# The relationship between erythrocyte parameters and metabolic syndrome components among patients with Type (2) Diabetes Mellitus

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## □ ABSTRACT □

Many previous studies reported an association between erythrocyte parameters and metabolic syndrome (MS). Due to the high prevalence of MS among patients with Type 2 Diabetes Mellitus (T2DM), our study aimed to examine the relationship between erythrocyte parameters and MS components among patients with T2DM. This current study took place in Tishreen University Hospital and the Diabetes Centre of Lattakia City in Syria. A total of 121 participants who were previously diagnosed with T2DM were included in this study. The results have shown that levels of erythrocyte parameters (RBC, Hb, HCT, and RDW) increased with the number of MS components from 1 to 5. There was a statically significant positive correlation between each of RBC, Hb, and HCT with BP, TG, WC, and BMI and a negative correlation with HDL among males and females. RDW had a positive correlation with BP, WC, and HDL and a negative correlation with TG and BMI in both males and females. In conclusion, high levels of erythrocyte parameters were associated with MS and its components among patients with T2DM. Due to this relationship, it is possible to use these parameters to investigate MS, especially with its high prevalence and dangerous complications.

**Keywords:** Metabolic Syndrome, Type 2 Diabetes Mellitus, Erythrocyte Parameters, Insulin Resistance

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# العلاقة بين مشعرات الكريات الحمراء ومكونات المتلازمة الاستقلابية لدى مرضى الداء السكري من النمط الثاني

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## □ ملخّص □

أشارت العديد من الدراساتِ السابقةِ إلى وجودِ علاقةٍ بين مشعرات الكريات الحمراء ومكونات المتلازمة الاستقلابيّة. نظراً إلى الانتشارِ الكبيرِ للمتلازمةِ الاستقلابيّةِ لدى مرضى الداء السكريّ من النمط الثاني، هدفت دراستنا إلى التحرّي عن العلاقة بين مشعرات الكريات الحمراء ومكونات المتلازمة الاستقلابية لدى مرضى الداء السكري من النمط الثاني.
أجريت الدراسة في مشفى تشرين الجامعيّ ومركز السكري في محافظة اللاذقيّة/سوريا. شملت هذه الدراسة 121 مشاركاً مشخّصين مسبقاً بالداء السكري النمط الثاني. أظهرت النتائج ازدياداً في مستويات مشعرات الكريات الحمراء (تعداد الكريات الحمراء، خضاب الدم، الهيماتوكريت وحجم توزّع الكريات الحمراء) مع ازدياد عدد مكونات المتلازمة الاستقلابيّة من 1 إلى 5. كان هنالك ارتباطاً إيجابيّاً هام إحصائياً بين كلّ من تعداد الكريات الحمراء، الخضاب والهيماتوكريت مع كلّ من الضغط الدمويّ، الشحوم الثلاثيّة، محيط الخصر ومشعر كتلة الجسم لدا كلا الجنسين. كان لحجم توزع الكريات الحمراء ارتباطاً إيجابيّاً مع الضغط الدموي، محيط الخصر والكولسترول عالي الكثافة، وارتباطاً سلبيّاً مع الشحوم الثلاثية ومشعر كتلة الجسم لدى الذكور والإناث. إذاً ارتبطت المستويات العالية من مشعرات الكريات الحمراء مع المتلازمة الاستقلابية ومكوناتها لدى مرضى الداء السكري من النمط الثاني. نظراً لهذه العلاقة، إنّه من الممكن استخدام هذه المشعرات للتقصّي عن المتلازمة الاستقلابيّة خاصّة مع معدل انتشارها الكبير واختلاطاتها الخطيرة.

**الكلمات المفتاحية:** المتلازمة الاستقلابية، الداء السكري من النمط الثاني، مشعرات الكريات الحمراء، مقاومة الأنسولين

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## Introduction:

Metabolic Syndrome (MS) can be defined as an accumulation of cardio-metabolic disorders characterized by the increase in fasting blood glucose (FBG), waist circumference (WC) ،blood pressure (BP), and triglycerides (TG), and the reduction in high-density lipoprotein cholesterol (HDL)[1]. This syndrome contributes to the occurrence of atherosclerotic and nonatherosclerotic cardiovascular diseases (CVD)[2] and the development of type 2 Diabetes Mellitus (T2DM)[3] and it is considered to be an important cardiovascular risk factor causing high rates of morbid mortality[4]. MS has a danger to the population's health and a real economic burden. The pathogenesis of MS is still not adequately explained. The main possible mechanisms were insulin resistance and chronic low-grade inflammation[5, 6]. Life style variables also affect the prevalence of the syndrome such as high-calorie diet and lack of exercise. MS also varies regarding age, sex, race, smoking, drinking alcohol, the diagnostic criteria that are used, and family history of T2DM[7].

A complete blood count (CBC) is a routine, inexpensive and noninvasive test, and many previous studies reported that erythrocyte parameters available from clinical examination including red blood cell count (RBC), hemoglobin (Hb), hematocrit (HCT), and red blood cell distribution width (RDW) had an association with insulin resistance and chronic low-grade inflammation[8, 9]. Many investigators around the world also confirmed that RBC[10], Hb[11], HCT[10], and RDW[12] were related to MS and its components. A longitudinal cohort in China[13] indicated that erythrocyte parameters that are RBC, HCT, and Hb could be used as predictive indexes for the risk of developing MS. Another study in Ethiopia[10] gave proof of using hematological markers such as RBC, HCT, and Hb for the early investigation of people who are at risk for cardiovascular diseases. A cross-sectional study that was conducted in Iran[14] suggested that high numbers of major hematological parameters such as Hb, and HCT could be new signs for the development of MS. RDW was considered a risk factor of MS among males according to research in China[15]. However, this relationship might be still regarded as controversial. That is why our study aimed to interpret the association between erythrocyte parameters that were mentioned before and the metabolic syndrome components among patients with T2DM.

## Materials and Methods:

### Study population:

Our study was carried out from November 2020 to December 2021 at Tishreen University Hospital and the Diabetes Centre of Lattakia City in Syria. A total of 121 participants (59 male and 62 female) who were previously diagnosed with T2DM, aged from (27 to 83) years were included in this study. Written consent was received from each subject. All participants agreed to complete a self-report questionnaire about personal and medical information (age, duration of diabetes, medical history and pre-existing diseases, drug history, systolic blood pressure (SBP), diastolic blood pressure (DBP), height, weight, waist circumference and at last body mass index (BMI) was calculated as the ratio of an individual's weight in kilograms (kg) divided by the height in meters squared ($m^2$). Patients were categorized according to BMI levels into underweighted when BMI was less than 18.5, healthy weighted when it was between 18.5-24.9, over weighted when it was between 25-29.9, and obese when it was 30 and above.

**Definition**:
Participants were categorized as patients with MS according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria[16]; patients must have three or more of the following parameters:

- WC (>102 cm for males and >88 cm for females)
- HDL (<40 mg/dl for males and <50 mg/dl for females or patients using antilipemic drugs)
- TG (≥150 mg/dl or patients using dyslipidemia drugs)
- BP (≥130/85 mm/Hg or patients using antihypertensive drugs)
- FBS (>100 mg/dl or patients using hypoglycemic drugs)

**Exclusion criteria:**
Patients who have :
- Inflammatory or infection diseases
- Immunologic diseases
- Liver, kidney, and gastrointestinal diseases
- Stroke or history of ischemic heart diseases
- Anemia

In addition, insulin-dependent patients or taking drugs that affect erythrocyte parameters (Iron supplements, B-complex supplements, corticosteroids…) were also excluded.

**Analytical Devices and Laboratory Methods:**
Blood samples were obtained from the superficial vein of the upper limb or dorsal hand vein in the morning after 8-12 hours of fasting. CBC was analyzed using a hematology analyzer (Nihon Kohden Celtac alpha MEK -64 1D®) while Biochemical assays for lipid profile were performed with commercially available kits from Biosystem® (Spain) by a Mindary BS-380 clinical chemistry analyzer from China (Total cholesterol; Cat. No. 11505, Triglycerides; Cat. No. 11528, LDL-C; Cat. No. 23585 and HDL-C; Cat. No. 23557). Fasting blood glucose was analyzed using a kit from Biosystem® with a Semi-Automatic Microprocessor Controlled Photometer (HumaLyzer Primus) from Germany: (Glucose; Cat. No. 11503).

## Statistical Analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS) version 20 for windows. Data were presented as mean ± standard deviation (SD). The student's t-test was used to compare the means of different variables between two independent samples. Analysis of variance (ANOVA) of one factor was used to identify differences in the mean. Receiver operating characteristic (ROC) was conducted to evaluate the ability of erythrocyte parameters in the diagnosis of MS in T2DM patients. Results with a p-value of $< 0.05$ were considered statistically significant.

## Results:

(Table 1) shows the demographic characteristics between the MS group and the non-MS group according to sex, 81.8% (n=99) of subjects were MS patients (male: 49 & female: 50) while 18.2% (n=22) were non-MS patients (male: 10 & female: 12). The prevalence of MS was higher in females (n=50) than in males (n=49) but with no significant difference ($p \geq 0.05$). There was a significant difference in the median age between the MS group and the non-MS group in both males (MS: 63.9±6.5 years & non-MS: 55.3±5.3 years) and females (MS: 59.6±8.2 years & non-MS:51.4±9.5 years) ($p<0.05$). According to the blood pressure, there was no significant difference between the MS group and the non-MS group in both males and females ($p \geq 0.05$). Regarding BMI, there was a significant difference

between the MS group and the non-MS group in both males (MS: 28.63±4.2 Kg/m$^2$ & non-MS: 24.42±2.3 Kg/m$^2$) and females (MS: 28.66±4.1 Kg/m$^2$& non-MS: 25.58±3.9 Kg/m$^2$) ($p<0.05$). There was a significant difference between the MS group and the non-MS group in the duration of diabetes in both males (MS: 10.9±6.3 years & non-MS: 7.5±3.8 years) and females (MS: 10.16±6.5 years & non-MS: 5.27±3.3 years) ($p<0.05$).
According to waist circumference, there was also a significant difference between the MS group and the non-MS group in both males (MS: 105.3±12.1 cm & non- MS: 93.7±5.1 years) and females (MS: 104.4±12.4 cm & non-MS: 87.9±11.5 years) ($p<0.05$).

**Table (1): The demographic characteristics between the MS group and the non-MS group according to sex**

**BP**; blood pressure, **SBP**; systolic blood pressure, **DBP**; diastolic blood pressure, **BMI**; body mass index, **WC**; waist circumference

(Table 2) shows the distribution of MS components between the MS group and the non-MS group stratified by sex. In both male and female groups, there was a significant difference in the distribution of the studied components (blood pressure, waist circumstance, TG, and HDL) between the MS group and the non-MS group ($p<0.05$). The most common criteria of MS (except for FBG) were blood pressure in males and waist circumstance in females.

| Demographic Characteristics | Male N=59 | | | Female N=62 | | |
|---|---|---|---|---|---|---|
| | Mets N=49 | Non-Mets N=10 | P-value | Mets N=50 | Non-Mets N=12 | P-value |
| Age (years) | 63.9±6.5 | 55.3±5.3 | 0.02 | 59.6±8.2 | 51.4±9.5 | 0.04 |
| BP(mmHg)<br>SBP<br>DBP | <br>13.19±1.6<br>8.25±1.1 | <br>12.29±1.2<br>7.72±0.9 | <br>0.1<br>0.1 | <br>13.4±2.03<br>7.8±1.01 | <br>12.15±1.1<br>7.46±0.6 | <br>0.05<br>0.2 |
| BMI (kg/m$^2$) | 28.63±4.2 | 24.42±2.3 | 0.004 | 28.66±4.1 | 25.58±3.9 | 0.02 |
| Duration of Diabetes (years) | 10.9±6.3 | 7.5±3.8 | 0.03 | 10.16±6.5 | 5.27±3.3 | 0.01 |
| WC (cm) | 105.3±12.1 | 93.7±5.1 | 0.005 | 104.4±12.4 | 87.9±11.5 | 0.001 |

**Table (2): The distribution of MS components between the MS group and non-MS group stratified by sex**

| MS components | Male | | | Female | | |
|---|---|---|---|---|---|---|
| | Mets | Non-Mets | P-value | Mets | Non-Mets | P-value |
| BP | 42(85.7%) | 3(30%) | 0.0001 | 32(64%) | 1(8.3%) | 0.0001 |
| TG | 35(71.4%) | 2(20%) | 0.002 | 28(56%) | 0(0%) | 0.0001 |
| HDL | 15(30.6%) | 0(0%) | 0.04 | 23(46%) | 1(8.3%) | 0.01 |
| WC | 34(69.4%) | 0(0%) | 0.001 | 44(88%) | 6(50%) | 0.003 |

**TG**; triglyceride**, HDL**; high density lipoprotein

(Table 3) shows a comparison of laboratory parameters between the MS and the non-MS groups according to sex. In the male group, there was a significant difference between the MS and the non-MS groups in relation to FBG (MS: 117.48±30.6 mg/dL & non MS: 143.1±51.2 mg/dL) ($p<0.05$).

As to a lipid profile, there was no significant difference between the two studied groups regarding to TC (MS: 128.20±26.5 mg/dL & non- MS: 114.9±24.5 mg/dL) and LDL (MS: 52.44±24.1 mg/dL & non MS: 41.4±18.1 mg/dL) ($p\geq0.05$), while there was an important significant statically difference in TG (MS: 142.14±55.8 mg/dL & non- MS: 92.5±37.3 mg/dL) and HDL (MS: 46.66±10.3 mg/dL & non- MS: 55.1±11.6 mg/dL) ($p<0.05$).

In the state of the erythrocyte parameters, there was a statically significant difference between the MS and the non-MS groups in RBC (MS: 4.79±0.5 $*10^6/mm^3$ & non MS: 4.31±0.5 $*10^6/mm^3$), Hb (MS: 13.8±0.7 g/dL & non- MS: 12.1±0.3 g/dL), HCT (MS: 40.33±3.5 % & non- MS: 38.67±4.1%) and RDW (MS: 13.66±0.8 % & non- MS: 13.27±0.7%) ($p<0.05$).

Concerning the female group, There was no significant difference between the studied groups regarding FBG (MS:142.74±43.3 mg/dL & non-MS: 144.25±84.3 mg/dL) ($p\geq0.05$). According to lipid profile, there was no significant difference between patients with MS and patients without MS in TC (MS: 146.32±30.8 mg/dL & non- MS: 138.16±20.6 mg/dL), HDL (MS: 55.28±13.9 mg/dL & non MS: 59.57±11.7 mg/dL) and LDL (MS: 61.70±26.2 mg/dL & non-MS: 56.30±25.4 mg/dL), where there was a significant difference in TG (MS: 148.32±52.6 mg/Dl & non- MS: 111.41±22.3 mg/dL).

In relation to erythrocyte parameters, there was a statically significant difference between the studied groups in RBC (MS: 4.32±0.6 $*10^6/mm^3$& non-MS: 3.71±0.2 $*10^6/mm^3$), Hb (MS: 13.1±0.4 gr/dL & non-MS: 11.65±0.9 gr/dL), HCT (MS: 39.49±3.2% & non- MS: 35.29±2.9%) and RDW (MS: 13.26±1.3% & non-MS: 12.97±3.1%) ($p<0.05$) as shown in (Table-3).

**Table (3): A comparison of laboratory parameters between MS and non-MS groups according to sex**

| Laboratory Parameters | Male | | | Female | | |
|---|---|---|---|---|---|---|
| | Mets | Non-Mets | P-value | Mets | Non-Mets | P-value |
| FBG(mg/dL) | 117.48±30.6 | 143.1±51.2 | 0.03 | 142.74±43.3 | 144.25±84.3 | 0.9 |
| TC(mg/dL) | 128.20±26.5 | 114.9±24.5 | 0.1 | 146.32±30.8 | 138.16±20.6 | 0.3 |
| TG(mg/dL) | 142.14±55.8 | 92.5±37.3 | 0.01 | 148.32±52.6 | 111.41±22.3 | 0.02 |
| HDL(mg/dL) | 46.66±10.3 | 55.1±11.6 | 0.02 | 55.28±13.9 | 59.57±11.7 | 0.3 |
| LDL(mg/dL) | 52.44±24.1 | 41.4±18.1 | 0.1 | 61.70±26.2 | 56.30±25.4 | 0.5 |
| RBC($*10^6$/ulL) | 4.79±0.5 | 4.31±0.5 | 0.01 | 4.32±0.6 | 3.71±0.2 | 0.0001 |
| Hb(g/dL) | 13.8±0.7 | 12.1±0.3 | 0.002 | 13.1±0.4 | 11.65±0.9 | 0.001 |
| HCT(%) | 40.33±3.5 | 38.67±4.1 | 0.0001 | 39.49±3.2 | 35.29±2.9 | 0.0001 |
| RDW(%) | 13.66±0.8 | 13.27±0.7 | 0.02 | 13.26±1.3 | 12.97±3.1 | 0.03 |

**FBG**; fasting blood glucose, **TC**; total cholesterol, **LDL**; low density lipoprotein, **RBC**; red blood cell count, **Hb**; hemoglobin, **HCT**; hematocrit, **RDW**; red blood distribution

(Table 4) shows a comparison of the erythrocyte parameters according to the number of metabolic syndrome components, the average of RBC, Hb, HCT and RDW increased as the number of MS components increased in both male and female groups ($p<0.05$).

**Table (4): A comparison of the erythrocyte parameters according to the number of metabolic syndrome components**

| Erythrocyte Parameters | 1 | 2 | 3 | 4 | 5 | P-value |
|---|---|---|---|---|---|---|
| | Male | | | | | |
| RBC | 4.19±0.5 | 4.34±0.4 | 4.39±0.3 | 4.61±0.2 | 5.22±0.4 | 0.0001 |
| Hb | 13.18±1.2 | 14.08±0.8 | 14.48±0.9 | 14.68±0.8 | 14.90±0.5 | 0.0001 |
| HCT | 38.98±2.2 | 39.58±2.7 | 41.68±2.4 | 41.96±2.6 | 42.21±3.1 | 0.002 |
| RDW | 13.57±0.6 | 13.68±0.3 | 13.83±0.5 | 14.11±0.9 | 14.73±0.4 | 0.001 |
| | Female | | | | | |
| RBC | 3.92±0.3 | 3.99±0.3 | 4.05±0.5 | 4.13±0.2 | 4.39±0.4 | 0.005 |
| Hb | 12.92±1.3 | 12.98±0.5 | 13.19±0.7 | 13.51±0.8 | 13.96±0.3 | 0.0001 |
| HCT | 38.28±2.3 | 38.58±1.9 | 38.97±1.2 | 39.12±1.5 | 39.34±1.1 | 0.0001 |
| RDW | 13.23±0.6 | 13.31±0.4 | 13.73±0.6 | 13.79±0.7 | 13.93±0.8 | 0.01 |

The correlation between the erythrocyte parameters and the MS components according to sex was shown in (table 5). In the male group, a positive correlation was observed between RBC and each DBP ($r=0.29$, $p<0.05$), TG ($r=0.30$, $p<0.05$), WC ($r=0.22$, $p<0.05$), and BMI ($r=0.29$, $p<0.05$), Hb and each of TG ($r=0.39$, $p<0.05$) and WC($r=0.32$, $p<0.05$), HCT and each of DBP ($r=0.24$, $p<0.05$) and TG ($r=0.42$, $p<0.05$), and RDW with HDL ($r=0.32$, $p<0.05$), while there was a significant negative association between RBC and HDL ($r= - 0.21$, $p<0.05$), Hb and HDL ($r= - 0.19$, $p<0.05$), and RDW with BMI ($r= - 0.31$, $p<0.05$). In the female group, a significant negative association was shown between RBC and HDL ($r= - 0.33$, $p<0.05$), Hb and HDL ($r= - 0.31$, $p<0.05$), HCT and HDL ($r= - 0.36$, $p<0.05$), and RDW with BMI ($r= - 0.19$, $p<0.05$). On the other hand, there was a positive correlation between DBP and each of RBC ($r=0.40$, $p<0.05$), Hb ($r=0.28$, $p<0.05$), and RDW ($r=0.16$, $p<0.05$), TG and each of RBC ($r=0.25$, $p<0.05$ ), Hb ($r=0.51$, $p<0.05$), and HCT ($r=0.37$, $p<0.05$), WC and each of RBC ($r=0.19$, $p<0.05$ ) and Hb ($r=0.26$, $p<0.05$), and BMI with RBC ($r=0.25$, $p<0.05$).

**Table (5): The correlation between the erythrocyte parameters and the MS components according to sex**

| Erythrocyte Parameters | DBP | TG | HDL | WC | BMI |
|---|---|---|---|---|---|
| | Male | | | | |
| RBC | 0.29** | 0.30** | - 0.21** | 0.22* | 0.29* |
| Hb | 0.11 | 0.39** | - 0.19* | 0.32** | 0.14 |
| HCT | 0.24* | 0.42** | - 0.17 | 0.10 | 0.11 |
| RDW | 0.11 | -0.10 | 0.32** | 0.09 | - 0.31** |
| | Female | | | | |
| RBC | 0.40** | 0.25** | - 0.33** | 0.19* | 0.25** |
| Hb | 0.28** | 0.51** | - 0.31** | 0.26** | 0.12 |
| HCT | 0.12 | 0.37** | - 0.36** | 0.09 | 0.13 |
| RDW | 0.16* | - 0.14 | 0.25 | 0.05 | - 0.19* |

Receiver operating characteristic (ROC) curves were generated to obtain the area under the curve (AUC) and to determine the cutoff points of erythrocyte parameters for MS diagnosis in T2DM patients as shown in (figure 1).

RBC greater than $3.89*10^6/mm^3$ has 84.9% sensitivity and 72.7% Specificity in the diagnosis of MS in T2DM (AUC: 0.86, $p<0.05$), Hb greater than 12.75 gr/dl has 87.9% sensitivity and 68.2% Specificity in the diagnosis of MS in T2DM (AUC: 0.88, $p<0.05$), HCT greater than 38.25% has 83.8% sensitivity and 77.3% Specificity in the diagnosis of MS in T2DM (AUC: 0.85, $p<0.05$), and RDW greater than 13.15% has 78.8% sensitivity and 71.1% Specificity in the diagnosis of MS in T2DM (AUC: 0.80, $p<0.05$).

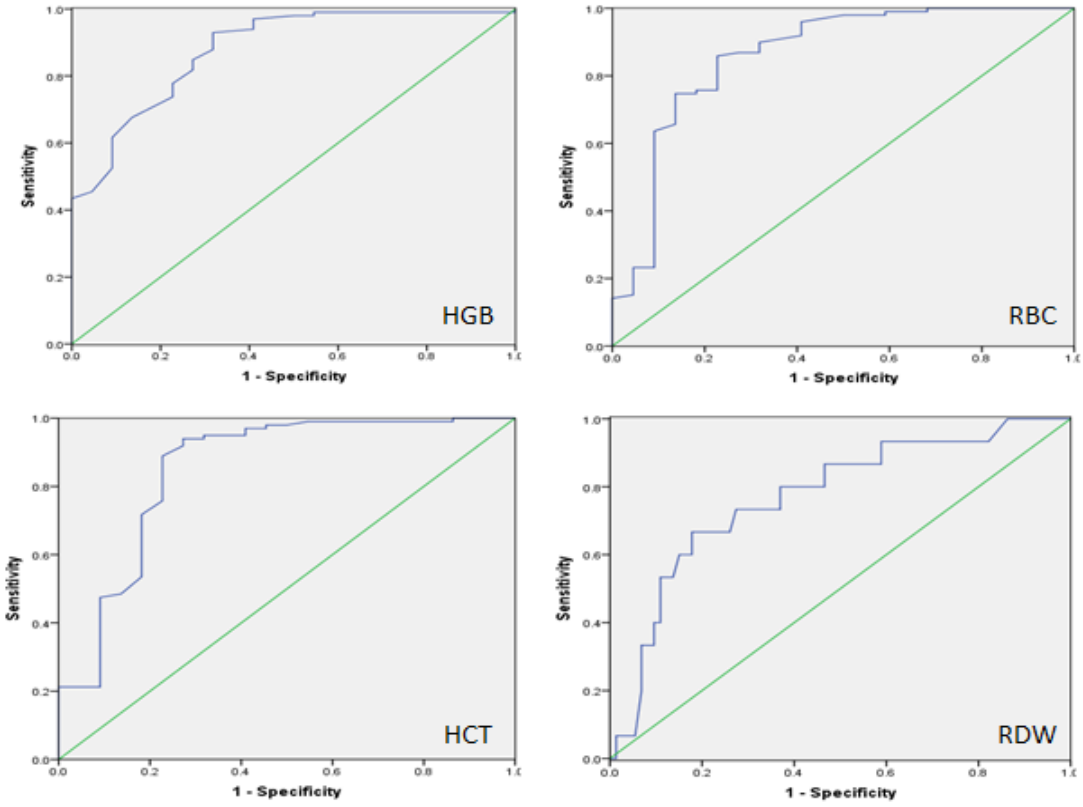


**Figure (1): ROC curve of RBC, Hb, Hct and RDW as a predictor for MS in T2DM patients**

## Discussion:

This study showed that there was a high prevalence of MS among patients with T2DM and this agreed with many previous studies conducted in Iraq[17], Brazil[18], India[19], and Ghana[20]. Many investigators confirmed that females had a higher prevalence of MS than males[21] and that was consistent with this present study. There was no significant difference according to the prevalence of MS between males and females, and this may be due to the limited sample size .

One of the main findings in our study was that levels of RBC, Hb, HCT, and RDW increased with the number of metabolic syndrome components from 1 to 5 among males and females. Our study was consistent with many previous studies[15]. RBC had been reported in many previous studies worldwide to be correlated with MS and its components[9, 10].

Our study demonstrated a positive correlation between RBC and BP, WC, and TG, while a negative correlation with HDL among males and females was observed. This result was in accordance with a study that was conducted in China[22] and reached the same results. The mechanism of the association between RBC and MS is still not enough clear. However, insulin resistance/hyperinsulinemia maybe is the causative of this relationship. The proliferation and differentiation of red blood cells are reported to be induced by insulin. Insulin and insulin growth factors I and II can support the proliferation and differentiation of erythroid progenitors in bone marrow and blood[23, 24]. The display of the insulin receptor(INS-R) during all phases of red blood cell formation suggests that insulin can be considered a co-factor in erythropoiesis[25]. The concentration of hypoxia-inducible factor-

1 alpha (HIF-1 alpha) can be elevated by hyperinsulinemia[26]. HIF-1 alpha stimulates the biosynthesis of erythropoietin and may play a role in the absorption of iron while passing throw the intestine. In the current study, Hb was reported to have a positive correlation with BP, WC, and TG which was in agreement with another study that took place in China[27]. We showed that Hb had a negative correlation with Hdl and this was consistent with the same result from research in Syria[28]. The relationship between Hb and MS may be explained by the following mechanism: Hb is known to be a major transporter and a buffer of nitric oxide(NO). The affinity between Hb and oxygen through blood circulation can be affected by different components of Hb with NO[29]. So, NO synthesis disorders may have negative actions on endothelial dysfunction[30] which was previously reported to be correlated with MS. Many researchers confirmed that Hb takes part in regulating the levels of sCD40L that is associated with thrombotic microenvironment and inflammation[31]. However, this can promote the development of atherosclerosis and MS[32]. HCT was shown to have a positive correlation with BP, WC, and TG and that was consistent with Chinese research[13] which reported that HCT was associated with hypertension, dyslipidemia, and obesity. Blood viscosity could be increased by the risen levels of HCT and this can promote peripheral resistance to blood flow. Data from previous studies suggested that the increasing numbers of hematocrit and WBV were related to insulin resistance and therefore to T2DM[33]. High WBV could result in the reduction of blood flow and this can lead to diminishing the transmission of insulin, glucose, and oxygen to the skeletal muscles[34]. Accordingly, higher WBV could be the direct reason for higher blood concentrations of glucose and insulin. A positive correlation was reported between RDW and each BP, WC, and HDL while there was a negative correlation with TG. Our study was in agreement with a study that was performed in China[12].

RDW is defined as the change in the volume of circulating red blood cells and is considered to be one of the main parameters that are used in the diagnosis of anemia. The mechanism that explains the relationship between RDW and MS is still unclear. MS was previously reported to be associated with low-grade inflammation. High levels of RDW reflect an inflammatory state. Erythropoietin-induced erythrocyte maturation can be inhibited by pro-inflammatory cytokines and this can be the causative of the risen in RDW levels[35, 36].

## Conclusion:

Our study showed that high levels of erythrocyte parameters (RBC, Hb, HCT, and RDW) were associated with metabolic syndrome and its components among patients with T2DM. Due to this relationship, it is possible to use these routine, inexpensive and noninvasive parameters to investigate metabolic syndrome, especially with its high prevalence and dangerous complications.

**References:**

1.Schlaich, M., et al., Metabolic syndrome: a sympathetic disease? Lancet Diabetes Endocrinol, 2015. **3**(2): p. 148-57.
2.Grundy, S.M., et al., Clinical management of metabolic syndrome: report of the American Heart Association/National Heart, Lung, and Blood Institute/American Diabetes Association conference on scientific issues related to management. Arterioscler Thromb Vasc Biol, 2004. **24**(2): p. e19-24.
3.Alberti, K.G., et al., Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation, 2009. **120**(16): p. 1640-5.
4.Misra, A. and L. Khurana, Obesity and the metabolic syndrome in developing countries. J Clin Endocrinol Metab, 2008. **93**(11 Suppl 1): p. S9-30.
5.Gonzalez, A.S., et al., Metabolic syndrome, insulin resistance and the inflammation markers C-reactive protein and ferritin. Eur J Clin Nutr, 2006. **60**(6): p. 802-9.
6.Musani, S.K., et al., Aldosterone, C-reactive protein, and plasma B-type natriuretic peptide are associated with the development of metabolic syndrome and longitudinal changes in metabolic syndrome components: findings from the Jackson Heart Study. Diabetes Care, 2013. **36**(10): p. 3084-92.
7.Ferrannini, E., Physiological and metabolic consequences of obesity. Metabolism, 1995. **44**(9 Suppl 3): p. 15-7.
8.Ellinger, V.C., et al., Relation between insulin resistance and hematological parameters in a Brazilian sample. Arq Bras Endocrinol Metabol, 2006. **50**(1): p. 114-7.
9.Kawamoto, R., et al., Hematological parameters are associated with metabolic syndrome in Japanese community-dwelling persons. Endocrine, 2013. **43**(2): p. 334-41.
10.Nebeck, K., et al., Hematological parameters and metabolic syndrome: findings from an occupational cohort in Ethiopia. Diabetes Metab Syndr, 2012. **6**(1): p. 22-7.
11.Hashimoto, Y., et al., Hemoglobin concentration and incident metabolic syndrome: a population-based large-scale cohort study. Endocrine, 2015. **50**(2): p. 390-6.
12.Yan, Z., et al., The relationship between red blood cell distribution width and metabolic syndrome in elderly Chinese: a cross-sectional study. Lipids Health Dis, 2019. **18**(1): p. 34.
13.Wu, S., et al., Association between erythrocyte parameters and metabolic syndrome in urban Han Chinese: a longitudinal cohort study. BMC Public Health, 2013. **13**(1): p. 989.
14.Ahmadzadeh, J., et al., The association between hematological parameters and metabolic syndrome in Iranian men: A single center large-scale study. Diabetes Metab Syndr, 2018. **12**(1): p. 17-21.
15.Huang, L.L., et al., Association of erythrocyte parameters with metabolic syndrome in the Pearl River Delta region of China: a cross sectional study. BMJ Open, 2018. **8**(1): p. e019792.
16.Grundy, S.M., et al., Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation, 2005. **112**(17): p. 2735-52.
17.Mansour, A., The prevalence of metabolic syndrome among patients with type 2 diabetes mellitus in Basrah. Middle East Journal of Family Medicine(MEJFM), 2007. **5**: p. 20-22.
18.Lira, J.C.G., et al., Prevalence of metabolic syndrome in individuals with type 2 diabetes mellitus. Revista brasileira de enfermagem, 2017. **70**: p. 265-270.
19.Yadav, D., et al., Prevalence of metabolic syndrome in type 2 diabetes mellitus using NCEP-ATPIII, IDF and WHO definition and its agreement in Gwalior Chambal region of Central India. Glob J Health Sci, 2013. **5**(6): p. 142-55.

20.Nsiah, K., et al., Prevalence of metabolic syndrome in type 2 diabetes mellitus patients. Int J Appl Basic Med Res, 2015. **5**(2): p. 133-8.
21.Sidorenkov, O., O. Nilssen, and A.M. Grjibovski, Metabolic syndrome in Russian adults: associated factors and mortality from cardiovascular diseases and all causes. BMC Public Health, 2010. **10**(1): p. 582.
22.Zhou, P., et al., The associations between leukocyte, erythrocyte or platelet, and metabolic syndrome in different genders of Chinese. Medicine (Baltimore), 2016. **95**(44): p. e5189.
23.Dainiak, N. and S. Kreczko, Interactions of insulin, insulinlike growth factor II, and platelet-derived growth factor in erythropoietic culture. J Clin Invest, 1985. **76**(3): p. 1237-42.
24.Bersch, N., J.E. Groopman, and D.W. Golde, Natural and biosynthetic insulin stimulates the growth of human erythroid progenitors in vitro. J Clin Endocrinol Metab, 1982. **55**(6): p. 1209-11.
25.Aoki, I., et al., Stimulatory effect of human insulin on erythroid progenitors (CFU-E and BFU-E) in human CD34+ separated bone marrow cells and the relationship between insulin and erythropoietin. Stem Cells, 1994. **12**(3): p. 329-38.
26.McCarty, M.F., Hyperinsulinemia may boost both hematocrit and iron absorption by up-regulating activity of hypoxia-inducible factor-1alpha. Med Hypotheses, 2003. **61**(5-6): p. 567-73.
27.He, S., et al., Hemoglobin concentration is associated with the incidence of metabolic syndrome. BMC Endocrine Disorders, 2021. **21**(1): p. 53.
28.Kaddar A.T, Bobo A.A and Yousif M.J. Association of hematological parameters with components of metabolic syndrome in the Syrian Coast population. Tishreen University Journal -Medical Sciences Series. (2017); 38(5).
29.Zinchuk, V.V., T.P. Pronko, and M.A. Lis, Blood oxygen transport and endothelial dysfunction in patients with arterial hypertension. Clin Physiol Funct Imaging, 2004. **24**(4): p. 205-11.
30.Toda, N., S. Tanabe, and S. Nakanishi, Nitric oxide-mediated coronary flow regulation in patients with coronary artery disease: recent advances. Int J Angiol, 2011. **20**(3): p. 121-34.
31.Kutlu, M., et al., Relationship between hemoglobin and CD40 ligand in prediabetes. Clin Invest Med, 2009. **32**(6): p. E244.
32.Missiou, A., et al., CD40L induces inflammation and adipogenesis in adipose cells--a potential link between metabolic and cardiovascular disease. Thromb Haemost, 2010. **103**(4): p. 788-96.
33.Tamariz, L.J., et al., Blood viscosity and hematocrit as risk factors for type 2 diabetes mellitus: the atherosclerosis risk in communities (ARIC) study. Am J Epidemiol, 2008. **168**(10): p. 1153-60.
34.Minato, S., et al., Association of Whole Blood Viscosity With Metabolic Syndrome in Type 2 Diabetic Patients: Independent Association With Post-Breakfast Triglyceridemia. J Clin Med Res, 2017. **9**(4): p. 332-338.
35.Arbel, Y., et al., Red blood cell distribution width and 3-year outcome in patients undergoing cardiac catheterization. J Thromb Thrombolysis, 2014. **37**(4): p. 469-74.
36.Pierce, C.N. and D.F. Larson, Inflammatory cytokine inhibition of erythropoiesis in patients implanted with a mechanical circulatory assist device. Perfusion, 2005. **20**(2): p. 83-90.