

# Hematological indices and their correlation with fasting blood glucose level and anthropometric measurements in type 2 diabetes mellitus patients in Gondar, Northwest Ethiopia

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**Background:** Diabetes mellitus is (DM) a global public health problem and a complex disease characterized by chronic hyperglycemia that leads to long-term macrovascular and microvascular complications. Recent studies have reported the role of hematological indices in contributing to the vascular injury in diabetic patients. Thus, the aim of this study was to determine hematological indices and their correlation with fasting blood glucose level and anthropometric measurement in type 2 DM patients in comparison with healthy controls.

**Methods:** A comparative cross-sectional study was conducted at the chronic illness clinic of Gondar University Hospital from February to April 2015. A total of 296 participants (148 cases and 148 healthy controls) were selected using systematic random sampling technique. Data were collected using a pretested structured questionnaire. Fasting blood glucose levels and hematological indices were determined by using Bio Systems A25 and Sysmex-KX 21N analyzers, respectively. Independent sample *t*-test, Mann–Whitney *U*-test, and correlation statistics were used. A *P*-value <0.05 was considered as statistically significant.

**Result:** There was significant difference in red blood cell distribution width ( $47.3 \pm 2.6$  fL vs  $45.2 \pm 3$  fL) between diabetic patients and controls. Total white blood cells in  $10^3/\mu\text{L}$  ( $6.59 \pm 1.42$  vs  $5.56 \pm 1.38$ ), absolute lymphocyte count in  $10^3/\mu\text{L}$  ( $2.60 \pm 0.70$  vs  $2.04 \pm 0.63$ ), and absolute neutrophil count in  $10^3/\mu\text{L}$  ( $3.57 \pm 1.46$  vs  $3.11 \pm 1.04$ ) increased significantly in diabetic patients compared with controls, respectively. Among platelet indices, mean platelet volume ( $10.4 \pm 1.1$  fL vs  $9.9 \pm 1.1$  fL) and platelet distribution width ( $14.5 \pm 2.1$  fL vs  $13.4 \pm 2.1$  fL) were found to be significantly increased in the diabetic patients ( $P < 0.05$ ). Anthropometric measurements significantly correlated with white blood cell and platelet indices.

**Conclusion:** The study showed statistically significant difference in some hematological parameters of diabetic patients compared to controls. Thus, hematological indices could be useful indicators of vascular complication and glycemic control in type 2 DM patients.

**Keywords:** Ethiopia, fasting blood glucose, Gondar, hematological indices, type 2 diabetes mellitus

## Introduction

Diabetes mellitus (DM) encompasses a heterogeneous group of disorders characterized by hyperglycemia associated with multiple disorders including metabolic, cellular, and blood disturbances leading to vascular complications.<sup>1</sup>

The number of people suffering from type 2 (T2) DM has been increasing due to the aging population, urbanization, and low physical activity. According to the International

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Diabetes Federation (IDF) estimate of 2013, 382 million (8.3%) adults had diabetes worldwide. The number has been increasing by twofold over the past 20 years, and 80% of the people with diabetes particularly live in low- and middle-income countries.<sup>2</sup> Ethiopia experiences a heavy burden of communicable infectious diseases and nutritional deficiencies. Currently, it is also being faced by the rising magnitude of noncommunicable diseases like DM. In Ethiopia, although a nationwide surveillance on occurrence of DM has not been documented, the 2012 IDF report indicated an estimated DM prevalence of 3.32%.<sup>3</sup>

The overall temporal burden of hyperglycemia is responsible for DM complications and adverse outcomes.<sup>4</sup> Patients with T2DM have increased risk of cardiovascular disease (CVD) related with atherogenic dyslipidemia, coronary artery disease, and myocardial infarction. Myocardial infarction is the leading cause of morbidity and mortality worldwide.<sup>5</sup> The increased vascular risk associated with T2DM is likely to be multifaceted, but lipid abnormalities play an important role. It is important to note that dyslipidemia is more atherogenic in diabetic than in nondiabetic patients.<sup>6</sup> T2DM is a part of metabolic syndrome that comprises dyslipidemia, hypertension, and impaired hematological indices.<sup>7</sup>

Several hematological changes affecting the red blood cells (RBCs), white blood cells (WBCs), and the coagulation factors are shown to be directly associated with DM.<sup>8</sup> Other hematological abnormalities reported in the DM patients include RBCs, WBCs, and platelet dysfunction.<sup>9,10</sup>

Systematic review and meta-analysis of cross-sectional and prospective studies have shown that the number of peripheral WBCs such as basophils, eosinophils, and neutrophils increased, with no change in the number of monocytes in patients with T2DM.<sup>10</sup>

Hyperglycemia results in disturbances in cellular metabolism due increased production of reactive oxygen species (ROS) and nonenzymatic glycation of many macromolecules, which lead to changes in cellular structure and function, and formation of advanced glycation end products (AGEs). The formation of AGEs enhances metabolic disturbances and also increases reactive oxygen species production via interaction with the specific receptor for AGE (RAGE).<sup>11,12</sup> This causes changes in structure and biophysical properties of the basement membrane which further causes changes in permeability and vasodilatation of blood vessels.<sup>13</sup>

A study suggested that high platelet activity enhances vascular complications in DM patients.<sup>14</sup> Mean platelet volume (MPV) is a marker showing platelet function and activation. Altered platelet morphology and function can be reflected

as a factor for risk of microvascular and macrovascular diseases.<sup>15-17</sup> Several studies have reported that increased platelet reactivation in patients with diabetes may confer less cardiovascular protection with antiplatelet therapy, particularly aspirin.<sup>18,19</sup> It has already been demonstrated that insulin resistance (IR) and hyperinsulinemia are associated with the stimulation of erythroid progenitors and increased levels of inflammatory markers.<sup>20,21</sup>

Epidemiological study has indicated a close relationship between the WBC count and components of metabolic syndrome.<sup>22</sup> These abnormalities have been shown to markedly increase blood viscosity that unfavorably affects the microcirculation, leading to microangiopathy.<sup>23</sup> Studies revealed that higher WBC count, as one of the major components of inflammatory process, contributes to atherosclerotic progression and CVD.<sup>22,24-26</sup> Hematological indices are important indicators for the evaluation of variations in size, number, and maturity of different blood cells. They are important for the assessment and management of patients with DM. Therefore, this study aimed at determining hematological indices and their correlation with fasting blood glucose level and anthropometric measurement in T2DM patients in comparison with apparently healthy controls in Gondar, Northwest Ethiopia.

## Materials and methods

### Study design, period, and area

A comparative cross-sectional study was conducted from February to April, 2015 at the chronic illness clinic of Gondar University Hospital, Northwest Ethiopia. Gondar University Hospital has more than 500 inpatient beds and provides health referral service to over 5 million inhabitants in Northwestern Ethiopia. As a teaching hospital, it plays an important role in providing teaching, research, and community service. The Diabetes Illness Care Follow-up Clinic, which was organized 2 decades ago in the Gondar University Hospital, has been providing service to more than 8,000 diabetic patients.

### Study participants

The study was conducted on 148 T2DM patients (59 males and 89 females) aged between 25 and 70 years who were followed up at the chronic illness clinic of Gondar University Hospital. One hundred forty-eight (59 males and 89 females) age- and sex-matched apparently healthy individuals who had no previous history of chronic diseases were included as control subjects. The control group included individuals who were working at the University of Gondar and volunteer

nonremunerated blood donors at Gondar blood bank. T2DM patients who were severely ill, pregnant women, smokers, alcoholics, on antihypertensive treatment, on statins for abnormal lipid treatment, on insulin therapy, on anticoagulant therapy, and who had other chronic diseases were excluded from the study.

## Sample size and sampling technique

Two population mean formulae were used to calculate the sample size using OpenEpi, version 2, open source calculator by considering the following assumptions: 95% confidence interval (two-sided), 80% power, and ratio of cases to control group was 1:1. Taking the mean and standard deviation (SD) of hemoglobin (Hgb) for T2DM and control group from a study conducted in Bangladesh,<sup>27</sup> 12.76 and 1.49 for T2DM group and 13.26 and 1.3 for control group, the sample size was determined to be 148 for each group. Systematic random sampling technique was employed to select the study participants.

## Data collection and laboratory methods

Sociodemographic data were collected by trained nurses at the chronic illness clinic of Gondar University Hospital by using semistructured questionnaire. The data regarding anthropometric variables such as height (to the nearest centimeter without shoes), weight (to the nearest 0.1 kg), and waist circumference (WC) (taken midway between the lowest rib and the iliac crest) were collected. Body mass index (BMI) was calculated as weight in kilograms divided by height in meter squared. Blood pressure (BP) was taken by qualified personnel using an analog sphygmomanometer and stethoscope. Measurements were taken from the upper arm with the hand at the heart level after the patient had been sitting for more than 5 minutes. The anthropometric and BP measurements were taken twice and the average values were used for data analysis. Five milliliters of fasting blood sample was collected by laboratory technologist for fasting blood glucose (FBG) determination after 10–12 hours of fasting with the exception of water and medication. FBG was estimated by following glucose oxidase method using Bio systems A25 (Costa Brava, Spain) automated clinical chemistry analyzer according to manufacturer's instructions. Three milliliters venous blood samples were collected in test tubes, containing EDTA anticoagulant, for hematological tests and were analyzed using Sysmex KX-21N (Sysmex Corporation, Kobe, Japan) hematology analyzer. The results of the evaluation of other parameters such as Hgb, hematocrit

(Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), MPV, platelet distribution width (PDW), red cell distribution width (RDW), and the count of RBCs, WBCs, platelets, absolute lymphocytes, mixed cells (monocyte, basophil, and eosinophil [MID]), and neutrophils were recorded.

## Data management and quality control

The questionnaire was pretested for its accuracy and consistency prior to actual data collection and a half-day training program was conducted for the data collectors. Furthermore, the principal investigator provided feedback and corrections on a daily basis to the data collectors. Completion, accuracy, and clarity of the collected data were checked carefully on a regular basis. The results obtained from quality control samples must be within mean  $\pm$  2 standard deviation (SD) of the given Levy Jennings chart. Therefore, to ensure the quality of the final results, preanalytical, analytical, and postanalytical precautions were taken. Finally, the samples were processed within 1 hour of specimen collection in the hematology and clinical chemistry laboratory.

## Data analysis and interpretation

Data were entered and analyzed by using Statistical Package for Social Sciences (SPSS) version 20 (IBM Corporation, Armonk, NY, USA). The data were tested for normality with the help of histograms, by comparison of means and medians, and by performing skewness and Kolmogorov–Smirnov tests. Data were reported as mean and SD for continuous variables, percentages for categorical variables, and interquartile range for non-normally distributed data. Variables were compared using an independent sample *t*-test for normally distributed data and the Mann–Whitney *U*-test for non-normally distributed data. The strength of association between the pairs of variables was assessed by Pearson's and Spearman's rank correlation coefficient. A *P*-value  $<0.05$  was considered statistically significant.

## Ethical consideration

Ethical clearance was obtained from Research and Ethical Review Committee of School of Biomedical and Laboratory Sciences, College of Medicine and Health Sciences, University of Gondar. A permission letter was also taken from the Hospital director and head of the chronic illness clinic. In addition, written informed consent was obtained from the study participants before data collection. The data were kept confidential by using codes rather than any personal identifier,

and the results were communicated to the physicians at the chronic illness follow-up clinic.

## Results

### Demographic, clinical, and anthropometric characteristics of study participants

A total of 296 (148 T2DM patients and 148 controls) study subjects were included in this study. Of the total T2DM patients, 59 (39.9%) were males and 89 (60.1%) were females. Similarly, of the total 148 healthy controls, 59 (39.9%) and 89 (60.1%) were males and females, respectively. The mean age (mean ± SD) was 49.09±8.1 and 47.8±6.7 years for T2DM patients and controls, respectively. The results showed that the mean levels of BMI, WHR (waist to hip ratio), systolic and diastolic blood pressure (BP), and FBG levels were significantly higher ( $P < 0.05$ ) in patients with T2DM compared to controls. The mean duration of illness since diagnosis was 4.07±3.1 years for T2DM patients. The mean waist circumference (WC) showed statistically significant difference between the two groups ( $P = 0.001$ ) (Table 1).

### Comparison of hematological profile of the study participants

Regarding the WBC indices, statistically significant increment in total WBC ( $P = 0.000$ ), absolute neutrophil ( $P = 0.012$ ), and absolute lymphocyte ( $P = 0.0001$ ) counts were observed in the T2DM patients as compared to the control group. Among the RBC indices, only RDW showed statistically significant

increment in T2DM ( $P = 0.000$ ) patients. In addition, statistically significant increments in MPV ( $P = 0.001$ ) and PDW ( $P = 0.000$ ) were observed in T2DM patients as compared to the control group for platelet indices (Table 2).

### Correlations of hematological indices with FBG, duration of DM, and anthropometric measurements of study participants

The correlation of BMI with neutrophil count, RBC count, Hgb, and RDW values achieved significant but weak positive correlation in T2DM groups. Likewise, WHR achieved significant but weak positive correlation with RBC count, Hct, and Hgb in T2DM groups. Except for WHR and neutrophils that showed weak positive correlation ( $r = 0.175$ ;  $P = 0.033$ ), there was no statistically significant correlation between hematological profile and WHR in the control groups (Table 3).

Regarding the correlation of hematological indices with systolic and diastolic BP, only MCHC was found to be positively correlated with systolic BP ( $P = 0.005$ ) and only WBC count was negatively correlated with diastolic BP in the control group ( $P = 0.006$ ). However, in T2DM groups, MCV ( $P = 0.036$ ), platelet count ( $P = 0.000$ ), lymphocyte count

**Table 1** Demographic, clinical, and anthropometric characteristics of the study participants at Gondar University Hospital, Northwest Ethiopia, 2015 (n=296)

Variables	T2DM (Mean ± SD)	Controls (Mean ± SD)	P-value
Age (years)	49.09±8.1	47.8±6.8	0.149
Male/female, n(%)	59 (39.9%)/89(60.15)	59 (39.9%)/89(60.15)	1.000
BMI(kg/m <sup>2</sup> )	25.4±3.2	23.2±3.1	0.000
WC(cm)	83.02±12.6	78.67±10.2	0.001
WHR	0.88±0.88	0.84±0.66	0.000
Blood pressure (mmHg)			
Systolic BP	130 (120–140)*	110 (110–120)*	0.000
Diastolic BP	80 (70–88)*	70 (70–80)*	0.000
FBG level (mg/dL)	163.7±1.33	81.3±1.08	0.000
Duration of DM in year	4.07±3.1		0.000

**Note:** \*Presented as median and interquartile range.

**Abbreviations:** DM, diabetes mellitus; T2DM, type 2 diabetes mellitus; SD, standard deviation; BMI, body mass index; WHR, waist to hip ratio; FBG, fasting blood glucose; BP, blood pressure; WC, waist circumference.

**Table 2** Comparison of hematological indices of the study participants at Gondar University Hospital, Northwest Ethiopia, 2015 (n=296)

Variables	Mean ± SD (T2DM)	Mean ± SD (Controls)	P-value
<b>White blood cell indices</b>			
WBCs (10 <sup>3</sup> /μL)	6.59±1.42	5.56±1.38	0.000
Lymphocytes (10 <sup>3</sup> /μL)	2.60±0.70	2.04±0.63	0.000
Neutrophils (10 <sup>3</sup> /μL)	3.57±1.46	3.11±1.04	0.012
MID (10 <sup>3</sup> /uL)	0.80±0.53	0.71±0.43	0.120
<b>Red blood cell indices</b>			
RBCs (10 <sup>6</sup> /μL)	5.12±0.57	5.1±0.54	0.755
Hgb (g/dL)	15.2±1.7	15.1±1.5	0.739
Hct (%)	46.7±5.1	46.4±4.2	0.609
MCV (fL)	91.7±5.0	90.7±4.3	0.056
MCH (pg)	29.7±2.6	30.0±5.3	0.086
MCHC (g/dL)	32.6±2.0	32.5±1.0	0.772
RDW (fL)	47.3±2.6	45.2±3.0	0.000
<b>Platelet indices</b>			
Platelet (10 <sup>3</sup> /μL)	255.7±82.0	246.3±67.4	0.280
MPV (fL)	10.4±1.1	9.9±1.1	0.001
PDW (fL)	14.5±2.1	13.4±2.1	0.000

**Note:** P-value <0.05 is considered statistically significant.

**Abbreviations:** T2DM, type 2 diabetes mellitus; WBC, white blood cell; MID, monocyte, basophil, and eosinophil; RBC, red blood cell; 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; PDW, platelet distribution width; SD, standard deviation.

**Table 3** Pearson's correlations(*r*) of hematological indices with BMI and WHR among T2DM patients and healthy controls at Gondar University Hospital, Northwest Ethiopia, 2015 (n=296)

Variables	T2DM group		Control group	
	BMI <i>r</i> ( <i>P</i> )	WHR <i>r</i> ( <i>P</i> )	BMI <i>r</i> ( <i>P</i> )	WHR <i>r</i> ( <i>P</i> )
WBC	0.089 (0.282)	0.088 (0.285)	0.070 (0.400)	0.161 (0.051)
Lymphocytes	0.031 (0.705)	0.114 (0.168)	0.189* (0.021)	0.145 (0.078)
Neutrophils	0.163* (0.048)	0.088 (0.287)	0.045 (0.591)	0.175* (0.033)
MID	-0.135 (0.101)	0.044 (0.598)	-0.095 (0.253)	-0.073 (0.381)
RBC	0.188* (0.022)	0.196* (0.017)	-0.132 (0.108)	-0.066 (0.427)
Hct	0.112 (0.174)	0.190* (0.021)	0.163* (0.048)	-0.048 (0.565)
Hgb	0.167* (0.042)	0.167* (0.042)	-0.156 (0.058)	-0.020 (0.807)
MCV	-0.091 (0.269)	-0.061 (0.461)	0.006 (0.945)	0.071 (0.389)
MCH	-0.167* (0.043)	-0.023 (0.779)	-0.084 (0.312)	-0.013 (0.871)
MCHC	-0.099 (0.230)	0.200* (0.015)	-0.028 (0.738)	-0.044 (0.596)
RDW	0.177* (0.032)	0.089 (0.281)	0.009 (0.918)	0.072 (0.385)
Platelets	-0.037 (0.659)	0.052 (0.528)	0.090 (0.277)	0.018 (0.830)
PDW	-0.123 (0.136)	-0.024 (0.771)	-0.032 (0.701)	-0.039 (0.641)
MPV	-0.101 (0.224)	0.070 (0.397)	-0.034 (0.680)	0.128 (0.120)

**Notes:** \*Correlation is significant at 0.05 level (two-tailed), *P*-value <0.05 is considered statistically significant; *r* is the correlation coefficient and *P* is the *P*-value.

**Abbreviations:** T2DM, type 2 diabetes mellitus; WHR, Waist to hip ratio; BMI, body mass index; WBC, white blood cell; MID, monocyte, basophil, and eosinophil; RBC, red blood cell; 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; PDW, platelet distribution width.

(*P*=0.002), and MPV count (*P*=0.046) achieved statistically significant correlation with systolic BP, while WBC count (*P*=0.013) and platelet count (*P*=0.000) showed significant negative correlation with diastolic BP (Table 4).

In the T2DM groups, FBG showed a significant positive correlation with total WBC count (*P*=0.007), absolute lymphocyte count (*P*=0.034), absolute neutrophil count (*P*=0.033), and MPV (*P*=0.042). However, no statistically significant correlation

was observed between hematological indices and FBG in the control group. Moreover, duration of illness in T2DM patients achieved significant positive correlation with MPV (*P*=0.004) and platelet count (*P*=0.011) (Table 5).

## Discussion

Research evidences suggest that hematological indices are altered in patients with T2DM.<sup>28</sup> In patients with DM,

**Table 4** Spearman's correlations (*rho*) of hematological indices with systolic and diastolic BP among T2DM patients and healthy controls at Gondar University Hospital, Northwest Ethiopia, 2015 (n=296)

Variables	T2DM group		Control group	
	SBP <i>rho</i> ( <i>P</i> )	DBP <i>rho</i> ( <i>P</i> )	SBP <i>rho</i> ( <i>P</i> )	DBP <i>rho</i> ( <i>P</i> )
WBC	0.110 (0.183)	-0.205* (0.013)	0.089 (0.284)	-0.277* (0.006)
Lymphocytes	0.062* (0.002)	-0.154 (0.061)	0.065 (0.435)	0.047 (0.570)
Neutrophils	0.094 (0.256)	-0.110 (0.182)	0.070 (0.398)	-0.259 (0.551)
MID	0.008 (0.920)	0.089 (0.282)	0.020 (0.807)	-0.109 (0.187)
RBC	0.190* (0.021)	0.122 (0.139)	0.046 (0.576)	0.095 (0.253)
Hct	0.116** (0.003)	0.150 (0.068)	0.239 (0.161)	0.107 (0.196)
Hgb	0.294** (0.000)	0.094 (0.254)	0.090 (0.274)	0.141 (0.088)
MCV	0.172* (0.036)	0.055 (0.504)	0.007 (0.937)	0.002 (0.982)
MCH	0.059 (0.473)	-0.045 (0.586)	0.106 (0.198)	0.067 (0.422)
MCHC	-0.059 (0.476)	-0.130 (0.116)	0.230* (0.005)	0.149 (0.071)
RDW	0.069 (0.407)	0.088 (0.287)	0.154 (0.062)	0.084 (0.311)
Platelets	0.640** (0.000)	-0.321** (0.000)	0.095 (0.250)	-0.148 (0.073)
PDW	-0.133 (0.107)	0.069 (0.406)	-0.092 (0.265)	0.027 (0.744)
MPV	0.579* (0.046)	0.040 (0.633)	0.066 (0.426)	0.073 (0.376)

**Notes:** \*\*Correlation is significant at 0.01 level; \*correlation is significant at 0.05 level (two-tailed); *P*-value <0.05 is considered statistically significant; *rho* is the correlation coefficient.

**Abbreviations:** BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; T2DM, type 2 diabetes mellitus; WBC, white blood cell; MID, monocyte, basophil, and eosinophil; RBC, red blood cell; 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; PDW, platelet distribution width.



**Table 5** Pearson's correlations(*r*) of hematological indices with FBG level and duration of illness among T2DM patients and healthy controls at Gondar University Hospital, Northwest Ethiopia, 2015 (n=296)

Variables	T2DM group		Control group
	FBG <i>r</i> ( <i>P</i> )	Duration of T2DM <i>r</i> ( <i>P</i> )	FBG <i>r</i> ( <i>P</i> )
Total WBC count	0.221** (0.007)	-0.004 (0.962)	0.008 (0.923)
Absolute lymphocytes	0.174* (0.034)	-0.023 (0.777)	0.119 (0.149)
Absolute neutrophils	0.175* (0.033)	0.003 (0.970)	-0.033 (0.692)
MID	0.083 (0.316)	-0.156 (0.058)	-0.014 (0.865)
RBC	0.129 (0.118)	0.081 (0.325)	0.047 (0.570)
Hct	0.106 (0.201)	0.013 (0.873)	0.010 (0.905)
Hgb	0.149 (0.070)	0.048 (0.566)	0.026 (0.758)
MCV	0.036 (0.663)	-0.073 (0.379)	-0.081 (0.328)
MCH	0.083 (0.315)	-0.057 (0.488)	-0.045 (0.587)
MCHC	0.159 (0.053)	0.038 (0.642)	-0.021 (0.798)
RDW	-0.120 (0.148)	-0.072 (0.384)	-0.094 (0.254)
Platelets	-0.048 (0.559)	0.234** (0.004)	0.029 (0.729)
PDW	0.038 (0.643)	-0.006 (0.945)	0.008 (0.927)
MPV	0.614* (0.042)	0.207* (0.011)	0.007 (0.936)

**Notes:** \*\*Correlation is significant at 0.01 level; \*correlation is significant at 0.05 level (two-tailed); *r* is the correlation coefficient.

**Abbreviations:** FBG, fasting blood glucose; T2DM, type 2 diabetes mellitus; WBC, white blood cell; MID, monocyte, basophil, and eosinophil; RBC, red blood cell; 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; PDW, platelet distribution width.

persistent hyperglycemia exposes RBCs to elevated glucose concentrations, thus resulting in glycation of hemoglobin, prothrombin, fibrinogen, and other proteins involved in clotting mechanisms.<sup>29</sup> In this study, RBC indices had shown increment in diabetic patients as compared to control group, although the difference was not statistically significant. This finding is in agreement with that reported by several previous studies.<sup>22,30,31</sup> This might be the indirect features of IR syndrome, since it is associated with increased WBC and RBC counts, and increased levels of Hgb and Hct.<sup>20</sup> Significant elevations of Hct and MCV might be due to the variety of morphological changes exhibited by RBCs and compositional changes in plasma associated with T2DM.<sup>32</sup>

In contrast to this study, a study conducted on Chinese patients with T2DM reported that a decreased RBC count is associated with microvascular complications.<sup>33</sup> Likewise, a study performed in Tobago (Caribbean) reported that RBC count, Hgb concentration, and Hct levels in T2DM patients are lower than in the control group.<sup>34</sup> The possible hypothesis for this difference might be that chronic hyperglycemia causes nonenzymatic glycosylation of RBC membrane proteins leading to accelerated aging of RBCs.<sup>35</sup> Similar study on middle-aged and elderly Chinese population in Taiwan also contradicts our finding as it is reported a reduced RBC count in patients with IR. But similar to the results obtained in our study, there was no statistically significant difference in Hgb levels between T2DM patients and control group.<sup>22</sup> Another study observed that diabetics are prone to anemia

due to reduced kidney functions and decreased production of erythropoietin hormone, which ultimately leads to decreased RBC count in the body.<sup>35</sup>

Among the RBC indices, only RDW values achieved statistically significant difference between T2DM and control groups. This finding is in accordance with the previous findings.<sup>22,36-39</sup> This is due to the fact that high RDW indicates impairment of erythropoiesis, reflecting chronic inflammation and increased levels of oxidative stress, both of which are significant signs of T2DM that result in the RBC size variation.<sup>40</sup> In contrary, studies in Turkey and Nigeria reported that significant difference was not observed between cases and controls in RDW level.<sup>39,40</sup> Differences in study design and ethnic and cultural differences across the study populations may account for the variability of RDW across studies.

In the present study, WBC indices increased significantly in the T2DM group compared with the control group. The reason for this variation might be due to the fact that the high WBC count in the T2DM group is in keeping with the increased oxidative stress triggered by the high levels of hyperglycemia. Thus, polymorphonuclear and mononuclear WBCs can be activated by AGEs and cytokines in a state of hyperglycemia.<sup>41</sup> One study has also indicated that WBC count is elevated in the T2DM patients and may contribute to the vascular complications.<sup>41</sup> Evidence from epidemiological studies suggested an association between WBC count, development of vascular complications, and diabetes risk,<sup>22,25,42</sup> and the authors reported that total and differential WBC

counts are higher in T2DM compared to apparently healthy individuals in congruence to our study.

In one study, the absolute MID count showed an increase but no significant difference was found to exist between the two groups. This is in agreement with the previously published reports of the Atherosclerosis Risk in Communities study.<sup>43</sup> Biological evidence suggests that inflammation might induce T2DM and epidemiological studies have also shown an association between higher WBC and T2DM.<sup>22,25</sup> However, the association has not been systematically investigated in this study. Several other previous studies, consistent to our study, reported that an increase in WBC count, even within the normal range, was found to be associated with the development of complications in T2DM patients.<sup>44-46</sup> The authors also reported that peripheral total WBC, monocyte, and neutrophil counts increased in parallel with the progression of complications.<sup>44-46</sup>

This study also included the comparison of the platelet indices between the control and the diabetic patients. We observed no significant difference in platelet count between diabetic and control groups. However, statistically significant increment in MPV and PDW were found in T2DM patients, which is in accordance with several studies that have shown an increased number of large circulating platelets compared with controls.<sup>39,47-51</sup> The reason might be related to the vascular complications in DM patients. There might be small vascular bleeds due the rupture of athrothrombotic plaques leading to bone marrow stimulation to recruit larger hyperactive platelets.<sup>30,52</sup> Moreover, osmotic swelling of platelets, as a result of hyperglycemia and the platelet granule secretions, may contribute to platelet size variation and MPV elevation in T2DM patients.<sup>30</sup> The other factors might be due to differences in platelet function between diabetic and control individuals.<sup>18</sup> Among the diabetic individuals, increased platelet aggregability and adhesiveness may be due to different reasons including reduced membrane fluidity, altered calcium and magnesium ion homeostasis, increased arachidonic acid metabolism leading to enhanced thromboxane A<sub>2</sub> (TXA<sub>2</sub>) production, decreased nitric oxide production, decreased antioxidant levels, and increased expression of activation-dependent adhesion molecules in DM patients.<sup>53,54</sup> Moreover, studies have reported that increment of immature platelet levels, platelet aggregation, and platelet activation are common in T2DM patients with coronary artery diseases, even on those who are on aspirin treatment aimed to protect vascular damage.<sup>18,19</sup> Besides, poor metabolic control, IR, low-grade inflammation, and hyperglycemia in T2DM patients have been suggested as factors influencing platelet function in addition to high platelet turnover.<sup>55</sup>

In this study, correlation of hematological indices with FBG, BP, duration of T2DM since diagnosis, BMI, and WHR was determined. The variables above the threshold cutoff values were found to be the forecasters of CVD in numerous populations. In our study, RBC, Hgb, MCH, and RDW achieved significant correlation with BMI and WHR. This is in harmony with a previous study conducted in Toronto and London, Ontario, Canada.<sup>56</sup> A similar study in Brazil demonstrated an association between the hematological indices and body adiposity.<sup>57</sup> A study on middle-aged and elderly Chinese people with T2DM found that WBC count was positively correlated with WHR and BMI.<sup>58</sup> In contrast to our study, a study in North-East Italy cohort reported that no associations were found between hematological indices and BMI in lean, overweight, or obese subgroups.<sup>59</sup> The discrepancy might be due to the differences in study design and study population.

With respect to the correlation of hematological indices with systolic and diastolic BP in T2DM groups, MCV, platelet count, lymphocyte count, and MPV achieved statistically significant correlation with systolic BP. Besides, WBC and platelet counts showed significant negative correlation with diastolic BP. The relationship between level of BP and hematological indices may be due to the development of diabetes-related hypertension and dyslipidemia.<sup>60,61</sup> Researchers reported an increased prevalence of hypertension in diabetics than in the non-diabetic individuals. They hypothesized that chronic hyperglycemia produces a direct, toxic effect on vascular endothelial cells, and this condition can lead to increased vasoconstriction and vascular remodeling ultimately affecting the blood cells.<sup>62</sup>

In the present study, we found significant correlation of MCV and WBC with levels of systolic and diastolic BP in T2DM patients. In the control group, RBC, Hct, Hgb, and MCHC values achieved significant correlation. Other recent cross-sectional survey on 32,004 patients showed that coexistence of high BP and abnormal glucose metabolism is common.<sup>63</sup> In our study, FBG level had statistically significant correlation with WBC, lymphocyte, and neutrophil counts in T2DM patients. Congruent to ours, a study in Pakistan indicated that granulocyte count was positively correlated with FBG.<sup>47</sup> Evidence suggests that disease chronicity and hyperglycemia have effects on sensorimotor control in DM patients.<sup>64</sup> Duration of DM since diagnosis achieved significant correlation with platelet count. Clinically elevated platelet counts are frequently observed in diabetics with a long duration of disease.

## Conclusion and recommendation

FBG, MPV, PDW, absolute lymphocyte count, absolute neutrophil count, total white cell count, RDW, BMI, and WHR are significantly higher among diabetic subjects compared to apparently healthy controls. This is a reflection of poor glycaemic control and lifestyle changes. FBG is significantly correlated with total WBC, absolute lymphocyte and neutrophil counts, and MPV. The routine hematological profile checking of patients with T2DM may help to prevent complications associated with aberrations in hematological values. The limitation of this study is it does not evaluate a cause–effect relationship between variables and diabetes because of cross-sectional nature of the study design.

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## Author contributions

BB designed and implemented the study, collected data, undertook statistical analysis, performed data interpretation, and drafted the manuscript. MA, SMA, and MM participated in data analysis and data interpretation and reviewed the manuscript. All authors contributed toward data analysis, drafting, and critically revising the paper and agree to be accountable for all aspects of the work.

## Disclosure

The authors report no conflicts of interest in this work.

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