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# Hematological and Inflammatory Cytokine Profiles in Subjects with Type 2 Diabetes Mellitus in Port Harcourt, Nigeria

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## Abstract

**Objective:** Type 2 diabetes mellitus (T2DM) is associated with chronic hyperglycemia and systemic inflammation, which contribute to hematological alterations and vascular complications. This study evaluated hematological indices, interleukin-1β (IL-1β), and tumor necrosis factor-α (TNF-α) in individuals with T2DM in Port Harcourt, Nigeria, and examined their relationship with glycated hemoglobin (HbA1c).

**Materials and Methods:** This case-control study involved 70 T2DM patients (HbA1c≥ 6.5%) and 70 age- and sex-matched healthy controls. Fasting blood glucose (FBG) was measured enzymatically, HbA1c by fluorescence immunoassay, complete blood count using an automated hematology analyzer, and cytokines by ELISA. Statistical analysis was performed using GraphPad Prism version 8.0.2, with effect sizes reported and $P \leq 0.05$ considered significant.

**Results:** T2DM subjects had significantly higher FBG, HbA1c, WBC, neutrophil percentage, and IL-1β, and significantly lower RBC, lymphocyte percentage, PLT, and PCT (adjusted $P < 0.05$). IL-1β was more than three-fold higher in diabetics, with a very large effect size. FBG increased significantly with longer disease duration ($P = 0.008$). HbA1c correlated positively with FBG ($P < 0.001$) WBC ($P = 0.044$), MPV ($P = 0.006$), and PDW ($P = 0.015$), and negatively with MCV ($P = 0.019$) and Mixed WBC population ($P = 0.001$).

**Conclusion:** This study simultaneously assessed complete blood count parameters alongside IL-1β and TNF-α in the same cohort. The findings demonstrate that T2DM in this population is characterized by clinically meaningful hematological and inflammatory alterations linked to poor glycemic control. Integrating routine complete blood count and selected inflammatory markers into diabetes monitoring may enhance early risk stratification, particularly in resource-limited settings.

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**Keywords**: Diabetes, Blood cell count, Interleukin-1beta, Inflammation

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## Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by hyperglycemia due to impaired insulin secretion, action, or both (1). Type 2 diabetes mellitus (T2DM) is the most prevalent form, accounting for 90-95% of cases. The global prevalence of T2DM has quadrupled over the past 35 years, with 536.6 million adults living with the disease in 2021 and projections reaching 783.2 million by 2045 (2). In Nigeria, as of 2021, the estimated prevalence was reported as 3.7% (3).

Type 2 DM arises when pancreatic β-cells fail to compensate for increasing insulin resistance (4). The persistent hyperglycemia triggers cellular and molecular changes that worsen the disease and lead to complications affecting the kidneys, eyes, nerves, blood vessels, and heart (5). Chronic inflammation is now recognized as a key contributor to the development and progression of these complications, marked by elevated levels of pro-inflammatory cytokines in diabetic individuals 6**)**. Notably, interleukin-1β (IL-1β) and tumor necrosis factor-α (TNF-α) impair insulin secretion and signalling, promote β-cell apoptosis, and drive oxidative stress and inflammatory pathways, thereby playing a central role in T2DM pathogenesis (6,7).

Alterations in hematological indices are closely associated with the chronic inflammatory state in T2DM. These changes are primarily driven by persistent hyperglycemia, increased oxidative stress from reactive oxygen species (ROS), and the accumulation of advanced glycation end products (AGEs), which impair red and white blood cells, platelets, and hemostatic functions (8,9). Red blood cell (RBC) abnormalities, such as reduced hematocrit and hemoglobin, are commonly reported (10,11), although findings vary, with some studies noting elevated RBC parameters (12,13), or no significant differences (14,15). Platelet dysfunction is also evident in diabetes, where hyperglycemia induces protein glycation, osmotic swelling, and activation. Insulin resistance and chronic inflammation further promote platelet hyperreactivity, fostering a prothrombotic state and increasing the risk of micro and macrovascular complications (16,17). White blood cell (WBC) indices are also altered in diabetes. Advanced glycation end products, angiotensin II, oxidative stress, and cytokines stimulate WBC activation and cytokine release, exacerbating inflammation and vascular damage (17). Elevated total WBC, neutrophil, and lymphocyte counts are consistently observed in diabetic patients, reflecting the systemic low-grade inflammation characteristic of T2DM (11,18).

In clinical settings, hematological indices and inflammatory markers can serve as useful tools for disease monitoring, risk assessment, and early detection of complications (19). Despite growing evidence linking hematological alterations and inflammation to T2DM, studies in Nigeria have largely evaluated these parameters independently, with limited data integrating inflammatory cytokines and hematological indices within the same cohort. Furthermore, there is a paucity of data in Port Harcourt, where rapid urbanization and lifestyle transitions may influence the inflammatory and metabolic profile of affected individuals. To the best of our knowledge, no previous study in this region has simultaneously assessed complete blood count parameters together with IL-1β and TNF-α and examined their relationship with glycated hemoglobin (HbA1c) as an indicator of long-term glycemic control. This integrated approach provides a more comprehensive understanding of the interplay between hyperglycemia, systemic inflammation, and hematological alterations in T2DM within this population.

## Material and methods

The study included 140 participants comprising 70 individuals with T2DM and 70 apparently healthy controls. T2DM was



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defined as HbA1c ≥ 6.5% in accordance with the American Diabetes Association criteria (1). Diabetic participants were selected by simple random sampling from the Family Medicine Department clinic attendance register; eligible individuals were assigned identification numbers and randomly selected until the required sample size was attained. Controls were recruited from hospital staff, patients' relatives, and community volunteers residing in Port Harcourt. They were frequency-matched to cases by age and sex and screened to exclude diabetes (HbA1c< 6.5%), inflammatory disorders, and other chronic systemic illnesses.

Sample size was determined using power analysis for comparison of two independent means. Assuming a moderate effect size (Cohen's d= 0.5), a two-sided alpha of 0.05, and 80% power, a minimum of 64 participants per group was required. To accommodate potential exclusions, 70 participants were recruited in each group**.**

Demographic and clinical information, including age, sex, family history of diabetes, and hypertension status, was obtained using a structured questionnaire. Venous blood samples were collected by standard venepuncture techniques as described by Cheesbrough (20). Three millilitres of blood were drawn into tripotassium ethylenediaminetetraacetic acid ($K_3$EDTA) tubes for HbA1c and complete blood count (CBC) analysis, three millilitres into fluoride oxalate tubes for fasting blood glucose (FBG) estimation, and four millilitres into plain tubes for serum separation. Clotted samples were centrifuged at 3200 rpm for 10 minutes using a NewLife Bucket Centrifuge (Model 800B), and the separated serum was stored for TNF-α and IL-1β assays.

All reagents were commercially sourced, and analyses were performed according to manufacturers' standard operating procedures. FBG was measured using the enzymatic oxidation method described by Yuen and McNeill (21) with ELITech Clinical Systems reagents (France) and analyzed on a Mindray BA-88A semi-auto chemistry analyzer. HbA1c was determined by fluorescence immunoassay using the Finecare™ system (Wondfo®, China), based on the method of Cox et al. (22). CBC parameters were analyzed using the Mindray BC-2800 automated haematology analyzer (Mindray Bio-Medical Electronics Co., Ltd., China). Serum TNF-α and IL-1β concentrations were quantified using human ELISA kits (Elabscience Biotechnology Co., Ltd., China) following standard enzyme-linked immunosorbent assay procedures, and absorbance was read using a Hinotek Microplate Reader (Model M201).

Statistical analysis was performed using GraphPad Prism version 8.0.2 (GraphPad Software Inc., USA). Normality of continuous variables was assessed using the Shapiro–Wilk test and homogeneity of variance using Levene's test. Normally distributed data are presented as mean ± standard deviation and compared using the independent samples t-test, whereas non-normally distributed data are expressed as median (interquartile range) and analyzed using the Mann-Whitney U test. Categorical variables are presented as frequencies and percentages and compared using the Chi-square test. Effect sizes were calculated as Cohen's d for parametric comparisons and rank-biserial correlation (r) for non-parametric comparisons. Spearman's correlation analysis was performed to assess the relationship between HbA1c and the studied parameters. To control for type I error arising from multiple comparisons, Bonferroni correction was applied and adjusted *P*-values are reported. Statistical significance was set at $P< 0.05$.

## Ethical considerations

Ethical approval for this study was obtained from the Research Ethics Committee of the Rivers State University Teaching Hospital, Port-Harcourt, Rivers State, Nigeria (Reference Number: RSUTH/REC/2024/577).

## Results

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The study included 70 individuals with T2DM and 70 apparently healthy controls. There were no significant differences between groups in mean age, weight, or sex distribution. A greater proportion of T2DM subjects reported a family history of diabetes, but this was not significant (OR= 1.44; 95% CI: 0.74-2.85; *P*= 0.385). In contrast, hypertension was significantly more prevalent among T2DM patients than controls (OR= 7.20; 95% CI: 3.33-15.12; *P*< 0.001). Among diabetic subjects, the largest proportion (44.3%) had been diagnosed within the preceding five years (Table 1).

FBG and HbA1c levels were significantly higher in T2DM subjects compared with controls (adjusted *P*< 0.001 for both), with large effect sizes (Table 2).

Red cell indices and leukocyte subpopulations were compared between T2DM subjects and healthy controls. After adjusting for multiple comparisons, T2DM patients showed significantly lower RBC counts (d= 0.57), higher neutrophil percentages (d= 0.61), and lower lymphocyte percentages (d= -0.63) compared with controls. Other parameters were not significantly different (Table 3a).

WBC count, platelet count (PLT), plateletcrit (PCT), and IL-1β remained significantly different between T2DM subjects and controls. T2DM participants demonstrated higher WBC and IL-1β levels, alongside reduced PLT and PCT values. These differences were associated with large effect sizes. No significant differences were observed for RDW-CV, PDW, or TNF-α following multiple comparison correction (Table 3b).

Among the studied parameters, only FBG differed significantly across diabetes duration. Post-hoc Tukey analysis revealed that participants with >10 years of diabetes had higher FBG compared with the 1-5 year and 6-10 year groups.

No significant differences were observed for HbA1c or any hematological and inflammatory parameters across duration categories (Table 4).

Spearman's correlation analysis was performed to assess the relationship between HbA1c and the studied hematological and inflammatory parameters. Significant positive correlations were observed with FBG, WBC, MPV, PDW, and MIXED (%), while MCV showed a significant negative correlation. Other parameters did not show statistically significant associations (Table 5).

**Table 1. Demographic information of study subjects**

| Variable | T2DM (n= 70) | Control (n= 70) | *P*-value | Effect size |
|---|---|---|---|---|
| **Continuous variables** | | | | |
| **Age** (years), mean± SD | 55.01 (± 11.80) | 52.33 (± 11.79) | 0.180 | Cohen's d= 0.23 |
| **Weight** (kg), mean± SD | 76.20 (± 16.87) | 76.89 (± 14.45) | 0.796 | Cohen's d= 0.044 |
| **Categorical variables** | | | | |
| **Male**, n (%) | 29 (41.4%) | 29 (41.4%) | 1.000 | OR= 1.0 (95% CI: 0.52-1.93) |
| **Female**, n (%) | 41 (58.6%) | 41 (58.6%) | 1.000 | OR= 1.0 (95% CI: 0.52-1.93) |
| **Family history of DM**, n (%) | 30 (42.9%) | 24 (34.3%) | 0.385 | OR= 1.44 (95% CI: 0.74-2.85) |
| **Hypertension**, n (**%**) | 45 (64.3%) | 14 (20.0%) | <0.0001 | OR= 7.20 (95% CI: 3.33-15.12) |
| **Duration of diabetes** (years) | | | | |
| **1–5** | 31 (44.3%) | – | – | – |
| **6–10** | 16 (22.9%) | – | – | – |
| **>11** | 23 (32.8%) | – | – | – |

OR: Odd Ratio, CI: Coefficient Interval

**Table 2. Comparison of glycemic parameters between diabetic and control subjects**

| Parameter | T2DM (n= 70) Median [IQR] | Control (n= 70) Median [IQR] | U | Median Difference (95% CI) | Effect Size (r) | *P*-value | Adjusted *P*-value |
|---|---|---|---|---|---|---|---|
| **FBG** (mmol/L) | 6.40 [5.18-8.83] | 4.50 [4.18-4.83] | 607 | 2.10 (1.50-2.70) | 0.65 | < 0.001 | < 0.001* |
| **HbA1c** (%) | 8.30 [7.25-9.30] | 5.30 [5.10-5.40] | 3 | 3.00 (2.60-3.30) | 0.86 | < 0.001 | < 0.001* |

FBG: Fasting Blood Glucose, HbA1c: Glycated Hemoglobin, IQR: Interquartile Range, U: Mann-Whitney U statistic, CI: Confidence Interval, r:rank-biserial correlation (effect size)

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**Table 3a. Comparison of hematological and inflammatory parameters between T2DM patients and healthy controls**

| Parameter | T2DM (n= 70) M(± SD) | Control (n= 70) M(± SD) | t value | Mean Difference (95% CI) | Cohen's d | Adjusted *P*-value |
|---|---|---|---|---|---|---|
| **RBC** (×10¹²/L) | 4.63 (± 0.68) | 4.99 (± 0.62) | 3.37 | 0.370 (0.153-0.587) | 0.57 | < 0.001* |
| **HGB** (g/dL) | 11.80 (± 1.51) | 12.49 (± 1.63) | 2.59 | 0.69 (0.162-1.213) | 0.44 | 0.011 |
| **HCT** (%) | 37.80 (± 4.63) | 39.37 (± 4.60) | 2.01 | -1.56 (-3.106–−0.023) | 0.34 | 0.047 |
| **MCV** (fl) | 80.32 (± 5.86) | 79.09 (± 5.35) | 1.29 | 1.23 (-0.648-3.100) | 0.22 | 0.198 |
| **MCH** (Pg) | 24.81 (± 2.09) | 25.02 (± 1.89) | 0.67 | 0.22 (-0.415-0.846) | 0.11 | 0.500 |
| **MCHC** (g/dl) | 31.26 (± 0.88) | 31.23 (± 1.08) | 0.16 | -0.03 (-0.356-0.302) | 0.03 | 0.870 |
| **RDW-SD** | 41.40 (± 3.37) | 40.54 (± 4.92) | 1.03 | 0.86 (-0.549-2.269) | 0.21 | 0.229 |
| **Neut** (%) | 50.19 (± 9.31) | 44.64 (± 8.93) | 3.70 | 5.54 (2.580-8.506) | 0.61 | < 0.001* |
| **Lym** (%) | 42.22 (± 8.77) | 47.98 (± 9.44) | 3.74 | -5.77 (-8.811–−2.721) | -0.63 | < 0.001* |
| **MIXED** (%) | 7.66 (± 1.93) | 7.73 (± 2.26) | 0.23 | -0.08 (-0.743-0.586) | -0.03 | 0.816 |
| **MPV** | 9.94 (± 0.76) | 9.79 (± 0.84) | 1.13 | 0.15 (-0.114-0.422) | 0.14 | 0.257 |

RBC: Red Blood Cell, HGB- Hemoglobin, HCT: Hematocrit, MCV: Mean Cell Volume, MCH: Mean Cell Hemoglobin, MCHC: Mean Cell Hemoglobin Concentration, RDW-SD: Red Cell Distribution Width Standard Deviation, Neut: Neutrophil, Lym: Lymphocyte, MPV:Mean Platelet Volume, SD: Standard Deviation, CI: Confidence Interval

**Table 3b.Comparison of hematological and inflammatory parameters between T2DM patients and healthy controls**

| Parameter | T2DM (n= 70) Median [IQR] | Control (n= 70) Median [IQR] | U | Median Difference (95% CI) | Effect Size (r) | *P*-value | Adjusted *P*-value |
|---|---|---|---|---|---|---|---|
| **RDW-CV** | 13.5 [13.2-14.3] | 13.7 [12.8-14.6] | 2685 | 0.00 (-0.30-0.40) | 0.08 | 0.839 | 1.000 |
| **WBC** (×10⁹/L) | 5.50 [4.90-6.40] | 4.90 [4.10-5.40] | 1413 | 0.80 (0.50-1.20) | 0.73 | < 0.001 | < 0.001* |
| **PLT** (×10⁹/L) | 247.5 [205.8-323.0] | 335.0 [244.3-379.5] | 1542 | -55.0 (-87.0 to -27.0) | 0.64 | 0.001 | 0.001* |
| **PDW** | 14.9 [14.5-15.1] | 14.7 [14.5-15.0] | 1961 | 0.10 (0.00-0.20) | 0.28 | 0.041 | 0.284 |
| **PCT** | 0.240 [0.210-0.290] | 0.315 [0.250-0.380] | 1417 | -0.060 (-0.090 to -0.030) | 0.72 | < 0.001 | < 0.001* |
| **IL-1β** (pg/mL) | 294.0 [116.9-393.6] | 84.75 [27.03-133.5] | 719.5 | 174.7 (113.6-222.1) | 0.84 | < 0.001 | < 0.001* |
| **TNF-α** (pg/mL) | 102.2 [46.8-208.7] | 85.70 [38.38-222.5] | 1661 | 7.65 (-22.40 to 42.50) | 0.19 | 0.636 | 1.000 |

RDW-CV: Coefficient of Variation, WBC: White Blood Cell, PLT: Platelet, PDW: Platelet Distribution Width, PCT: Plateletcrit, IL-1β: Interleukin 1-Beta, TNF-α: Tumor Necrosis Factor-Alpha, IQR: Interquartile Range, U: Mann–Whitney U statistic, CI: Confidence Interval, r: rank-biserial correlation coefficient (effect size)

**Table 4. Relationship between duration of diabetes and studied parameters**

| Parameters/Duration | 1-5 (Yrs) (n=31) Mean± SD | 6-10 (Yrs) (n=16) Mean± SD | >10 (Yrs) (n=23) Mean± SD | F value | *P*-value |
|---|---|---|---|---|---|
| **FBG** (mmol/L) | 6.881 (±3.033)[a] | 6.206 (±1.824)[a] | 9.274 (±4.245)[b] | 5.150 | 0.008 |
| **HBA1c** (%) | 8.452 (± 2.106) | 8.150 (± 1.243) | 9.039 (± 1.558) | 1.329 | 0.272 |
| **RBC** (×10¹²/L) | 4.793 (± 0.646) | 4.454 (± 0.615) | 4.521 (± 0.739) | 1.769 | 0.178 |
| **HGB** (g/dL) | 12.29 (± 1.250) | 11.31 (± 1.573) | 11.48 (± 1.655) | 3.129 | 0.050 |
| **HCT%** | 39.14 (± 3.647) | 36.26 (± 4.965) | 37.07 (± 5.236) | 2.576 | 0.084 |
| **MCV** (fl) | 79.91 (± 5.385) | 81.65 (± 5.040) | 79.93 (± 7.000) | 0.530 | 0.591 |
| **MCH** (Pg) | 24.92 (± 1.985) | 25.22 (± 1.750) | 24.65 (± 2.636) | 0.327 | 0.722 |
| **MCHC** (g/dl) | 31.35 (± 1.060) | 31.09 (± 0.581) | 31.27 (± 0.792) | 0.425 | 0.655 |
| **RDW-CV** | 13.96 (± 0.899) | 13.85 (± 1.007) | 13.58 (± 1.381) | 0.774 | 0.465 |
| **RDW-SD** | 41.16 (± 3.482) | 42.62 (± 3.375) | 40.88 (± 3.142) | 1.412 | 0.251 |
| **WBC** (×10⁹/L) | 5.542 (± 1.152) | 5.444 (± 0.931) | 6.396 (± 2.891) | 1.734 | 0.184 |
| **Neut** (%) | 47.46 (± 9.018) | 51.79 ± 8.695 | 52.27 (± 9.316) | 2.258 | 0.112 |
| **Lym** (%) | 44.53 (± 8.475) | 40.21 (± 8.335) | 40.50 (± 9.066) | 1.993 | 0.144 |
| **MIXED** (%) | 8.006 (± 1.779) | 7.994 (± 2.215) | 7.226 (± 1.869) | 1.270 | 0.288 |
| **PLT** (×10⁹/L) | 266.6 (± 83.63) | 254.6 (± 74.78) | 273.9 (± 80.93) | 0.271 | 0.764 |
| **MPV** | 10.06 (± 0.882) | 9.688 (± 0.608) | 9.961 (± 0.663) | 1.270 | 0.288 |
| **PDW** | 14.84 (± 0.526) | 14.81 (± 0.394) | 14.88 (± 0.357) | 0.136 | 0.873 |
| **PCT** | 0.258 (±0.067) | 0.251 (±0.061) | 0.255 (±0.059) | 0.081 | 0.922 |
| **IL-1β** (pg/mL) | 248.6 (± 44.11) | 252.2 (± 42.68) | 247.5 (± 39.34) | 0.061 | 0.941 |
| **TNF- α** (pg/mL) | 176.3 (± 44.54) | 184.1 (± 57.88) | 182.4 (± 52.34) | 0.159 | 0.853 |

FBG : Fasting Blood Glucose, HbA1c: Glycated Hemoglobin, RBC: Red Blood Cell, HGB: Hemoglobin, HCT: Hematocrit, MCV: Mean Cell Volume, MCH: Mean Cell Hemoglobin, MCHC: Mean Cell Hemoglobin Concentration, RDW-SD: Red Cell Distribution Width Standard Deviation, Neut: Neutrophil, Lym: Lymphocyte, PLT- Platelet, MPV: Mean Platelet Volume, PDW: Platelet Distribution Width, PCT: Plateletcrit, IL-1β: Interleukin 1-Beta, TNF-α: Tumor Necrosis Factor-Alpha, SD: Standard Deviation.
Values with the same superscript does not differ significantly when compared.

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**Table 5. Correlation between HbA1c levels and studied parameters**

| Variables | HbA1c | |
|---|---|---|
| | Spearman r | *P*-value |
| **FBG** (mmol/L) | 0.680 | < 0.001* |
| **RBC** (×10¹²/L) | 0.013 | 0.916 |
| **HGB** (g/dL) | -0.020 | 0.873 |
| **HCT** (%) | -0.038 | 0.753 |
| **MCV** (fl) | -0.280 | 0.019* |
| **MCH** (Pg) | -0.157 | 0.195 |
| **MCHC** (g/dL) | 0.034 | 0.780 |
| **RDW-CV** | -0.043 | 0.722 |
| **RDW-SD** | -0.161 | 0.183 |
| **WBC** (×10⁹/L) | 0.242 | 0.044* |
| **Neut** (%) | 0.064 | 0.597 |
| **Lym** (%) | 0.025 | 0.839 |
| **MIXED** (%) | -0.378 | 0.001* |
| **PLT** (×10⁹/L) | -0.160 | 0.187 |
| **MPV** | 0.326 | 0.006 |
| **PDW** | 0.291 | 0.015* |
| **PCT** | -0.085 | 0.486 |
| **IL-1β** (pg/mL) | 0.116 | 0.338 |
| **TNF-α** (pg/mL) | -0.092 | 0.447 |

FBG: Fasting Blood Glucose, HbA1c: Glycated Hemoglobin, RBC: Red Blood Cell, HGB: Hemoglobin, HCT: Hematocrit, MCV: Mean Cell Volume, MCH: Mean Cell Hemoglobin, MCHC: Mean Cell Hemoglobin Concentration, RDW-SD: Red Cell Distribution Width Standard Deviation, Neut- Neutrophil, Lym: Lymphocyte, MPV: Mean Platelet Volume, IL-1β: Interleukin 1-Beta, TNF-α: Tumor Necrosis Factor-Alpha, r: Spearman Correlation Coefficient

## Discussion

The significant elevation of FBG and HbA1c in diabetic subjects confirms persistent hyperglycemia, a hallmark of T2DM. The median HbA1c of 8.3% in the diabetic group substantially exceeds the ADA-recommended target for most adults (1), indicating suboptimal glycemic control. This degree of hyperglycemia places patients at significantly increased risk for microvascular and macrovascular complications (18,23), underscoring the need for more intensive glycemic management in this population.

The diabetic subjects exhibited significantly lower RBC compared to healthy controls, with moderate effect size. This finding is consistent with previous studies reporting reduced RBC counts in patients with T2DM (11,24,25). Hyperglycaemia as seen in this study can promote oxidative stress and non-enzymatic glycation of hemoglobin and red cell membrane proteins, which can accelerate erythrocyte aging and shorten red cell lifespan (8). Although HGB and HCT were lower in diabetic subjects, these differences did not remain statistically significant after correction. However, the absolute reduction is clinically noteworthy: the mean HGB level of 11.8 g/dL approaches the WHO diagnostic threshold for anemia in adults (26). Even mild HGB reductions in T2DM have important practical implications, as anemia is associated with accelerated progression of nephropathy and increased cardiovascular risk (26,27). Importantly, the normocytic nature of the anemia observed in this study (indicated by normal MCV, MCH, and MCHC) points toward anemia of chronic disease rather than nutritional deficiencies (26). This distinction is important in guiding evaluation and management, particularly in settings where iron supplementation may otherwise be initiated empirically. These findings support the value of routine full blood count assessment in diabetic patients as part of comprehensive risk monitoring.

The significantly higher WBC count and neutrophil percentage, coupled with lower lymphocyte percentage in diabetic subjects (large effect sizes: r= 0.73, Cohen's d= 0.61

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and -0.63 respectively), provide evidence of chronic low-grade inflammation. Neutrophilia in diabetes contributes to endothelial damage through release of proteolytic enzymes and reactive oxygen species, accelerating atherosclerosis (28). Hyperglycemia not only increases neutrophil count but also alters their function (11). They play a central role in promoting adipose tissue inflammation and further exacerbating insulin resistance (28). The relative lymphopenia observed may indicate impaired adaptive immunity, potentially explaining the increased susceptibility to infections reported in diabetic populations (29,30). These findings are consistent with previous studies reporting elevated WBC and neutrophil counts, alongside reduced lymphocyte levels in individuals with diabetes (10,11,31).

Although platelet counts remained within reference ranges among the study population, the approximately 26% lower median platelet count in diabetics compared to controls, together with elevated PDW, suggests altered platelet production and increased heterogeneity in platelet size. Kim et al. (32) suggested that ineffective thrombopoiesis may contribute to lower platelet counts in diabetic patients, while Hekimsoy et al. (33) attributed this to altered platelet production and turnover. Additionally, during inflammation, platelets are recruited to inflammatory sites and form aggregates with white blood cells, reducing circulating platelet numbers (34). The elevated PDW in diabetics reflects greater variation in platelet size, indicating enhanced platelet activation. This has been associated with inflammation, atherosclerosis, and increased cardiovascular risk in individuals with diabetes (35). Such platelet abnormalities may contribute to the development of both macrovascular and microvascular complications commonly seen in T2DM. These findings are consistent with those of Ahmed (31), who reported lower PLT counts and higher PDW in diabetic patients. However, studies have shown mixed results, some reported higher platelet counts in diabetic subjects compared to controls (10,36,37), while others (25,38), found no significant differences in platelet counts. Notably, the higher PDW observed in this study aligns with findings by Kizilgul et al. (15) and Ebrahim et al. (38).

The markedly elevated IL-1β levels in diabetic subjects (more than three-fold higher than controls, with a very large effect size of r= 0.84) represent the most striking finding of this study. This elevation has profound clinical implications, as IL-1β is an active participant in diabetes pathogenesis. Chronically elevated IL-1β promotes β-cell apoptosis, impairs insulin secretion, and contributes to insulin resistance in peripheral tissues (39,40). The magnitude of elevation observed, a median of 294.0 pg/mL in diabetics versus 84.75 pg/mL in controls underscores the relevance of inflammatory dysregulation in this population. The findings highlight IL-1β as a potentially informative biomarker of inflammatory burden in T2DM. Therapeutically, these findings support emerging evidence for IL-1β blockade as a potential treatment strategy in diabetes. While anti–IL-1 therapies have shown cardiovascular benefit in selected high-risk populations, their applicability in routine diabetes management remains an area of ongoing research (41,42).

In contrast, TNF-α levels did not differ significantly between groups. The wide interquartile range in both groups (46.8-208.7 pg/mL in diabetics versus 38.4-222.5 pg/mL in controls) suggests substantial individual variability. This variability may reflect differences in obesity status, medication use, or genetic factors as its expression may be influenced by these factors (43). In contrast to the findings of the present study, Tong et al. (40) reported elevated TNF-α levels in diabetic individuals compared to controls, while Babandina et al. (44) observed lower TNF-α concentrations in diabetics than in healthy subjects. These inconsistencies highlight the variability in TNF-α expression in T2DM, suggesting its role may depend on individual


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characteristics, disease progression, or methodological differences across studies.

The observation that FBG, but not HbA1c, increased significantly with longer diabetes duration has practical implications. While HbA1c remains the standard marker of long-term glycemic control, it may be influenced by factors affecting red cell lifespan and turnover (45). The finding that patients with longer disease duration exhibited higher fasting glucose despite similar HbA1c levels suggests that reliance on HbA1c alone may underestimate glycemic burden in certain individuals. This supports current recommendations for complementary glycemic assessment strategies, particularly in patients with longstanding disease or hematological abnormalities (46).

The lack of significant variation in hematological and inflammatory parameters across duration groups suggests that these alterations may develop early in the disease course and persist rather than progressively worsen. Clinically, this emphasizes the importance of comprehensive baseline evaluation at diagnosis, as inflammatory and hematological disturbances may already be established.

The positive correlations between HbA1c and WBC (r= 0.242, *P*= 0.044) and MPV (r= 0.326, *P*= 0.006), although modest, indicate that worsening glycemic control is associated with increasing inflammatory burden and platelet activation. These relationships are clinically meaningful, as even incremental increases in WBC and MPV have been associated with elevated cardiovascular risk (47). Previous studies have shown that increase in WBC is associated with increased risk of cardiovascular events in diabetic populations (48). Similarly, elevated MPV correlates with increased platelet aggregation and microvascular problems (49). The negative correlation between HbA1c and MCV observed in this study, (r= -0.280, *P*= 0.019), may reflect subtle erythrocyte morphological changes induced by chronic hyperglycemia and oxidative stress (50). Additionally, the negative relationship with mixed white cell populations suggests that poor glycemic control may differentially affect specific immune cell subsets, though the clinical implications require further investigation.

This study is limited by its single-centre design, modest sample size, and absence of detailed data on obesity status, iron indices, vitamin B12 levels, and medication use, all of which may influence hematological parameters and inflammatory markers. Nevertheless, the consistent pattern of abnormalities across red cell, white cell, platelet, and inflammatory markers, supported by moderate-to-large effect sizes strengthens the robustness of the findings.

Overall, these results suggest that routine complete blood count assessment in patients with T2DM may provide clinically meaningful information beyond basic hemoglobin measurement. Hematological indices can serve as accessible adjunct markers of inflammatory status, thrombotic tendency, and potential anemia, particularly in resource-constrained settings. Careful interpretation of HbA1c is also warranted in the presence of hematological abnormalities. Early and integrated evaluation of glycemic, inflammatory, and hematological parameters may enhance risk stratification and support more individualized management strategies in T2DM.

## CONCLUSION

This study demonstrates that patients with T2DM exhibit significant alterations in glycemic, hematological, platelet, and inflammatory parameters. Beyond statistical differences, the magnitude of hyperglycemia, the reduction in red cell indices approaching anemic thresholds, the evidence of leukocyte-mediated inflammation, altered platelet indices suggestive of increased thrombotic tendency, and the marked elevation of IL-1β collectively indicate clinically meaningful disturbances that may contribute to cardiovascular and microvascular risk. The persistence of these

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abnormalities irrespective of disease duration further suggests that such changes may occur early and remain sustained throughout the disease course. Routine evaluation of complete blood count parameters, alongside glycemic assessment, may therefore provide additional, accessible tools for risk stratification, particularly in resource-limited settings. Integrating inflammatory and hematological markers into diabetes monitoring frameworks may enhance individualized management and support early identification of patients at higher risk of complications.

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## Conflict of Interest

Authors have declared that no competing interests exist.

## Authors' contributions

Conceptualization: CH.AS, SG.CH and SU.K.
Data Collection and Laboratory Analysis: CH.AS.
Data Analysis and Interpretation: CH.AS, SG.CH and SU.K.
Writing – Original Draft Preparation: CH.AS.
Writing – Review and Editing: SG.CH and SU.K.
Supervision: SG.CH and SU.K.
All authors read and approved the final manuscript.

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