# Hematological Indices as Surrogate Markers in Hypertension: an Observational Clinical Study

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## Abstract

Hematological indices are used as markers for diagnostic and prognostic purposes in medicine.

**Aims:** This study aimed to assess the levels of hematological indices in hypertensive patients taking in consideration the status of the blood pressure control and the metabolic derangements.

**Materials and Methods:** A total number of 82 hypertensive patients were enrolled in this study. They were grouped into Group I (controlled hypertension, n=14)) and Group II (Uncontrolled hypertension, n=68). Anthropometric measurements, fasting serum lipid profile, and hematological indices were determined.

**Results:** Significant high serum levels of triglyceride were observed among Group II. There is insignificant difference between Group I and II in the hematological indices. Group II patients showed a significant correlation of plateletcrit (PCT) with mean arterial pressure, and platelet distribution width (PDW) with triglycerides. In Group I, a significant positive correlation between PCT with body mass index, and mean platelet volume (MPV) with cholesterol and apolipoprotein B100 were observed.

**Conclusion:** We conclude that the MPV values tended to be lower while the PCT is higher than the normal values in hypertension whether controlled or uncontrolled. The red blood cell width (RDW) values do not discriminate between controlled and uncontrolled hypertension.

**Keywords:** Hypertension, Hematological indices, Metabolic risk factors.

## Introduction

Hematological indices are thoroughly studied in hypertensive patients and they are considered as surrogate markers of vascular risk. The mean platelet volume (MPV) was found to be higher in non-dipper hypertensive patients treated with antihypertensive drugs and significantly correlated with systolic, diastolic and nocturnal pulse pressure[1]. Boose et al demonstrated a stepwise increase of MPV in hypertensive patients and it significantly correlated with platelet distribution width (PDW) and systolic blood pressure[2]. Recently, plateletcrit (PCT) was found to be a predictor for the proteinuria that complicated or associated with hypertension[3]. In untreated hypertension, the mean value of red cell width

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distribution (RWD) is significantly higher in patients who have left ventricular hypertrophy[4]. The link between hypertension and significant changes in the hematological indices is related to the activation of blood platelet which is implicated in the alteration of the blood vessel function and thereby implicated in the pathogenesis of many diseases including hypertension[5]. Therefore, these hematological indices are not specific for hypertension and they tended to be increased significantly in many diseases of heterogenous eitopathology. They increase in pre-eclampsia[6], acute coronary syndrome[7], chronic pulmonary hypertension[8], stroke[9], dyslipidemia[10] and obesity [11]. In obese subjects, the MPV inversely and significantly correlated with systolic blood pressure and triglycerides[11]. Siviri et al. (2013) demonstrated a non-significant correlation between MPV with triglycerides or total cholesterol or low density lipoprotein-cholesterol[12]. The rationale of this study is related to the concept that these markers tended to be increased in the active disease as with inflammatory markers and then declined when the disease became inactive with treatment. Therefore, this study aimed to assess the levels of hematological indices in hypertensive patients treated with different drug modalities and to link these levels to the controlled status of the blood pressure and to the metabolic derangements usually associated with hypertension including obesity and dyslipidemia.

**Methods**

This observational clinical study was performed at the Departments of Physiology and Pharmacology, College of Medicine, Al-Mustansiriya University, Baghdad, Iraq in accordance with the Declaration of Helsinki

from 1st January 2014 to 30th January 2015. The study protocol was approved by the Institutional Scientific Committee. The study included hypertensive patients who were followed up with a diagnosis of essential hypertension at the private clinics. All patients provided informed consent to participate in the study. The criteria of inclusion were essential hypertension treated with antihypertensive drugs and related medications including acetylsalicylic acid (100 mg/daily) and one of the lipid lowering agents. The criteria of exclusion included secondary hypertension, diabetes mellitus, pregnancy, renal and hepatic failure. From each patient, the subjective data related to the current medical and the other associated illness were obtained. Each patient was examined clinically and subjected to the following measurements; blood pressure, anthropometric indices, fasting serum lipid profile, complete blood count and related hematological indices. The blood pressure was measured in the sitting position and the mean of three readings was taken. The mean arterial blood pressure was determined using the following equation: Mean arterial blood pressure (mmHg) = Diastolic + $\frac{1}{3}$ pulse pressure. The pulse pressure is equal to systolic *minus* diastolic blood pressure.

The anthropometric measurements included height, weight and waist circumference. Body mass index (BMI) was calculated by applying the Quetlete's equation:
Body mass index (kg/m$^2$) = weight (kg)/height$^2$(m).

Peripheral venous blood was drawn immediately after admission into a plane and EDTA-tubes Plane tubes that contained blood were centrifuged at 2500 RPM for 10 min, and the sera were separated for determination of lipid profile. The determinants of lipid profile included fasting serum cholesterol,

triglycerides, and high density lipoprotein. The levels of the apolipoprotein B100 were calculated by using the following equation: $0.65 \times$ (non-HDL-c) + 6.3[13]. The EDTA tubes were used for determination of hematological indices using hematology analyzer.

A total number of 82 hypertensive patients were enrolled in this study; 14 of them have a blood pressure < 140 mm Hg (systolic) and < 90 mm Hg (diastolic) and they were assigned as controlled hypertension (Group I) and 68 of them have a blood pressure > 140 mm Hg (systolic) and/or >90 mm Hg (diastolic) and they were assigned as uncontrolled hypertension (Group II).

**Statistical analysis**

The statistical analysis was performed by using SPSS v.20.0 for Windows (IBM Corp., Armonk, NY, USA). The results are expressed as a number and mean ± SD. Difference between percentages test was used to compare categorical variables. The differences in means were analyzed by using the two tailed unpaired t-test and a simple correlation test was used to determine the relationship between hematological indices and the variables related to the mean blood pressure and the other metabolic derangement determinants. The level of statistical significance was set at $p \leq 0.05$.

**Results**

The characteristics data of the patients showed uneven distribution of the gender in each group. The male to female ratio in Group I and II is 1:6 and 1:2.6 (Table 1). The mean age of Group II patients is non-significantly higher than the corresponding mean age of Group I (Table 1). Group II patients had a non-significant long duration of hypertension compared with Group I patients (Table 1).

Current smoking was observed in a significant high frequency among Group II patients compared with Group I patients (Table 1). Among the past history of diseases related to the hypertension, significant high frequency of stoke was observed in Group II compared to Group I. No significant differences in the prescribed drugs between Group I and II patients (Table 1). Significant high systolic (p<0.001), diastolic (p<0.001), pulse (p=0.004) and mean arterial blood pressure (p<0.001) were observed in patients of Group II compared with Group I (Table 2). Table 3 showed a significant high value of mean height of Group II patients. Otherwise there were no significant differences in body mass index or the waist measurement between Group I and Group II. The mean levels of fasting serum triglycerides were significantly lower in Group II compared with Group I while the fasting serum cholesterol, high density lipoprotein-cholesterol and apolipoprotein B100 levels did not show significant difference between Group I and Group II (Table 4). The hematological indices related to white blood cells and red blood cells were non-significantly higher in Group II compared with Group I while the indices related to platelets showed non-significant low values in Group II compared with Group I (Table 5). In Group I the PCT is significantly and directly correlated with body mass index (Table 6) while the mean platelet volume is significantly and negatively correlated with fasting serum cholesterol and the calculated apolipoprotein levels (Table 6). In Group II, the PCT is positively and significantly correlated with mean arterial blood pressure (Table 6) while the PDW is significantly and positively correlated with fasting serum triglycerides (Table 6).

**Table 1. Characteristics of the study population**

| Characteristics | Group I (n=14) | Group II (n=68) | Probability |
|---|---|---|---|
| Gender (M:F) | 2:12 | 19:49 | |
| Age (Year) | 61.5±6.0 | 64.0±8.4 | 0.175 |
| Duration of Hypertension (Year) | 11.3±4.5 | 14.0±4.8 | 0.083 |
| Current smoking | 3 (21.4) | 36 (52.9) | 0.031* |
| Previous history:<br>Hypertensive crisis<br>Transient ischemic attack<br>Migraine<br>Stroke<br>Ischemic heart disease | 0(0)<br>0(0)<br>1(7.1)<br>1(7.1)<br>4(28.6) | 0(0)<br>4(5.9)<br>1(1.5)<br>30(44.1)<br>25(36.8) | 0.0<br>0.352<br>0.210<br>0.009*<br>0.559 |
| Current medications<br>Lipid lowering agents<br>ACEI<br>ARBs<br>β-adrenoceoptor blockers<br>α-adrenoceptor blockers<br>Thiazides | 12(85.7)<br>5(35.7)<br>4(28.6)<br>4(28.6)<br>3(21.4)<br>3(21.4) | 44(64.7)<br>19(27.9)<br>28(41.2)<br>35(51.5)<br>8(11.8)<br>12(17.6) | 0.124<br>0.560<br>0.378<br>0.118<br>0.334<br>0.739 |

The results are expressed as number and mean ± SD. *Significant difference between Group I and II.ACEI: angiotensin converting enzyme inhibitors; ARBs: angiotensin receptor blockers;

**Table 2. Blood pressure measurements**

| Blood pressure (mmHg) | Group I (n=14) | Group II (n=68) | Probability |
|---|---|---|---|
| Systolic | 127.1±8.0 | 152.3±19.7 | 0.000 |
| Diastolic | 82.1±2.6 | 97.8±9.6 | 0.000 |
| Pulse | 45.0±8.5 | 54.5±17.4 | 0.004 |
| Mean arterial | 97.1±3.1 | 115.9±11.1 | 0.000 |

The results expressed as mean ± SD

**Table 3. Anthropometric measurements**

| Anthropometric measurements | Group I (n=14) | Group II (n=68) | Probability |
|---|---|---|---|
| Weight (kg) | 81.9±12.1 | 86.5±15.5 | 0.226 |
| Height (m) | 1.59±0.06 | 1.63±0.09 | 0.036 |
| Body mass index (kg/m$^2$) | 32.31±4.39 | 32.51±5.83 | 0.088 |
| Waist circumference (cm) | 95.1±14.2 | 102.6±15.1 | 0.088 |

The results expressed as mean ± SD

**Table 4. Fasting lipid profile measurements**

| Fasting lipid profile (mg/dl) | Group I (n=14) | Group II (n=68) | Probability |
|---|---|---|---|
| Total cholesterol | 186.8±35.1 | 187.2±31,5 | 0.970 |
| Triglycerides | 180.0±41 | 148.6±48.4 | 0.019 |
| High density lipoprotein-cholesterol | 45.6±5.8 | 47.6±6.2 | 0.258 |
| Apolipoprotein B100 | 95.9±21.0 | 93.5±21.7 | 0.704 |

The results expressed as mean ± SD

**Table 5. Hematological indices**

| Hematological indices | Group I (n=14) | Group II (n=68) | Probability |
|---|---|---|---|
| White cell count (per mm$^3$) | 8985±2821 | 9826±4072 | 0.359 |
| Red blood cell count(x10$^6$ per mm$^3$) | 4.446±0.643 | 4.612±0.806 | 0.410 |
| Hemoglobin (g/dl) | 12.9±2.1 | 13.4±1.5 | 0.385 |
| Hematocrit (%) | 38.0±6.0 | 39.3±4.2 | 0.443 |
| Mean cell volume (fL) | 85.5±6.8 | 85.6±9.1 | 0.988 |
| Mean corpuscular hemoglobin (pg/cell) | 29.0±2.7 | 29.5±3.4 | 0.576 |
| Mean corpuscular hemoglobin concentration (g/dl) | 33.9±1.0 | 34.2±1.1 | 0.314 |
| Platelet count (x10$^3$ per mm$^3$) | 340.7±161.7 | 323.5±97.8 | 0.706 |
| Red cell distribution width (%) | 12.91±1.73 | 12.43±0.98 | 0.329 |
| Plateletcrit(%) | 0.177±0.09 | 0.158±0.043 | 0.441 |
| Mean platelet volume (fL) | 5.28±0.89 | 5.01±0.79 | 0.304 |
| Platelet distribution width (%) | 17.34±1.17 | 17.14±0.77 | 0.559 |

The results expressed mean ± SD.

**Table 6. Correlation between hematological indices and the cardio-metabolic risk factors**

| | Red cell distribution width | | Plateletcrit | | Mean platelet volume | | Platelet distribution width | |
|---|---|---|---|---|---|---|---|---|
| | Group I | Group II | Group I | Group II | Group I | Group II | Group I | Group II |
| Mean arterial blood pressure (mm Hg) | -0.079 | -0.113 | +0.207 | +0.240 p=0.048 | -0.5 | +0.223 | -0.338 | 0.072 |
| Body mass index (kg/m$^2$) | -0.155 | +0.230 | +0.690 p=0.006 | +0.034 | -0.113 | +0.003 | -0.055 | -0.097 |
| Waist circumference (cm) | +0.071 | +0.163 | +0.322 | +0.178 | +0.072 | +0.008 | +0.277 | -0.068 |
| Total cholesterol (mg/dl) | -0.185 | -0.123 | +0.106 | -0.002 | -0.758 p=0.0016 | +0.120 | -0.226 | +0.03 |
| Triglycerides (mg/dl) | -0.314 | -0.158 | +0.114 | +0.044 | -0.385 | +0.044 | +0.188 | +0.248 p=0.041 |
| High density lipoprotein (mg/dl) | +0.187 | -0.040 | -0.171 | -0.028 | -0.305 | -0.025 | +0.080 | -0.053 |
| Apolipolipoprotein B100 (mg/dl) | -0.235 | -0.045 | +0.145 | 0.054 | -0.768 (p=0.001) | +0.160 | -0.259 | +0.056 |

The results are expressed as a correlation factors (r) and the significant probability (p) values

**Discussion**

The results of this study show that there is non-significant difference in the hematological indices between Group I and II. In Group I patients, there is significant positive correlation between BMI with PCT and significant negative correlation between lean platelet volume with total cholesterol and apolipoprotein B100 while in Group II significant positive correlation between mean platelet volume with mean arterial blood pressure and platelet distribution with triglycerides. The status of blood pressure control may be attributed to the significant correlations between hematological indices with cardio-metabolic risk factors. The values of mean platelet volume in both groups are less than the normal range (7.5-11.5fL). Previous studies demonstrated that MPV values were significantly higher in hypertension associated with proteinuria, which reflected the relationship between activated platelets and abnormal renal function[3]. Surgit et al (2015) reported a significant high value of MPV in patients with resistant uncontrolled hypertension (8.97±0.99 fL) compared with controlled hypertension patients (8.46±0.84 fL) and normotensive subjects (8.17±0.63fL). Taking in consideration the normal range of MPV, the MPV values of normotensive and hypertensive patients are within normal values[14]. Furthermore, a significant positive correlation between office systolic or diastolic blood pressure with MPV is reported in the Surgit's study[14]. In this study, the mean arterial blood pressure is significantly correlated with the PCT in uncontrolled hypertension. The PCT percent values are less than normal value (0.23%) despite a non-significantly higher value among Group I compared with Group II. Plateletcrit, a useful marker of active inflammation is significantly and directly correlated with mean arterial blood pressure and body mass index among Group II and I respectively, indicating that there is a link between the cardio-metabolic risk factors and inflammation[15]. In this study the PDW is higher than 17%, which means that hypertensive patients are at high risk of mortality, as the results of Zhang et al study (2015) recently reported[16]. Moreover, our study documented a significant positive correlation between PDW with serum triglyceride levels, an atherogenic lipid and one component of metabolic syndrome, in Group II. This indicates that our patients are more vulnerable to the prothrombotic tendency[17]. The results of this study do not show significant correlation with any component of cardio-metabolic risk factors and these results are in agreement with Laufer Perl 's study[18] which showed that patients with RDW values > 14% are positively and significantly correlated with the components of metabolic syndrome and long term all-cause mortality. One of the limitations of this study is the small sample size of Group I.

We conclude that all hematological indices should be considered in the assessment of hypertension. The MPV values tended to be lower while PCT is higher than the normal values in hypertension, whether controlled or uncontrolled. The RDW values do not discriminate between controlled and uncontrolled hypertension and do not show significant correlations with any cardio-metabolic risk factors.

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# المؤشرات الدموية كعلامات بديلة في ارتفاع ضغط الدم: دراسة بينة سريرية

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## الملخص

**خلفية:** ارتفاع ضغط الدم قد يكون أولي أو ثانوي ويتزامن بامراضية أو بفقدان الحياة.

**أهداف الدراسة:** تقييم المؤشرات الدموية عند مرضى ارتفاع ضغط الدم أخذين بنظر الاعتبار مدخل السيطرة على ضغط الدم والتقلبات الأيضية.

**المواد وطرائق العمل:** تم ضم 82 مريضا بارتفاع ضغط الدم في هذه الدراسة وتصنيفهم إلى المجموعة I (ارتفاع ضغط الدم المسيطر وعليه عددهم 14) وبمجموعة II (ارتفاع ضغط الدم غير المسيطر وعليه عددهم 68). تم احتساب القياسات الأنثروبومترية ومفردات مستويات الشحوم في المصل الصائم والمؤشرات الدموية. إضافة إلى المؤشرات الدموية.

**النتائج:** لوحظ ارتفاع مستويات الشحوم الثلاثية في المصل عند المجموعة II بدلالة نوعية متميزة ولم يكن هناك اختلاف ذو دلالة نوعية متميزة في المؤشرات الدموية بين المجموعتين I وII. لوحظ وجود ارتباط ذو دلالة نوعية متميزة بين نسبة تكدس الصفيحات الدموية وارتفاع ضغط الدم وكذلك بين التوزيع العرضي للصفيحة الدموية والشحوم الثلاثية. كما كان ارتباط ذو دلالة نوعية متميزة بين تكدس الصفيحات الدموية مع مؤشر كتلة الجسم، وكذلك بين معدل حجم الصفيحة الدموية مع الكوليستيرول وأبولايبوبروتيب–ب 100.

**استنتاج:** نستنج من هذه الدراسة أن قيم معدل حجم الصفيحة الدموية تنخفض في حين قيم تكدس الصفيحات الدموية تزداد عند ارتفاع ضغط الدم سواءً كان مسيطر أو غير مسيطر عليه. ولم تميز قيم توزيع كريات الدم الحمر العرضي ما بين ارتفاع ضغط الدم المسيطر وغير المسيطر عليه.

**الكلمات الدالة:** ارتفاع ضغط الدم، المؤشرات الدموية، عوامل أخطار أيضية.