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Comparison of Blood Cells Parameters and Complete Blood Count in Diabetic Patients: A Cross-sectional Study

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background and Aim: Diabetes is a type of metabolic disorder characterized by increased blood glucose, which is due to insulin resistance, insulin deficiency, or both. Changes in blood cell parameters in diabetes are controversial. The present study aimed to assess the blood cell parameters in diabetic patients compared to healthy individuals.
Methods: This cross-sectional study was performed on 540 cases (270 diabetic patients and 270 healthy individuals) over 20 years old who were referred to the clinics affiliated to Semnan University of Medical Sciences, Semnan, Iran, in 2018. The complete blood count (CBC) parameters were assessed in both groups, and demographic information was also collected via questionnaires. All the analyses were performed in SPSS software (version 22).

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Results: In terms of gender, the majority of participants (61.2%) were female. The white blood cell (WBC) count in diabetic patients was significantly higher than that in the control group (*P<0.001*), and the hemoglobin (HGB) level was significantly lower in diabetic patients (*P=0.009*). There was no significant difference in the level of other indices between diabetic and control groups. There was a significant difference between the gender of diabetic patients in HGB, red blood cell (RBC) count, and platelets (PLT) (P<0.001). Moreover, HBG and RBC were less in patients with longer diabetes duration (*P<0.001*).
Conclusion: The obtained results pointed to a statistically significant difference in some hematological parameters of diabetic patients compared to non-diabetic individuals. More studies are needed to clarify the causal relationship between diabetes and these indices.

Keywords: Blood cells parameters; diabetes; Red Blood Cell (RBC); White Blood Cell (WBC).

HIGHLIGHTS:

- The White Blood Cell (WBC) count in diabetic patients was higher than non-diabetic.
- The Hemoglobin (HGB) level was lower in diabetic patients than non-diabetic.
- The difference in some hematological parameters of diabetic patients compared to non-diabetic individuals.

1. INTRODUCTION

Diabetes is a metabolic disorder characterized by hyperglycemia due to low insulin secretion or insulin resistance [1]. The prevalence of this global public health problem is on the rise in both developed and developing countries [2], highlighting its crucial social and economic importance. This disease has become a matter of significant clinical concern due to its numerous complications, increasing mortality, and imposition of high costs on the health care system [3].

The evidence demonstrated that inflammation might perform a critical intermediary role in the pathogenesis of diabetes; therefore, relating diabetes to an amount of usually coexisting situations is thought to originate from inflammatory mechanisms [4]. Inflammatory markers, such as C-reactive protein (CRP), interleukin-6, and tumor necrosis factor, are associated with the progression of diabetes. Numerous hematological and biochemical markers are used to measure systemic inflammation [5]. White blood cell (WBC) count in the complete blood count (CBC) test indicates a common inflammation in many diseases [6]. Some investigations have recently reported that other blood parameters, such as blood cell subtype ratios, red blood cell distribution width (RDW), mean platelet volume (MPV), platelet-to-lymphocyte ratio (PLR), and neutrophil to lymphocyte ratio (NLR), can be used as anti-inflammatory parameters in a variety of diseases [7]; nonetheless, these biomarkers are not clinically evaluated.

Based on recent studies, elevated blood glucose levels affect red blood cells (RBC) and vascular endothelial cells, leading to alterations in the RBC and vascular endothelial parameters [8]. Nevertheless, WBC count is a test available almost everywhere and can be used as a risk factor for diabetes. Chronic inflammation causes an increase in WBC count, which in turn can increase the incidence of metabolic syndrome in patients with type 2 diabetes [9]. Diabetes is a clinically important public health problem, the most common cause of blindness and kidney failure, as well as one of the major risk factors for cardiovascular diseases [10]. Therefore, finding a simple, inexpensive, and frequently used biomarker to predict the development of diabetes is essential to prevent the progression of diabetes [11]. In light of the aforementioned issues, the present study aimed to assess alterations in some blood parameters, including WBC count, RBC count, hemoglobin (HGB), platelets (PLT), MPV, and RDW in diabetic compared to healthy individuals.

2. MATERIALS AND METHODS

2.1 Study Population

This cross-sectional study included 540 cases over 20 years old who were selected via convenience sampling from those who were referred to the clinics affiliated to Semnan University of Medical Sciences, Semnan, Iran, in 2018. The inclusion criteria entailed definite diabetes, absence of diabetes complications, and the age range of over 20 years old for the case group, as well as healthy people aged over 20 years old without any specific diseases who had

been referred to clinics for a check-up for the control group. On the other hand, the exclusion criteria were as follows: liver, lung, and kidney malignancies, immunological disorders, infectious diseases in a recent month, macrocytic anemia, hematologic diseases, hemodialysis, smoking, drinking alcohol, as well as the use of steroids, immunosuppressants, and erythropoietin.

2.2 Study Protocol

Before the commencement of the study, the subjects were provided with the objectives of the study and signed the informed written consent. Diabetic subjects were considered the case group, and healthy individuals without any specific diseases were regarded as the control group. Information about age, gender, body mass index (BMI), and duration of diabetes were collected via a questionnaire. The CBC parameters, including HGB, WBC, RBC, RDW, MPV, and PLT, were collected according to the annual patient control test. Finally, in a supplementary analysis, diabetic patients were compared with non-diabetic controls in terms of CBC parameters.

2.3 Statistical Analysis

The descriptive data were summarized as mean±SD and percentage. Data normality was checked prior to data analysis using the One-Sample Kolmogorov-Smirnov Test. The student's t-test, Mann-Whitney U test, and chi-square were employed in order to analyze the data. All the analyses were performed in SPSS software (version 22, Chicago, IL, USA), and a p-value less than 0.05 was considered statistically significant.

3. RESULTS

A total of 540 subjects were included in this study, including 210 (38.8%) males and 330 (61.2%) females. The demographic characteristics of participants in the two groups are displayed in Table 1. The gender was not significantly different between the two groups (*P=0.289*) based on the Chi-square test, and the two groups were homogeneous. The mean age scores of participants in the case and control groups were obtained at 51.62±11.81 and 58.99±10.64, respectively. The minimum age scores were 30 and 31 years in the control and case groups, respectively, while the maximum age score was 87 years in both groups. Based on the t-test, the two groups were significantly different in terms of age (*P<0.001*). The mean±SD of BMI in the case and control groups were 27.00±4.41 kg/m^2 and 28.71±4.33 kg/m^2, respectively. The BMI was a significant difference between the two groups based on the Mann-Whitney test (*P<0.001*).

Table 1. Demographic characteristics of participants

Variable		Groups		P-value
		Case	Control	
Gender n (%)	Male	111 (41.1)	99 (36.7)	0.289
	Female	159 (58.9)	171 (63.3)	
Age n (%)	Less than 40 years	11 (4.1)	42 (15.6)	<0.001
	40-49 years	44 (16.3)	88 (32.6)	
	50-59 years	84 (31.1)	79 (29.3)	
	60-69 years	87 (32.2)	40 (14.8)	
	70 years and more	44 (16.3)	21 (7.8)	
BMI n (%)	<25 kg/m^2	51 (18.9)	93 (34.4)	<0.001
	25-30 kg/m^2	122 (45.2)	117 (49.0)	
	≥ 30 kg/m^2	97 (35.9)	60 (22.2)	

BMI: Body Mass Index

Table 2. Mean±SD of CBC indices in the study groups

Variable	Control group	Case group
WBC 10^3/µL (mean±SD)	6446.96±1590.63	6977.66±1723.36
RBC 10^3/µL (mean±SD)	4.63±0.588	4.73±0.593
HGB g/dL (mean±SD)	13.45±1.49	13.11±1.55
RDW % (mean±SD)	13.08±0.974	13.03±1.34
PLT 10^3/µL (mean±SD)	242355.55±61600.15	248074.07±66415.79
MPV Femtoliter (mean±SD)	9.22±1.124	9.06±1.29

WBC: White blood cell, RBC: Red blood cell, HGB: Hemoglobin, RDW: Red blood cell distribution width, PLT: Platelets, MPV: Mean platelet volume

Table 3. Count of complete blood cell indices in the study groups

Variable		Groups		P-value
		Case	Control	
WBC n (%)	< 4000	8 (3.0)	7 (2.6)	<0.001
	4000-10000	249 (92.2)	259 (95.9)	
	>10000	13 (4.8)	4 (1.5)	
RBC n (%)	Less than 4.2 in female Less than 4.7 in male	69 (25.6)	94 (34.8)	0.051
	4.2-6.1 in female 4.7-6.1 in male	195 (72.2)	172 (63.7)	
	>6.1	6 (2.2)	4 (1.5)	
HGB n (%)	Less than 12 in female Less than 14 in male	142 (52.6)	71 (26.3)	0.009
	12-16 in female 14-18 in male	127 (47.0)	198 (73.3)	
	More than 16 in females More than 18 in males	1 (0.4)	1 (0.4)	
RDW n (%)	< 11.6	12 (4.4)	9 (3.3)	0.463
	11.6-14.6	236 (87.4)	248 (91.9)	
	>14.6	22 (8.1)	13 (4.8)	
PLT n (%)	< 150000	9 (3.3)	16 (5.9)	0.300
	150000-400000	251 (93)	251 (93)	
	>400000	10 (3.7)	3 (1.1)	
MPV n (%)	< 9.7	183 (67.8)	169 (62.6)	0.134
	9.7-12.8	84 (31.1)	101 (37.4)	
	>1.8	3 (1.1)	0 (0.0)	

WBC: White blood cell, RBC: Red blood cell, HGB: Hemoglobin, RDW: Red blood cell distribution width, PLT: Platelets, MPV: Mean platelet volume

The mean±SD of diabetes duration was 7.20±5.34 years in the case group. The duration of diabetes was ≤5 years in 131 (48.5%) cases, 5-10 years in 70 (25.9%) subjects, and > 10 years in 69 (25.6%) participants. The mean±SD of CBC indices are displayed in Table 2, and CBC indices are depicted in Table 3. The WBC count was a significant difference between the two groups based on the t-test (*P<0.001*); nonetheless, the two groups did significantly differ in RBC count based on the t-test (*P=0.051*).

The HGB count was a significant difference between the two groups based on the t-test (*P=0.009*). The HGB levels was lower in the case group as compared to those in the control group. The amount of RDW (*P=0.463*), PLT (*P=0.300*), and MPV (*P=0.134*) were not significantly different between the two groups based on the Mann-Whitney test.

The results of regression analysis indicated that the WBC count was significantly different between the two groups based on BMI (*P=0.001*). The RBC, HGB, and PLT count was significantly different between the two groups based on age (*P<0.001*). The evaluation of the level of CBC indices by considering age, gender, BMI, and duration of diabetes in the case group showed that the RBC level (*P<0.001*) and HGB level (*P<0.001*) were higher in men than in women, while PLT level (*P=0.001*) was higher in women than in men. The WBC count was higher in patients with higher BMI (*P=0.023*). However, there was a significant difference between the levels of diabetes duration in RBC (*P=0.002*) and HGB (*P=0.004*). This demonstrated that the HGB level and RBC counts were lower in patients with a longer duration of diabetes. In other parameters, no significant differences were observed.

4. DISCUSSION

All the cellular components in the blood, including RBC, platelets, and WBC, have a role to play in the underlying pathogenesis of inflammatory factors [12]. Therefore, the present study assessed the alterations in CBC indices in diabetic compared to healthy individuals. The results of this study pointed out that the WBC count was higher in the diabetic group; however, the HGB level was lower in the diabetic group

than that in healthy individuals. Based on the duration of diabetes, RBC and HGB levels were higher in men, while PLT level was higher in women. Nevertheless, the number of WBCs was higher in patients with higher BMI, while the HGB level and RBC counts were lower in patients with a longer duration of diabetes. In the same direction Adane et al. demonstrated that the mean values of RBC, HGB, hematocrit (Hct), and mean cell volume (MCV) parameters were be significantly lower in diabetes mellitus patients than in healthy person [13]. Therefore, for the better prognosis and quality of life can be achieved by periodically evaluating and treating RBC parameters abnormalities in diabetes mellitus patients.

The use of new inflammatory markers in models for predicting the risk of diabetes has been considered since chronic inflammation plays a major role in insulin resistance in peripheral tissues. Since the WBC is known as a marker of systemic inflammation, its high levels can be a predictor of further decreased insulin activity and the progression of diabetes mellitus. Naredi et al. reported that the WBC counts on the higher side of the normal range can be indicative of subclinical inflammation in diabetic patients [14]. However, numerous studies reported that WBC counts are significantly higher in diabetic patients than in healthy individuals [7,15-17]. The results of the present research are in line with the findings of other studies that reported that the WBC count was higher in the diabetic group. Along the same lines, Twig et al. demonstrated that the WBC count was related to increased diabetes risk in obese individuals, and the WBC count was significantly higher in overweight men with diabetes [18]. The results of the current study pointed out that the number of WBC was higher in patients with higher BMI. That is to say, BMI is directly related to WBC counts. This can be ascribed to the fact that obesity can cause an inflammatory condition in the body [19]. Adipose tissue has been shown to increase the production of granulocytes in bone marrow by releasing inflammatory cytokines, such as TNF-α, as well as interleukins 1 and 8 [20]. Therefore, the elevated WBC count in diabetic patients with high BMI may be associated with a higher rate of diabetes incidence [21].

Diabetic nephropathy, inflammation, nutritional deficiencies, comorbid autoimmune diseases, medications, and hormonal changes can also cause anemia in diabetics [22]. Moreover, it has been demonstrated that hyperglycemia can reduce the lifespan of RBC by glycosylation of hemoglobin and decrease the plasticity of erythrocytes, thereby aggravating anemia in diabetic patients [23]. In accordance with the findings of the present research, some studies suggested that HGB levels are significantly reduced in all diabetic patients [24,25]. Mushlih et al. reported that the RBC and HGB significantly lower in T2DM with ulcers compare with T2DM without ulcers and they suggested the identifying HGB levels to get proper treatment for T2DM [26]. Nonetheless, in some studies, there was no significant difference in HGB levels between diabetic and non-diabetic individuals [15,27]. This discrepancy can be attributed to differences in gender distribution and participants' nutritional status.

In agreement with the present research, some studies reported that the mean RBC was not significantly different between the healthy and diabetic groups [15,27,28]. However, another study found that the mean RBC count was higher in people with diabetes, although the increase in RBC was more frequently observed in people who had just been diagnosed with diabetes [29]. In the present study, the RBC count was higher in people with a lower duration of diabetes. This may be the main reason for the difference between the results of the stated study and the findings of the present research. Different sample sizes and racial and geographical differences are the other reasons for this difference.

In the present study, the RDW, PLT, and MPV were not significantly different between the two study groups. Ziaee et al. reported that the RDW, PLT, and MPV were not significantly different in diabetic patients [28]; nonetheless, Biadgo et al. [15] and Engström et al. detected that the reduction of RDW significantly increased the risk of diabetes. Nevertheless, a case-control study reported a significant positive correlation between the RDW and diabetes [30]. Moreover, some studies suggested that the RDW may be a predictor of the onset of diabetic macrovascular complications. A high RDW increased the levels of oxidative stress and showed chronic inflammation, both of them revealing signs in type 2 diabetics, which may be meaningfully contributed to the expansion of atherosclerotic diseases [31,32].

Numerous factors, such as increased erythropoiesis (e.g., after bleeding or hemolysis) and anemia due to nutritional deficiencies, can affect RDW levels [33]. In line with the results of the present study, a cross-sectional study

reported that the PLT and MPV are not different between diabetic and non-diabetic groups; moreover, MPV was significantly higher in diabetic patients than that in non-diabetic patients [34]. On the other hand, Kachekouche et al. reported that people with low platelets were five times more likely to develop type 2 diabetes compared to people with normal PLT [27]. A case study demonstrated that PLT is significantly lower and MPV is higher in diabetic patients [35]. In the present study, the presence of hematological diseases was considered the exclusion criterion, and the observed discrepancies in the results of studies in this field can be ascribed to differences in exclusion criteria and the possible effect of these factors. However, the type of anticoagulant in the test tube may be effective in PLT. If EDTA is used in the CBC test tube, there is a possibility of pseudo-thrombocytopenia due to platelet agglutination by antibodies, thereby decreasing the calcium content as a result of collecting blood in a tube containing EDTA. Other reasons include differences in the design and method of study, different sample sizes, as well as racial and genetic differences.

The present study reported that RBC and HGB levels were lower in women than men, while PLT was higher in women than men. The results of previous studies are consistent with the findings of the present research [28,36]. Based on recent studies, diabetic men have lower testosterone levels than non-diabetic men, and it has been suggested that one of the factors increasing the prevalence of anemia in diabetic men may be decreased testosterone levels [37,38]. Nevertheless, it has not been determined to what extent this affects the gender difference in HGB levels in diabetic patients, and its assessment requires more extensive studies.

Consistent with the results of our study, Shim et al. did not find a significant relationship between age and WBC count in diabetic patients [39]. Harusato et al. detected an inverse relationship between age and HGB levels in men with diabetes. In this study, only HGB was studied in diabetic men, and the reduction of testosterone with increasing age was mentioned as the cause of the inverse relationship observed between age and hemoglobin level [40].

Based on the results of this study, HGB levels and RBC counts were lower in patients with a longer duration of diabetes. Decreased HGB is a common finding in diabetic patients, and recent studies suggested that HGB levels are inversely associated with diabetes duration. It has been demonstrated that people with a history of more than 5 years of diabetes are 1.5 times more at risk of anemia than people with a history of less than 5 years of diabetes [41]. The progress of erythropoietin resistance due to chronic inflammation in diabetes has been suggested as a possible cause [42]. The results of other studies were consistent with the findings of the present research [34,35,39,40].

5. LIMITATIONS AND SUGGESTIONS

One of the limitations of this study is that it is cross-sectional, which is limited in determining the causal relationship between CBC parameters and diabetes and only shows the association of changes in parameters with diabetes. Moreover, the statistical population of the present study was restricted to patients referring to the clinics affiliated to Semnan University of Medical Sciences; therefore, the results may not be generalizable to the general population of diabetic patients. Indeed, there are many known and unknown factors that may affect changes in the level of CBC parameters in diabetes, especially nutritional status, genetics, cardiovascular risk factors (such as hypertension and lipid disorders), and other socio-demographic risk factors. The assessment of all these factors is not possible in one study and will require more comprehensive studies and wider statistical communities.

6. CONCLUSION

The results of this study pointed out that the number of WBC is higher in diabetic patients. On the other hand, the number of WBC in diabetics was directly related to BMI, indicating that obesity is associated with an inflammatory condition in diabetic patients. The HGB levels in diabetic patients are also inversely associated with the duration of diabetes. Given the importance of para-clinical indicators indicating future problems and complications and CBC testing as one of the most common, inexpensive, and widely available tests, these results raise hopes and motivation for further valuable studies in the future to better understand the role of these indices in predicting the incidence and burden of diabetes.

ETHICAL APPROVAL

The study protocol was reviewed and approved by the Ethics Committee of Semnan University of

Medical Sciences, Semnan, Iran (No: IR.SEMUMS.REC.1397.082).

CONSENT

Before the commencement of the study, the subjects were provided with the objectives of the study and signed the informed written consent.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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