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RESEARCH ARTICLE

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Associations of complete blood count parameters with pancreatic beta-cell function and insulin resistance in prediabetes and type 2 diabetes mellitus

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Abstract

Introduction: Previous studies found controversial associations of CBC parameters with pancreatic beta-cell function (BCF) and insulin resistance (IR). The aim of this was to determine the independent associations of CBC parameters with BCF and IR in prediabetes and type 2 diabetes mellitus (T2DM).

Methods: This study selected subjects who underwent health checkups at 16 health-promotion centers in 13 Korean cities during 2021. The subjects comprised 1470 patients with normoglycemia, 1124 with prediabetes, and 396 with T2DM. BCF and IR were assessed using the homeostasis model assessment (HOMA)-β and HOMA-IR, respectively. Correlation and multiple linear regression analyses were used to determine the correlation between CBC parameters and HOMA.

Results: While HOMA-IR gradually increased according to red blood cell count quartiles (1.22, 1.40, 1.47, and 1.91, in the first, second, third, and fourth quartiles, respectively; $p < 0.001$), there was no correlation after adjusting for waist circumference (WC) and HbA1c. The red blood cell distribution width (RDW) was associated with HOMA-β [coefficient (β) = 15.527, $p = 0.002$], but not with HOMA-IR. White blood cells (WBCs) were associated with HOMA-IR and HOMA-β, which was stronger in HOMA-β ($\beta = 0.505$ vs 15.171, $p = 0.002$) after adjusting for WC and HbA1c. The platelet count was correlated with HOMA-IR and HOMA-β, which only remained in HOMA-β ($\beta = 15.581$, $p = 0.002$) after adjusting for WC and HbA1c.

Conclusion: RDW, WBC, and platelet counts were independently associated with only HOMA-β in prediabetes and T2DM. This suggests that these CBC parameters could represent BCF in prediabetes and T2DM.

KEYWORDS
complete blood count parameters, homeostasis model assessment, insulin resistance, pancreatic beta-cell function, type 2 diabetes mellitus

1 | INTRODUCTION

The pathophysiology of type 2 diabetes mellitus (T2DM) involves insulin resistance (IR) and progressive deterioration of beta-cell function (BCF).[1-3] Estimation of IR and BCF is essential for screening subjects at a high risk of T2DM and making treatment plans in clinical practice. There are several methods for estimating the underlying status of glucose tolerance in hyperglycemia.[4] The homeostasis model assessment (HOMA) has been used to assess the relationship between glucose and insulin balance during fasting.[5-7] HOMA-β therefore evaluates BCF by calculating the ratio of fasting insulin to fasting blood glucose (FBG) concentrations. The reverse equation is performed to determine the HOMA-IR, an index of fasting IR.

Along with other routine tests, the complete blood count (CBC) is widely used by physicians in health checkups to determine the status of patients and healthy people. Due to its low cost and easy accessibility, CBC can be an appropriate approach for investigating and diagnosing various diseases such as anemia, infection, coagulation disorder, and hematologic malignancies.[8-10] Advances in technology make it possible for automatic cell counters to measure hematologic parameters related to variations in the shape and size of cells in addition to quantitative blood cell measurements, which contribute to the diagnosis and monitoring of many diseases.

T2DM and related conditions are associated with subclinical inflammation. Several CBC parameters have been reported as a marker of inflammatory burden in T2DM.[11-13] Mean platelet volume was considered as a marker of the inflammatory burden in T2DM. The red cell distribution width (RDW) was also suggested as an important predictor of vascular complications of diabetes mellitus. Some studies have found associations between T2DM and CBC parameters such as the RDW[14-16] and the red blood cell (RBC) count.[17,18] In a 5-year follow-up study, high RDW was associated with a high risk of developing diabetes in Chinese adults.[14] Meanwhile, Engström et al.[15] found an independent association between low RDW and increased diabetes incidence. Furthermore, a study of a sample of Chinese patients with T2DM[16] demonstrated that RDW values were significantly associated with HOMA2-β and HbA1c, but found no correlation between RDW and HOMA2-IR.

This study therefore aimed to determine the associations of CBC parameters from a health checkup cohort with prediabetes and T2DM, and HOMA-β and HOMA-IR after adjusting for potential confounding factors.

2 | METHOD

2.1 | Study subjects and data

We analyzed data from health examinees that underwent health checkups at 16 health-promotion centers in 13 Korean cities during 2021. The subjects comprised 1470 patients with normoglycemia, 1124 with prediabetes, and 396 with diabetes. Prediabetes and T2DM were defined according to the guidelines of the American Diabetes Association.[19] Subjects with missing results on laboratory tests for HOMA or with no information on age, sex, or laboratory data were excluded. The medical records of the subjects were also reviewed. The study protocol was reviewed and approved by the institutional review board of the Korea Association of Health Promotion (approval no. 130750-202109-HR-007). The requirement for informed consent was waived due to the retrospective study design, and the analysis used anonymous clinical data.

2.2 | Laboratory measurements

CBC parameters including hemoglobin level, RBC indices, and white blood cell (WBC), and platelet counts were measured using the Sysmex XE-2100D analyzer (Sysmex, Kobe, Japan). Examinees discontinued using antiplatelet agents or other nonsteroidal anti-inflammatory drugs 1 week before the health checkup. Blood samples were collected from the antecubital vein of each subject while in a sitting position after fasting for >8 h. Blood samples in EDTA tubes were stored at room temperature and analyzed by a technician within 2 h of collection. Biochemical measurements, including those of fasting serum glucose, triglycerides, high-density lipoprotein cholesterol, and creatinine were made using the Hitachi 7600 analyzer (Hitachi, Tokyo, Japan). HbA1c levels were measured using ion-exchange high-performance liquid chromatography using the HLC-723 G8 analyzer (Tosoh, Tokyo, Japan). Serum insulin was measured using an electrochemiluminescence immunoassay with the Cobas e801 (Roche Diagnostics, Mannheim, Germany).

2.3 | Calculation of HOMA-β and HOMA-IR

HOMA-β and HOMA-IR were calculated using the following formulas[5,6]:

$$\text{HOMA-}\beta = [20 \times \text{fasting insulin level } (\mu\text{U/mL})]/[\text{FBG (mmol/L)} - 3.5].$$

$$\text{HOMA-IR} = [\text{fasting insulin level } (\mu\text{U/mL}) \times \text{FBG (mmol/L)}]/22.5.$$

2.4 | Statistical analyses

Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA). The Kolmogorov–Smirnov test was performed to assess the normality of each variable. ANOVA with the Scheffe test was used for multiple comparisons, and the chi-square tests were used to compare parameters of the study subjects according to their FBG levels. Differences in HOMA-IR and HOMA-β among CBC parameter quartiles were analyzed using the Kruskal–Wallis tests, with the Dunn's test used for multiple comparisons. The association of CBC parameters with HOMA-IR and HOMA-β was analyzed by stratifying CBC parameters into quartiles. Multiple

TABLE 1 Characteristics of study subjects

	Total	NG	Pre-DM	T2DM		Multiple comparison[†]
	(*N* = 2990)	(*N* = 1470)	(*N* = 1124)	(*N* = 396)	*P*	
Sex, male	1564 (52.3)	659 (44.8)	654 (58.2)	251 (63.4)	<0.001	
Age, years	47.1 ± 12.3	42 ± 10.7	50.6 ± 11.7	55.9 ± 10.9	<0.001	a<b<c
BMI, kg/m^2	24.1 ± 3.6	23.2 ± 3.3	24.8 ± 3.4	26.4 ± 4.1	<0.001	a<b<c
WC, cm	81.6 ± 10.2	78.8 ± 9.6	84 ± 9.5	88.5 ± 10.8	<0.001	a<b<c
SBP, mmHg	116.6 ± 14.3	113.6 ± 13.5	118.7 ± 14.2	124.3 ± 14.6	<0.001	a<b<c
DBP, mmHg	73.4 ± 9.5	71.7 ± 9.0	74.8 ± 9.7	77.1 ± 9.6	<0.001	a<b<c
TC, mmol/L	5.2 ± 1.0	5.2 ± 0.9	5.4 ± 1	5 ± 1.3	<0.001	c<a<b
TG, mmol/L	1.4 ± 1.3	1.2 ± 0.9	1.6 ± 1.2	2.1 ± 2.3	<0.001	a<b<c
HDLC, mmol/L	1.4 ± 0.3	1.5 ± 0.4	1.4 ± 0.3	1.3 ± 0.3	<0.001	c<b<a
LDLC, mmol/L	3.2 ± 0.9	3.2 ± 0.9	3.3 ± 0.9	2.9 ± 1.1	<0.001	c<a<b
FPG, mmol/L	5.5 ± 1.4	4.9 ± 0.4	5.6 ± 0.6	8.1 ± 2.5	<0.001	a<b<c
HbA1C, mmol/mol	40.3 ± 10.9	34.8 ± 2.5	40.1 ± 3.3	60.1 ± 17.8	<0.001	a<b<c
Insulin, μU/mL	6.07 ± 5.89	5 ± 3.2	6.3 ± 4.1	9.3 ± 12.7	<0.001	a<b<c
HsCRP, mg/dL	0.14 ± 0.31	0.11 ± 0.24	0.13 ± 0.19	0.28 ± 0.68	<0.001	a,b<c
Creatinine, μmol/L	84.2 ± 18.1	82 ± 19	87.2 ± 16.6	84.9 ± 17.2	<0.001	a<b,c
eGFR, mL/min/1.73 m^2	81.42 ± 14.21	83.7 ± 14.22	78.36 ± 13.27	80.63 ± 15.43	<0.001	b,c<a
Complete blood count						
RBC characteristics						
RBC count, 10^{12}/L	4.7 ± 0.5	4.6 ± 0.5	4.7±0.4	4.8±0.5	<0.001	a<b<c
Hb, g/dL	14.3±1.5	14.1±1.5	14.3±1.5	14.8±1.5	<0.001	a<b<c
MCV, fL	90.9±4.4	90.8±4.4	91.1±4.6	90.7±4.2	0.238	
MCH, pg/cell	30.6±1.9	30.5±1.9	30.6±1.9	30.8±1.7	0.021	a<c
MCHC, g/dL	33.6±1	33.6±1	33.6±1	34±1.1	<0.001	a,b<c
RDW, %	12.6±1	12.6±1.1	12.7±1	12.5±0.9	0.002	c<b
WBC characteristics						
WBC count, 10^9/L	5.9±1.6	5.6±1.5	6±1.5	6.7±1.8	<0.001	a<b<c
Platelet characteristics						
PLT count, 10^9/L	251±55.7	251±52.9	253.6±58.8	243.3±56	0.007	c<a,b
MPV, %	10±0.83	10.03±0.84	9.97±0.81	10±0.81	0.183	
PDW, %	11.3±1.7	11.4±1.7	11.3±1.7	11.4±1.7	0.255	
HOMA-IR	1.5±1.8	1.1±0.7	1.6±1.1	3.2±4.1	<0.001	a<b<c
HOMA-β	66.8±57.6	72.7±54.9	63.5±44.5	52.5±92.5	<0.001	c<b<a

Note: Data are N (%) or mean ± SD values.

There are missing data.

Multiple comparison method is the Scheffe's test.

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; Hb, hemoglobin; HDLC, high-density lipoprotein cholesterol; HOMA, homeostasis model assessment; hsCRP, high-sensitivity C-reactive protein; LDLC, low-density lipoprotein cholesterol; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; MPV, mean platelet volume; NG, normoglycemia; PDW, platelet distribution width; PLT, platelet; RBC, red blood cell; RDW, red blood cell distribution width; SBP, systolic blood pressure; T2DM, type 2 diabetes mellitus; TC, total cholesterol; TG, triglycerides; WBC, white blood cell; WC, waist circumference.

[†]a: NG, b: pre-DM, c: T2DM.

linear regression analyses were conducted to determine whether CBC parameters were associated with HOMA-IR and HOMA-β before and after adjusting for potential confounding factors. Model 1 was unadjusted, model 2 was adjusted for age and sex, and model 3 was adjusted for age, sex, waist circumference (WC), and HbA1c. $p < 0.05$ was considered statistically significant.

TABLE 2 Correlation coefficient between insulin resistance and the complete blood count (CBC) parameters in hyperglycemia

	HOMA-IR						HOMA-β					
	Total		Pre-DM		T2DM		Total		Pre-DM		T2DM	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*
RBC parameters												
RBC count, 10^{12}/L	**0.218**	**<0.001**	**0.185**	**<0.001**	**0.204**	**<0.001**	0.04	0.13	**0.118**	**<0.001**	−0.042	0.441
Hb, g/dL	**0.183**	**<0.001**	**0.137**	**<0.001**	**0.166**	**0.002**	**−0.069**	**0.009**	0.002	0.96	**−0.138**	**0.011**
MCV, fL	**−0.114**	**<0.001**	**−0.097**	**0.001**	**−0.149**	**0.006**	**−0.137**	**<0.001**	**−0.196**	**<0.001**	−0.035	0.523
MCH, pg/cell	−0.048	0.069	**−0.07**	**0.02**	−0.099	0.068	**−0.206**	**<0.001**	**−0.21**	**<0.001**	**−0.173**	**0.001**
MCHC, g/dL	**0.078**	**0.003**	0.01	0.739	0.073	0.178	**−0.164**	**<0.001**	**−0.114**	**<0.001**	**−0.198**	**<0.001**
RDW, %	−0.043	0.103	−0.019	0.534	0.02	0.716	**0.202**	**<0.001**	**0.124**	**<0.001**	**0.326**	**<0.001**
WBC parameters												
WBC count, 10^9/L	**0.273**	**<0.001**	**0.219**	**<0.001**	**0.242**	**<0.001**	**0.14**	**<0.001**	**0.218**	**<0.001**	**0.168**	**0.002**
Platelet parameters												
PLT count, 10^9/L	**0.071**	**0.007**	**0.112**	**<0.001**	**0.09**	**0.097**	**0.161**	**<0.001**	**0.158**	**<0.001**	**0.113**	**0.037**
MPV, %	0.016	0.54	−0.018	0.543	**0.129**	**0.017**	0.045	0.084	0.037	0.219	0.067	0.218
PDW, %	**0.053**	**0.043**	0.012	0.699	**0.153**	**0.005**	0.049	0.061	0.055	0.067	0.059	0.281

Note: Bold face indicates statistical significance.

Abbreviations: RBC, red blood cell; Hb, hemoglobin; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; RDW, red blood cell distribution width; WBC, white blood cell; PLT, platelet; MPV, mean platelet volume; PDW, platelet distribution width; DM, diabetes mellitus.

3 | RESULTS

3.1 | Study subject characteristics according to FBG group

Table 1 lists the characteristics of all 2990 study subjects, who were aged 47.1 ± 12.3 years (mean ± SD; 1564 males and 1426 females). Those with higher FBG had higher serum insulin levels (p <0.001). The mean HOMA-β values were significantly lower (p < 0.001) and HOMA-IR levels were significantly higher in the prediabetes and diabetes groups (p < 0.001). RBC and WBC counts were higher in patients with prediabetes and T2DM than in those with normoglycemia (p < 0.001). RDW was higher in prediabetes than in T2DM (p = 0.002) (Table 1).

TABLE 3 HOMA-IR and HOMA-β according to the complete blood count (CBC) quartiles

	Quartile					
	Q1	Q2	Q3	Q4	$P^{\dagger}$	Multiple comparisons
RBC count, 10^{12}/L						
Range (min, max)	(3.1, 4.39)	(4.4, 4.69)	(4.7, 5.01)	(5.02, 6.12)		
HOMA-IR	1.22 (0.07, 12.75)	1.40 (0.07, 56.81)	1.47 (0.17, 22.52)	1.91 (0.22, 25.64)	<0.001	Q1<Q3<Q4, Q2<Q4
HOMA-β	49.25 (4.42, 298.30)	47.04 (2.18, 1470.83)	44.23 (2.65, 457.66)	54.45 (1.00, 394.01)	0.007	Q3<Q4
Hb, g/dL						
Range (min, max)	(8.4, 13.4)	(13.5, 14.4)	(14.5, 15.4)	(15.5, 18.3)		
HOMA-IR	1.3 (0.07, 12.75)	1.42 (0.13, 56.81)	1.4 (0.07, 25.64)	1.83 (0.17, 22.52)	<0.001	Q1,Q2,Q3<Q4
HOMA-β	52.72 (4.42, 303.90)	49.07 (5.10, 1470.83)	43.23 (2.46, 394.01)	48.77 (1.00, 457.66)	<0.001	Q1>Q3
RDW, %						
Range (min, max)	(10.8, 11.9)	(12.0, 12.4)	(12.5, 12.9)	(13.0, 21.7)		
HOMA-IR	1.54 (0.18, 22.52)	1.58 (0.07, 56.81)	1.38 (0.11, 8.11)	1.44 (0.13, 25.64)	0.204	
HOMA-β	39.71 (2.65, 457.66)	46.31 (1, 1470.83)	48.24 (5.47, 282.28)	57.12 (2.18, 586.50)	<0.001	Q1<Q2,Q3<Q4
WBC count, 10^{9}/L						
Range (min, max)	(2.6, 4.9)	(5.0, 5.8)	(5.9, 6.8)	(6.9, 15.2)		
HOMA-IR	1.17 (0.07, 8.46)	1.31 (0.07, 25.64)	1.63 (0.13, 8.83)	1.95 (0.17, 56.81)	<0.001	Q1<Q2<Q3<Q4
HOMA-β	42.9 (2.46, 167.18)	46.77 (4.76, 394.01)	50.34 (1.00, 586.50)	54.05 (2.18, 1470.83)	<0.001	Q1<Q3,Q4, Q2<Q4
PLT count, 10^{9}/L						
Range (min,max)	(105, 208)	(209, 245)	(246, 284)	(285, 554)		
HOMA-IR	1.49 (0.07, 17.68)	1.3 (0.13, 14.98)	1.52 (0.07, 9.27)	1.58 (0.17, 56.81)	0.003	Q2<Q3,Q4
HOMA-β	43.33 (4.55, 342.91)	45.61 (2.18, 298.3)	49.15 (1.00, 196.87)	56.98 (5.10, 1470.83)	<0.001	Q1,Q2,Q3<Q4
PDW, %						
Range (min, max)	(7.6, 10.0)	(10.1, 11.0)	(11.1, 12.2)	(12.3, 22.2)		
HOMA-IR	1.43 (0.11, 11.39)	1.375 (0.17, 56.81)	1.545 (0.07, 25.64)	1.51 (0.15, 14.98)	0.189	
HOMA-β	44.86 (2.65, 282.28)	46.65 (5.32, 1470.83)	51.59 (1.00, 586.50)	49.35 (2.18, 342.91)	0.035	Q1<Q3

Note: Data are median (min, max) values except where indicated otherwise.

Multiple comparison method is the Dunn's method.

Abbreviations: RBC, red blood cell; Hb, hemoglobin; RDW, red blood cell distribution width; WBC, white blood cell; PLT, platelet; PDW, platelet distribution width.

†Kruskal–Wallis test.

3.2 | Correlations of CBC parameters with HOMA-IR and HOMA-β in prediabetes and T2DM

RBC and WBC counts were correlated with HOMA-IR ($r = 0.218$ and $r = 0.273$, respectively; $p < 0.001$), while WBC and platelet counts were correlated with HOMA-β ($r = 0.140$, $p < 0.001$, and $r = 0.161$, $p = 0.037$, respectively). RDW was only correlated with HOMA-β ($r = 0.202$, $p < 0.001$) (Table 2). HOMA-IR and HOMA-β differed significantly among RBC, WBC, and platelet count quartiles ($p < 0.001$) in prediabetes and T2DM. HOMA-β differed significantly among RDW quartiles whereas HOMA-IR did not (Table 3).

3.3 | Multiple linear regression analyses of CBC parameters with HOMA-IR and HOMA-β in prediabetes and T2DM

Multiple linear regression analyses were conducted to further explore the association of CBC parameter quartiles with HOMA-IR

TABLE 4 Association between hematology parameters and HOMA-IR

	Model 1			Model 2			Model 3		
	ß	SE	*P*	*ß*	SE	*P*	*ß*	SE	*P*
RBC count									
Q1 (ref)	1			1			1		
Q2	0.289	0.175	0.099	0.327	0.179	0.069	0.14	0.192	0.466
Q3	**0.4**	**0.172**	**0.02**	**0.499**	**0.195**	**0.011**	0.145	0.209	0.488
Q4	**0.997**	**0.176**	**<0.001**	**1.117**	**0.214**	**<0.001**	0.253	0.236	0.282
Hb									
Q1 (ref)	1			1			1		
Q2	0.286	0.173	0.098	0.353	0.181	0.052	0.138	0.191	0.47
Q3	0.33	0.173	0.056	**0.476**	**0.213**	**0.025**	0.072	0.227	0.751
Q4	**0.803**	**0.168**	**<0.001**	**0.961**	**0.223**	**<0.001**	0.177	0.242	0.464
RDW									
Q1 (ref)	1			1			1		
Q2	0.108	0.177	0.542	0.124	0.176	0.484	0.158	0.189	0.403
Q3	−0.286	0.183	0.118	−0.279	0.183	0.126	−0.156	0.194	0.421
Q4	0.074	0.177	0.678	0.123	0.178	0.491	0.043	0.191	0.821
WBC count									
Q1 (ref)	1			1			1		
Q2	**0.348**	**0.172**	**0.043**	**0.339**	**0.172**	**0.05**	0.157	0.182	0.389
Q3	**0.571**	**0.172**	**0.001**	**0.558**	**0.172**	**0.001**	0.142	0.186	0.448
Q4	**1.303**	**0.167**	**<0.001**	**1.269**	**0.168**	**<0.001**	**0.505**	**0.188**	**0.007**
PLT count									
Q1 (ref)	1			1			1		
Q2	−0.271	0.173	0.119	−0.26	0.174	0.136	−0.204	0.186	0.273
Q3	−0.007	0.171	0.968	−0.01	0.175	0.956	−0.131	0.185	0.479
Q4	**0.441**	**0.172**	**0.01**	**0.494**	**0.181**	**0.007**	0.31	0.191	0.106
PDW									
Q1 (ref)	1			1			1		
Q2	0.299	0.176	0.09	0.277	0.176	0.117	0.316	0.185	0.089
Q3	0.265	0.169	0.118	0.247	0.17	0.145	0.175	0.18	0.329
Q4	0.285	0.175	0.103	0.262	0.175	0.134	0.023	0.184	0.9

Note: ß, coefficient; SE, standard error.

Model 1: Unadjusted.

Model 2: Adjusted age and sex.

Model 3: Adjusted age, sex, WC, and HbA1c.

Bold face indicates statistical significance.

Abbreviations: RBC, red blood cell; Hb, hemoglobin; RDW, red blood cell distribution width; WBC, white blood cell; PLT, platelet; PDW, platelet distribution width.

and HOMA-β. In model 1 (unadjusted), higher RBC, WBC, and platelet count quartiles had a stronger correlation with HOMA-IR. However, in model 3 (adjusted for age, sex, WC, and HbA1c), only the highest WBC count quartile had a remaining weak correlation with HOMA-IR [coefficient (β) = 0.505, p = 0.007] (Table 4). The highest RDW (β = 15.527, p = 0.002), WBC (β = 15.171, p = 0.002), and platelet (β = 15.581, p = 0.002) count quartiles were still significantly correlated with HOMA-β after adjusting for potential confounding factors (Table 5).

4 | DISCUSSION

This study found that RBC and WBC counts were increased at higher hyperglycemia levels, while RDW was higher in prediabetes than in T2DM. HOMA-β was significantly associated with RDW, WBC, and platelet counts after adjusting for the potential confounding factors of age, sex, WC, and HbA1c, but this association between CBC parameters and HOMA-IR ceased after adjusting for potential confounding factors.

TABLE 5 Association between hematologic parameters and HOMA-β

	Model 1			Model 2			Model 3		
	ß	SE	P	ß	SE	P	ß	SE	P
RBC count									
Q1 (ref)	1			1			1		
Q2	6.938	4.553	0.128	6.225	4.623	0.178	5.502	5.072	0.278
Q3	1.047	4.475	0.815	1.934	5.039	0.701	0.43	5.53	0.938
Q4	**9.725**	**4.586**	**0.034**	8.312	5.529	0.133	2.253	6.24	0.718
Hb									
Q1 (ref)	1			1			1		
Q2	2.043	4.487	0.649	2.353	4.655	0.613	0.59	5.047	0.907
Q3	−7.527	4.477	0.093	−7.713	5.463	0.158	−9.738	6.016	0.106
Q4	0.404	4.358	0.926	−1.654	5.73	0.773	−6.742	6.389	0.292
RDW									
Q1 (ref)	1			1			1		
Q2	**12.478**	**4.525**	**0.006**	**12.865**	**4.482**	**0.004**	8.061	4.984	0.106
Q3	**9.677**	**4.684**	**0.039**	**10.239**	**4.637**	**0.027**	4.425	5.124	0.388
Q4	**22.793**	**4.54**	**<0.001**	**22.372**	**4.532**	**<0.001**	**15.527**	**5.043**	**0.002**
WBC count									
Q1 (ref)	1			1			1		
Q2	6.044	4.491	0.179	6.35	4.452	0.154	2.656	4.813	0.581
Q3	**13.977**	**4.488**	**0.002**	**14.513**	**4.453**	**0.001**	**10.262**	**4.931**	**0.038**
Q4	**22.034**	**4.355**	**<0.001**	**21.201**	**4.355**	**<0.001**	**15.171**	**4.971**	**0.002**
PLT count									
Q1 (ref)	1			1			1		
Q2	2.544	4.443	0.567	0.625	4.442	0.888	3.328	4.922	0.499
Q3	4.382	4.389	0.318	0.178	4.467	0.968	−1.436	4.896	0.769
Q4	**22.527**	**4.407**	**<0.001**	**16.842**	**4.634**	**<0.001**	**15.581**	**5.058**	**0.002**
PDW									
Q1 (ref)	1			1			1		
Q2	**12.515**	**4.534**	**0.006**	**10.755**	**4.503**	**0.017**	**10.252**	**4.905**	**0.037**
Q3	**11.39**	**4.359**	**0.009**	**9.536**	**4.33**	**0.028**	8.662	4.749	0.068
Q4	7.028	4.492	0.118	5.484	4.459	0.219	0.173	4.869	0.972

Note: ß-coefficient; SE, standard error.

Model 1: Unadjusted.

Model 2: Adjusted age and sex.

Model 3: Adjusted age, sex, WC, and HbA1c.

Bold face indicates statistical significance.

Abbreviations: RBC, red blood cell; Hb, hemoglobin; RDW, red blood cell distribution width; WBC, white blood cell; PLT, platelet; PDW, platelet distribution width.

Insulin needs to be released and act to meet the precise metabolic demand, which involves mechanisms such as insulin synthesis and release, and the insulin response in tissues, which must be tightly regulated. Defects in any of the involved mechanisms can lead to a metabolic imbalance and then T2DM pathogenesis. These defects begin in the early stages of prediabetes.[20] The relationship of CBC parameters with IR and BCF therefore needs to be explored from the prediabetic stage.

In the present study, RDW was correlated with HOMA-β, which persisted after adjusting for age, sex, WC, and HbA1c. IR is fully compensated by a proportionate oversecretion of pancreatic beta-cell insulin. As IR reaches near to its maximum level, clinically relevant hyperglycemia manifests. This is coincidental with further BCF deterioration, characterized by a progressive failure to secrete sufficient insulin to maintain normoglycemia.[21] Hyperinsulinemia exerts its effects on erythropoiesis through various mechanisms.[18,22-24] The insulin receptor in human erythropoietic cells suggests that insulin is a co-factor in erythropoiesis.[22] Furthermore, some studies have found that insulin exerts growth-promoting effects on erythropoietic cells in vitro,[23] with hyperinsulinemia increasing the hypoxia-inducible factor-1 concentration, which promotes erythropoietin the synthesis and may also mediate intestinal iron absorption.[24] An increase in RDW reflects a deregulation of erythrocyte homeostasis.[25-27] However, chronic hyperglycemia in decreased BCF could be sufficient to change the mechanical properties of RBCs, reduce cell survival, and create a more homogenous cell population, resulting in decreased RDW.[28-31] This could explain the correlation between RDW and HOMA-β and RDW and BCF being lower in T2DM than in prediabetes in this study. Our results were partially consistent with a previous Chinese study[13] suggesting that the correlation between RDW and HOMA2-β only present in males, since the present study found a correlation between RDW and HOMA-β after adjusting for sex. Furthermore, a study based on the Malmö Diet and Cancer cohort[15] indicated that low RDW is independently associated with an increased incidence of diabetes mellitus.

Some previous studies have demonstrated a relationship between WBC count and IR.[32-34] Increased WBC count was associated with IR, which may contribute to an increased risk of cardiovascular disease.[18,34,35] The association between IR and increased WBC count may represent evidence that chronic inflammation is part of metabolic syndrome. We found that the correlation between IR and WBC count was attenuated after adjusting for WC and HbA1c. A study of non-obese Japanese patients with T2DM found a correlation between IR and platelet count.[36] However, our study found that the above-mentioned correlation ceased after adjusting for WC and HbA1c. Possible explanations for the inconsistency between studies include the study design, sample size, data source, and other variance in population characteristics.

Our study had some limitations. First, we could not evaluate the causal relationship between the CBC parameters and BCF and IR due to the cross-sectional study design. Second, HOMA was used to assess BCF and IR. Applying the HOMA model may be more convenient and relatively simple, but its results are less sensitive in detecting BCF changes and are restricted to assessments of pancreatic reserve alone.[37,38] Third, we could not entirely explain the biologic mechanisms underlying the relationships between CBC parameters and BCF in this study, and so these need to be clarified by further studies. Notwithstanding these limitations, this study has identified the relationships of CBC parameters with IR and BCF in a health checkup cohort of patients with both diabetes and prediabetes. Moreover, we investigated this relationship after adjusting for anthropometric measurements and HbA1c levels.

In conclusion, RDW, WBC, and platelet counts were independently associated with HOMA-β in prediabetes and T2DM. This suggests that these CBC parameters could represent BCF in prediabetes and T2DM. Due to its cost-effectiveness and easy accessibility, these CBC parameters could be screened periodically in prediabetes and T2DM, along with HbA1c, to keep both physicians and patients aware of the BCF of these diseases.

AUTHORS CONTRIBUTION

All the authors participated in designing this study. SC and HP performed data collection. SK undertook the statistical analyses. EN, SK, HC, and HP analyzed and interpreted the data. EN wrote the first draft of the manuscript, which was reviewed by all the other authors, who also provided further contributions and suggestions.

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CONFLICT OF INTERESTS

No potential conflicts of interest relevant to this article were reported.

DATA AVAILABILITY STATEMENT

The data used to support the findings of this study are included in the article.

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