative marker of the homogeneity/heterogeneity of the RBC size, which is normally obtained as an auxiliary index in the CBC. It is widely used for the differential diagnosis of subtypes of microcytic anemia. High values of RDW in microcytic anemia are mainly associated with iron deficiency anemia, unlike thalassemia. RDW is associated with increased risk factors for CVD and overall cardiovascular mortality.[21]

The current study reported no effect of T2DM on WBC count, similar to other studies,[7,22] as the counts of WBCs were in the normal ranges. The WBC count reflects the inflammatory response of the body.[23] The chronic inflammatory process contributes to the pathogenesis of T2DM. It was found that the inflammatory pathways were upregulated in T2DM.[23,24] The chronic inflammatory response is a key player in the development of DM complications.[25] The association between WBCs and inflammation is well documented.[25]

CBC-derived parameters, including NLR, PNR, PLR, and MPR, were also investigated in the study. These parameters are considered novel markers to predict the inflammatory process.[26] The NLR was slightly higher but within the normal range in diabetic patients compared to healthy controls (P<0.0001). The mean value of NLR in the current study was 1.4 ±0.7, which is similar to reported NLR values from diabetic patients[27] and less than NLR reported from viral infections, including COVID-19.[28] However, the increase in NLR among large-scale diabetic patients from[1,13] NLR in quartile 1 (Q1) to 3.08 NLR in quartile 2 (Q4) has been suggested to be associated with diabetic complications, including CVD and diabetic kidney disease.[27] Furthermore, the mean value of NLR in the current study was slightly increased with increasing HbA1C levels: 1.5 (HbA1C >9.0%), >1.4 (HbA1C 7.0–9.0%), and >1.3 (HbA1C <7.0%) (Table 4).[22] Hence, it is very important to mention that an NLR in the 2.3–3.0 range can suggest an early sign of worsening the inflammatory state.[26] Moreover, the NLR has been reported to increase in poorly controlled diabetic patients.[29]

In addition to their key role in hemostasis and thrombosis, platelets participate in inflammation, immunity, angiogenesis, and cancer.[30] The role of platelets in deriving the prothrombotic state in DM, including T2DM, has been suggested.[31]

In the current study, platelet count was comparable in diabetic patients and healthy controls (290±72 vs 286±67; P>0.05),[32,33] and both counts were within the reported normal ranges.[34] Platelet count has been suggested to be associated with diabetic complications, including nephropathy.[35] The platelet count with diabetic nephropathy was around 281±65, as reported by Sterner et al.[35] However, it is worth mentioning that platelet counts have shown variable results, being either higher or lower[36] in patients with diabetes as compared to controls.

Platelet indices, including mean platelet volume (MPV; reflects the rate of platelet production, average size, and activity), platelets distribution width (PDW; measures platelets' heterogeneity), and platelet-large cell ratio (P-LCR; measures larger platelets), were investigated in the current study. MPV was significantly lower in our patient cohort compared to healthy controls. The MPV was reported to be higher in diabetic patients with and without complications compared to healthy controls.[32,33] Increased MPV is associated with a variety of complications, including myocardial infarction[37] and an increased risk of microvascular complications in DM.[38] In addition, the current study reports no correlation between MPV and HbA1C or the duration of the disease.[36] PDW and P-LCR were significantly higher in diabetic patients as compared to controls (P<0.01) in the current study and elsewhere.[32,33] The data on these two parameters are limited in diabetes and need further exploration.[32] The PDW and P-LCR have been found to be raised in patients with acute coronary artery disease compared to controls and stable coronary artery disease patients.[37] The study exhibits notable strengths, including a robust sample size with comprehensive assessment of comorbidities and a valuable comparison with HbA1C levels. However, one of the limitations lies in the omission of evaluating additional inflammatory markers and their correlation with CBC and CBC-derived parameters and potential association with T2DM.

Conclusion

Complete blood count is a routine, simple test with significant results. The CBC can show the contribution of RBCs, WBCs, and platelets to the progression of T2DM and the inflammatory activity using the calculated parameters, including NLR, PLR, MPR, and PNR. Therefore, CBC and CBC-calculated parameters are inexpensive tools for follow up of patients with T2DM. These parameters could be providing an early sign of alteration in the blood cell including the development of anemia. Further studies are needed to explore these parameters to predict the pathogenesis and progression of T2DM, and therefore, intervention is made to reduce severe complications, mortality and morbidity in those patients.

Ethical Approval

All procedures performed in the current studies involving human participants were in accordance with the ethical standards of the Jazan Health Ethics Committee, Ministry of Health, Saudi Arabia and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent

Informed consent was obtained from all study participants.

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

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References

1. IDF. *Diabetes Atlas*. 10th ed. Brussels, Belgium: IDF Diabetes Atlas; 2021.
2. Sobczak AIS, Stewart AJ. Coagulatory defects in type-1 and type-2 diabetes. *Int J Mol Sci*. 2019;20(24):6345. doi:10.3390/ijms20246345
3. Twig G, Afek A, Shamiss A, et al. White blood cells count and incidence of type 2 diabetes in young men. *Diabetes Care*. 2013;36(2):276–282. doi:10.2337/dc11-2298
4. Demirtunc R, Duman D, Basar M, Bilgi M, Teomete M, Garip T. The relationship between glycemic control and platelet activity in type 2 diabetes mellitus. *J Diabetes Complications*. 2009;23(2):89–94. doi:10.1016/j.jdiacomp.2008.01.006
5. Ezenwaka CE, Jones-Lecointe A, Nwagbara E, Seales D, Okali F. Anaemia and kidney dysfunction in Caribbean type 2 diabetic patients. *Cardiovasc Diabetol*. 2008;7(1):25. doi:10.1186/1475-2840-7-25
6. Cho YI, Mooney MP, Cho DJ. Hemorheological disorders in diabetes mellitus. *J Diabetes Sci Technol*. 2008;2(6):1130–1138. doi:10.1177/193229680800200622
7. Ziaee A, Ghorbani A, Kalbasi S, Hejrati A, Moradi S. Association of hematological indices with prediabetes: a cross-sectional study. *Electron Physician*. 2017;9(9):5206–5211. doi:10.19082/5206
8. Biadgo B, Melku M, Abebe SM, Abebe M. Hematological indices and their correlation with fasting blood glucose level and anthropometric measurements in type 2 diabetes mellitus patients in Gondar, Northwest Ethiopia. *Diabetes Metab Syndr Obes*. 2016;9:91–99. doi:10.2147/DMSO.S97563
9. Ebrahim H, Fiseha T, Ebrahim Y, Bisetegn H, Akash MSH. Comparison of hematological parameters between type 2 diabetes mellitus patients and healthy controls at Dessie comprehensive specialized hospital, Northeast Ethiopia: comparative cross-sectional study. *PLoS One*. 2022;17(7):e0272145. doi:10.1371/journal.pone.0272145
10. Hamali HA, Saboor M, Dobie G, et al. Procoagulant microvesicles in COVID-19 patients: possible modulators of inflammation and prothrombotic tendency. *Infect Drug Resist*. 2022;15:2359–2368. doi:10.2147/IDR.S355395
11. Zhong Q, Peng J. Mean platelet volume/platelet count ratio predicts severe pneumonia of COVID-19. *J Clin Lab Anal*. 2021;35(1):e23607. doi:10.1002/jcla.23607

12. Sayed AA, Allam AA, Sayed AI, Alraey MA, Joseph MV. The use of neutrophil-to-lymphocyte ratio (NLR) as a marker for COVID-19 infection in Saudi Arabia. *Saudi Med J*. 2021;42(4):370 LP–376 . doi:10.15537/smj.2021.42.4.20200818

13. Nada AM. Red cell distribution width in type 2 diabetic patients. *Diabetes Metab Syndr Obes*. 2015;8:525–533. doi:10.2147/DMSO.S85318

14. Arkew M, Yemane T, Mengistu Y, Gemechu K, Tesfaye G, Johnson C. Hematological parameters of type 2 diabetic adult patients at debre berhan referral hospital, Northeast Ethiopia: a comparative cross-sectional study. *PLoS One*. 2021;16(6):e0253286. doi:10.1371/journal.pone.0253286

15. Wang Z-S, Song Z-C, Bai J-H, et al. Red blood cell count as an indicator of microvascular complications in Chinese patients with type 2 diabetes mellitus. *Vasc Health Risk Manag*. 2013;9:237–243. doi:10.2147/VHRM.S43211

16. Keane WF, Brenner BM, de Zeeuw D, et al. The risk of developing end-stage renal disease in patients with type 2 diabetes and nephropathy: the RENAAL study. *Kidney Int*. 2003;63(4):1499–1507. doi:10.1046/j.1523-1755.2003.00885.x

17. Thomas MC. Anemia in diabetes: marker or mediator of microvascular disease? *Nat Clin Pract Nephrol*. 2007;3(1):20–30. doi:10.1038/ncpneph0378

18. Hamali HA, Saboor M. Undiagnosed hemoglobinopathies: a potential threat to the premarital screening program. *Pakistan J Med Sci*. 2019;35(6):1611–1615. doi:10.12669/pjms.35.6.976

19. Hamali HA, Mobarki AA, Saboor M, et al. Prevalence of anemia among Jazan University students. *Int J Gen Med*. 2020;13:765–770. doi:10.2147/IJGM.S275702

20. Vlagopoulos PT, Tighiouart H, Weiner DE, et al. Anemia as a risk factor for cardiovascular disease and all-cause mortality in diabetes: the impact of chronic kidney disease. *J Am Soc Nephrol*. 2005;16(11):3403–3410. doi:10.1681/ASN.2005030226

21. Pan J, Borné Y, Engström G. The relationship between red cell distribution width and all-cause and cause-specific mortality in a general population. *Sci Rep*. 2019;9(1):16208. doi:10.1038/s41598-019-52708-2

22. Duman TT, Aktas G, Atak BM, Kocak MZ, Erkus E, Savli H. Neutrophil to lymphocyte ratio as an indicative of diabetic control level in type 2 diabetes mellitus. *Afr Health Sci*. 2019;19(1):1602–1606. doi:10.4314/ahs.v19i1.35

23. Duncan BB, Schmidt MI, Pankow JS, et al. Low-grade systemic inflammation and the development of type 2 diabetes: the atherosclerosis risk in communities study. *Diabetes*. 2003;52(7):1799–1805. doi:10.2337/diabetes.52.7.1799

24. Pradhan AD, Manson JE, Rifai N, Buring JE, Ridker PM. C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. *JAMA*. 2001;286(3):327–334. doi:10.1001/jama.286.3.327

25. Fujita T, Hemmi S, Kajiwara M, et al. Complement-mediated chronic inflammation is associated with diabetic microvascular complication. *Diabetes Metab Res Rev*. 2013;29(3):220–226. doi:10.1002/dmrr.2380

26. Zahorec R. Neutrophil-to-lymphocyte ratio, past, present and future perspectives. *Bratisl Lek Listy*. 2021;122(7):474–488. doi:10.4149/BLL_2021_078

27. Wan H, Wang Y, Fang S, et al. Associations between the neutrophil-to-lymphocyte ratio and diabetic complications in adults with diabetes: a cross-sectional study. *J Diabetes Res*. 2020;2020:6219545. doi:10.1155/2020/6219545

28. Mobarki AA, Dobie G, Saboor M, et al. MPR and NLR as prognostic markers in ICU-admitted patients with COVID-19 in Jazan, Saudi Arabia. *Infect Drug Resist*. 2021;14:4859–4864. doi:10.2147/IDR.S342259

29. Sefil F, Ulutas KT, Dokuyucu R, et al. Investigation of neutrophil lymphocyte ratio and blood glucose regulation in patients with type 2 diabetes mellitus. *J Int Med Res*. 2014;42(2):581–588. doi:10.1177/0300060513516944

30. Hamali HA. The mighty role of platelets in immunity, inflammation, cancer and angiogenesis. *Majmaah J Heal Sci*. 2020;8(1):65–81. doi:10.5455/mjhs.2020.01.008

31. Schneider DJ. Factors contributing to increased platelet reactivity in people with diabetes. *Diabetes Care*. 2009;32(4):525–527. doi:10.2337/dc08-1865

32. Jindal S, Gupta S, Gupta R, et al. Platelet indices in diabetes mellitus: indicators of diabetic microvascular complications. *Hematology*. 2011;16(2):86–89. doi:10.1179/102453311X12902908412110

33. Ebrahim H, Asrie F, Getaneh Z. Basic coagulation profiles and platelet parameters among adult type 1 and type 2 diabetes patients at Dessie Referral Hospital, Northeast Ethiopia: comparative cross-sectional study. *J Blood Med*. 2021;12:33–42. doi:10.2147/JBM.S287136

34. Kodiatte TA, Manikyam UK, Rao SB, et al. Mean platelet volume in Type 2 diabetes mellitus. *J Lab Physicians*. 2012;4(1):5–9. doi:10.4103/0974-2727.98662

35. Sterner G, Carlson J, Ekberg G. Raised platelet levels in diabetes mellitus complicated with nephropathy. *J Intern Med*. 1998;244(6):437–441. doi:10.1111/j.1365-2796.1998.00349.x

36. Hekimsoy Z, Payzin B, Örnek T, Kandoğan G. Mean platelet volume in type 2 diabetic patients. *J Diabetes Complications*. 2004;18(3):173–176. doi:10.1016/S1056-8727(02)00282-9

37. Khandekar MM, Khurana AS, Deshmukh SD, Kakrani AL, Katdare AD, Inamdar AK. Platelet volume indices in patients with coronary artery disease and acute myocardial infarction: an Indian scenario. *J Clin Pathol*. 2006;59(2):146–149. doi:10.1136/jcp.2004.025387

38. Papanas N, Symeonidis G, Maltezos E, et al. Mean platelet volume in patients with type 2 diabetes mellitus. *Platelets*. 2004;15(8):475–478. doi:10.1080/0953710042000267707