# Exploring the Hematological Disorders among Normotensive, Prehypertensive and Hypertensive in an Adult Population 

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#### Abstract

Objective: To explore the disorders in the hematological index among normotensive, prehypertensive and hypertensive patients and help detect the predictive and preventive factors of hypertension-related complications.

Methods: A comparative cross-sectional study was conducted from January to December 2018 on a total of 3000 study participants classified as hypertensive (HTN, blood pressure $\geq 140 / 90 \mathrm{mmHg}$ ), prehypertensive ( PHTN , blood pressure $=120-139 / 80-89 \mathrm{mmHg}$ ), and normotensive (NTN, blood pressure $<120 / 80 \mathrm{mmHg}$ ) with 1000 participants in each group. Cross tabulation and Chi-square tests were used for categorical variables. The Kruskal-Wallis and Mann-Whitney U-test were used to compare the difference between groups.

Result: There were 2005(66.8\%) males and 995(33.2\%) females out of 3000 study participants. The progression from normotensive to hypertensive was associated with an increase in age, body mass index (BMI), fasting plasma glucose (FPG), and predominantly more in males. There was a statistically significant ( $P<0.001$ ) difference between all the hematological factors and the blood pressure category (NTN, PHTN, and HTN) except red blood cell distribution width (RDW) $(P=0.150)$ and platelets, PLT $(P=0.357)$. A Mann-Whitney $U$ test results indicated a significant difference between Red Blood Cell (RBC), white blood cell (WBC), hematocrit (HCT), mean erythrocytic hemoglobin concentration (MEHC), and the pairwise comparison of blood pressure category. However, mean corpuscular volume, MCV ( $P=0.885$ ), mean corpuscular hemoglobin concentration, MCHC $(P=0.153)$ and mean platelet volume, MPV $(P=0.188)$ showed no statistically significant difference between NTN and PHTN groups. Hgb $(P=0.055)$ did not show a statistically significant difference between PHTN and HTN.

Conclusion: There was a statistically significant difference in hematological factors across blood pressure categories with observed similarities between PHTN and HTN compared to the NTN population. Clinicians can use hematological disorders to detect hypertension-related complications and improve overall health.


Keywords: Hypertension; Blood Pressure; Prevalence; Hematological Factors

List of abbreviations: BP: Blood Pressure; NTN: Normotensive; PHTN: Prehypertensive; HTN: Hypertensive; WHO: World Health Organization; CBC: Complete Blood Cell Count; DBP: Diastolic Blood Pressure; HCT: Hematocrit; Hgb: Hemoglobin; HTN: Hypertension; MCHC: Mean Cell Hemoglobin Concentration; MCV: Mean Cell Volume; MmHg: Millimeters mercury; MPV: Mean Platelet Volume; PLT: Platelets; RBC: Red Blood Cells; RDW: Red Blood Cell Distribution Width; SBP: Systolic Blood Pressure; WBC: White Blood Cells

## Introduction

Hematological factors are components of blood that serve as markers for diagnosing disease, conditions, and infections [1]. Hematological disorders have an impact on hypertension and present challenges in its clinical diagnosis and prognosis [2]. Blood pressure (BP) is the force exerted via circulating blood against arteries' walls and the major blood vessels given as systolic pressure by diastolic pressure (SBP/DBP) mmHg. BP less than $120 / 80 \mathrm{mmHg}$, within $120-139 / 80-89 \mathrm{mmHg}$, and $\geq 140 / 90 \mathrm{mmHg}$ are termed as normotensive (NTN), prehypertensive (PHTN), and hypertensive (HTN), respectively [3].

Hematological factors such as hematocrit (HCT), hemoglobin (Hgb), red blood cell (RBC) count, white blood cell (WBC) count, and platelet (PLT) count are associated with functional and structural defects to organs that involve in the formation and development of blood cells [4,5]. Hypertensive end-organ deformities, such as cardiovascular diseases and kidney failure, are due to hematological disorders [6,7]. Low Hgb levels cause anemia and heart failure [8], while increased Hgb levels may cause left ventricular hypertrophy and blood disorders in hypertensive patients [9].

Hypertension contributes about $55 \%$ of the global mortality caused by cardiovascular diseases and $7 \%$ of all disability-adjusted life years [10]. China's population is aging with some public health problems such as hypertension, lifestyle changes, diabetes, and increased urbanization. In China, about 244.5 million adults ( $23 \%$ ), 435 million ( $41.3 \%$ ) had prehypertension, and less than $18 \%$ of such individuals effectively controlled their blood pressure [11]. Prevention and early diagnosis of hypertension in adults is an essential strategy for the control of cardiovascular diseases [12]. Prehypertension and hypertension are major health problems worldwide associated with hematological disorders and cardiovascular diseases. Hematological disorders may also enhance endorgan damages. Knowledge of the hematological changes of prehypertensive and hypertensive in comparison with normotensive individuals may enable the clinician to establish an effective and early therapeutic intervention in order to prevent the occurrence of significant complications. We, therefore, aimed to explore the hematological disorders across the BP category in the general population to help guide physicians in the diagnosis and prevention of hypertension-related complications.

## Methods

## Study area and study subjects

This comparative cross-sectional study involved 3000 Nanjing residents aged 35 years or over who took part in a routine health screening at the Health Management Center of the First Affiliated Hospital of Nanjing Medical University in 2018. A simple questionnaire was used to collect demographic characteristics and behavior factors. Blood samples were collected to measure the blood cell count (CBC) using an automatic hematology analyzer. We extracted demographic characteristics, behavioral factors, anthropometric, biochemical parameters, body mass index (BMI), blood glucose values, blood pressure, total cholesterol (TC), triglyceride (TG), and fasting blood glucose (FBG) of the subjects from the health examination database. Adoption of informed consent was not applicable since we did not involve study participants in the enrollment and conduct of this study.

The hematological factors included in this study were white blood cell ( $\mathrm{WBC}, 10^{9} / \mathrm{L}$ ), red blood cell ( $\mathrm{RBC}, 10^{12} / \mathrm{L}$ ), hemoglobin (HGB), hematocrit (HCT), mean corpuscular volume (MCV, fl), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), platelet count (PLT), and platelet distribution width (PDW).

## Definition and measurement

BP categories were estimated according to the 2017 American College of Cardiology/American Heart Association High Blood Pressure Guideline [13]. We defined hypertension as blood pressure at or above $140 / 90 \mathrm{mmHg}$ following repeated examination. BP was classified as normotensive, prehypertensive, and hypertensive. BP was measured using a standard mercury sphygmomanometer, and values were approximated to the nearest number $(\mathrm{mmHg})$.

## Statistical analysis

## Kruskal-Wallis test statistics

The Kruskal Wallis test statistics are given as $H=\frac{12}{N(N+1)} \sum_{j=1}^{k} \frac{R_{j}^{2}}{n_{j}}-3(n+1)$ where $k=$ the number of groups, $n_{j}$ is the size of the jth group, $\mathrm{R}_{\mathrm{j}}$ is the rank sum for the $j$ th group, and N is the total sample size. H is approximately equal to Chi-square with $\mathrm{k}-1$ degrees of freedom when $\mathrm{n}_{\mathrm{j}}$ is greater or equal to 5 , and the distribution of scores is similar across all groups. It is considered statistically significant at $P<0.05$.

## Test hypothesis

$\mathrm{H}_{0}$ : The medians of hematological factors across BP category are equal
$H_{1}$ : The medians of hematological factors across BP category are not equal

For multiple comparisons, the significance level ( $\alpha$ ) for each comparison should be adjusted by the Bonferroni method, $\alpha^{*}=\alpha / c$ wherect is the number of times of comparison. Kruskal-Wallis test was considered appropriate for our analysis since the hematological factors were continuous and did not follow the normal distribution.

We performed a Kruskal-Wallis test on three independent samples based on BP category as HTN (BP $\geq 140 / 90 \mathrm{mmHg}$ ), PHTN $(\mathrm{BP}=120-139 / 80-89 \mathrm{mmHg})$ and $\mathrm{NTH}(\mathrm{BP}<120 / 80 \mathrm{mmHg})$. The total study participants were 3000 , with 1000 in each group. The normality of data was evaluated using Kolmogorov-Smirnov test. Data were expressed as mean $\pm$ standard deviation (SD) for normally distributed or median $\pm$ interquartile range (IQR) for non-normally distributed variables. Cross tabulation and Chi-square tests were used for categorical variables. Kruskal-Wallis test was used to test the null hypothesis that medians of hematological factors are equal or not different between BP categories. The Mann-Whitney U test was used to evaluate pairwise differences of NTN versus PHTN, NTN versus HTN, and PHTN versus HTN by using the Dunn-Bonferroni approach to control for type 1 error. All analyses were performed with SPSS 25 (IBM, NY, USA), were two-sided, and differences were considered statistically significant at a $\mathrm{P}<0.05$.

## Results

There were 2005(66.8\%) males and 995(33.2\%) females out of 3000 study participants. The progression from normotensive to hypertensive was associated with an increase in age, BMI, fasting plasma glucose (FPG) and predominantly more in males than in females. There was statistically significant correlation between $\operatorname{sex}\left(\chi^{2}=231.2, \mathrm{P}<0.001\right)$, age group ( $\chi^{2}=340.5, \mathrm{P}<0.001$ ), BMI $\left(\chi^{2}=\right.$
473.8, P $<0.001$ ), smoking status ( $\chi^{2}=44.2, \mathrm{P}<0.001$ ), FPG $\left(\chi^{2}=83, \mathrm{P}<0.001\right)$ and BP category. Patients with FPG $<7 \mathrm{mmol} / \mathrm{l}$ were the majority ( $94 \%$ ). Comparison by BMI showed $54 \%, 40.2 \%$ and $5.7 \%$ as normal, overweight and obesity respectively (Table 1).

| Variable |  | $\begin{array}{\|l\|} \hline \text { NTN } \\ \text { N (\%) } \\ \hline \end{array}$ | $\begin{array}{\|l\|} \hline \text { PHTN } \\ \text { N (\%) } \\ \hline \end{array}$ | $\begin{aligned} & \text { HTN } \\ & \text { N (\%) } \end{aligned}$ | $\begin{array}{\|l} \hline \text { TOTAL } \\ \mathrm{N} \text { (\%) } \\ \hline \end{array}$ | Chi-square | $P$ value |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Sex |  |  |  |  |  |  |  |
|  | Male | 487(24.3) | 790(39.4) | 728(36.3) | 2005(66.8) | 231.18 | <0.001 |
|  | Female | 513(51.6) | 210(21.1) | 272(27.3) | 995(33.2) |  |  |
| Age group |  |  |  |  |  |  |  |
|  | 35-49 | 702(42.3) | 577(34.7) | 382(23.0) | 1661(55.4) | 340.49 | <0.001 |
|  | 50-64 | 278(25.0) | 395(35.5) | 441(39.6) | 1114(37.1) |  |  |
|  | $\geq 65$ | 20(8.9) | 28(12.4) | 177(78.7) | 9200(7.5) |  |  |
| BMI |  |  |  |  |  |  |  |
|  | <25 | 798(49.2) | 472(29.1) | 351(21.7) | 1621(54.0) | 473.85 | <0.001 |
|  | 25-30 | 194(16.1) | 483(40.0) | 530(43.9) | 1207(40.2) |  |  |
|  | >30 | 8(4.7) | 45(26.2) | 119(69.2) | 172(5.7) |  |  |
| Smoking status |  |  |  |  |  |  |  |
|  | Never | 733(35.4) | 629(30.4) | 707(34.2) | 2069(69.0) | 44.22 | <0.001 |
|  | Quitting | 10(16.1) | 23(37.1) | 29(46.8) | 3842(2.2) |  |  |
|  | Smoking | 190(28.4) | 286(42.8) | 193(28.8) | 6268(23.9) |  |  |
| FPG(mmol/L) |  |  |  |  |  |  |  |
|  | <7.0 | 974(34.5) | 962(34.1) | 885(31.4) | 2821(94.0) | 83.14 | $<0.001$ |
|  | $\geq 7.0$ | 26(14.5) | 28(21.2) | 115(64.2) | 179(6.0) |  |  |

BMI: body mass index; FPG: fasting plasma glucose; BP: blood pressure: NTN: normotensive; PHTN: prehypertensive; HTN: hypertensive
Table 1: Prevalence of BP category by sex, age-group, smoking status and FPG

|  |  |  | Variable |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
|  |  | Test <br> statistics | Age | BMI | SBP | DBP | FPG | Trigly <br> ceride | HDL | TC |
| BP category |  |  |  |  |  |  |  |  |  |  |
|  | NTN |  |  |  |  |  |  |  |  |  |
|  |  | Mean $\pm$ SD | $45.5 \pm 8.1$ | $23.0 \pm 2.7$ | $110.2 \pm 6.7$ | $68.6 \pm 6.2$ | $5.3 \pm 1.1$ | $1.4 \pm 1.0$ | $1.5 \pm 0.3$ | $5.4 \pm 0.9$ |
|  |  | Median | 45.0 | 22.9 | 112.0 | 69.0 | 5.0 | 1.1 | 1.4 | 5.4 |
|  |  | Q1 | 38.0 | 21.3 | 106.0 | 65.0 | 5.0 | 0.8 | 1.2 | 4.8 |
|  |  | Q3 | 51.0 | 24.6 | 115.0 | 73.0 | 5.0 | 1.6 | 1.7 | 6.0 |
|  |  | Mean $\pm$ SD | $47.8 \pm 8.0$ | $25.2 \pm 3.0$ | $130.4 \pm 5.3$ | $84.0 \pm 2.8$ | $5.6 \pm 1.2$ | $1.8 \pm 1.2$ | $1.3 \pm 0.3$ | $5.5 \pm 1.0$ |
|  |  | Qedian | 48.0 | 25.2 | 131.0 | 84.0 | 5.0 | 1.5 | 1.3 | 5.5 |
|  |  | Q3 | 51.0 | 23.2 | 126.0 | 82.0 | 5.0 | 1.0 | 1.1 | 4.9 |
|  |  |  |  | 27 | 135 | 86 | 6.0 | 2.2 | 1.5 | 6.2 |
|  |  | MTN |  |  |  |  |  |  |  |  |
|  |  | Mean $\pm$ SD | $54.0 \pm 11.6$ | $26.3 \pm 3.2$ | $155.3 \pm 12.3$ | $97.2 \pm 6.2$ | $6.2 \pm 1.5$ | $2.0 \pm 1.9$ | $1.2 \pm 0.3$ | $5.5 \pm 1.1$ |
|  |  | Q1 | 46.0 | 24.1 | 146.0 | 92.0 | 5.0 | 1.1 | 1.0 | 5.5 |
|  |  | Q3 | 61.0 | 28.3 | 162.0 | 100 | 6.0 | 2.3 | 1.4 | 6.1 |

BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; FPG: fasting plasma glucose; HDL: high-density lipoprotein; TC: total cholesterol, BP: blood pressure: NTN: normotensive, PHTN: prehypertensive, HTN: hypertensive; Q1: 25th percentile; Q3: 75th percentile Table 2: Comparison of biochemical characteristics of study participants across BP category

The mean $\pm$ SD age was $45.5 \pm 8.1$ years, $47.8 \pm 8.0$ years, and $54.0 \pm 11.6$ years for NTN, PHTN, and HTN, respectively. The median values of BMI, SBP, DBP and FPG were: 22.9, 25.2, 26.1; 112.0, 131.0, 152; 69.0, 84.0, 96; and 5.0, 5.0, 6.0 for NTN, PHTN and HTN respectively. The median values of HDL decreased across the BP category, whereas triglyceride and total cholesterol increased across the BP category (Table 2).


Figure 1: Multiple plot (A, B); A: showing SBP and DBP by sex across BP category and B: showing SBP and DBP by age group across BP category

A plot of BP indices (SBP and DBP) against sex and age group showed a high prevalence of prehypertensive and hypertensive with increased SBP/DBP in males than females. With an increase in SBP and DBP, age increased accordingly across the BP category (Figure 1).

|  | $\begin{gathered} \text { BP } \\ \text { category } \end{gathered}$ | $\begin{gathered} \text { RBC } \\ (1012 / \mathrm{L}) \end{gathered}$ | $\begin{gathered} \text { WBC } \\ (109 / \mathrm{L}) \end{gathered}$ | $\begin{aligned} & \mathrm{HCT} \\ & (\mathrm{~g} / \mathrm{dl}) \end{aligned}$ | $\begin{gathered} \text { HGB } \\ (\mathrm{g} / \mathrm{l}) \\ \hline \end{gathered}$ | MCV <br> (fl) | $\begin{gathered} \text { MECH } \\ (\mathrm{pg}) \\ \hline \end{gathered}$ | MCHC <br> (g/dl) | RDW | MPV | PLT |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Male |  |  |  |  |  |  |  |  |  |  |  |
|  | NTN |  |  |  |  |  |  |  |  |  |  |
|  | $\begin{aligned} & \text { Mean } \pm \text { SD } \\ & (\mathrm{Q} 2 \pm \mathrm{IQR}) \end{aligned}$ | $\begin{gathered} 4.4 \pm \\ 0.3 \\ (4.4 \pm \\ 0.5) \end{gathered}$ | $\begin{gathered} 5.6 \pm \\ 1.4 \\ (5.4 \pm \\ 1.0) \\ \hline \end{gathered}$ | $\begin{gathered} 39.7 \pm \\ 3.4 \\ (40.0 \pm \\ 3.1) \end{gathered}$ | $\begin{gathered} 134.1 \pm \\ 11.0 \\ (135.0 \pm \\ 10.3) \end{gathered}$ | $\begin{gathered} 90.8 \pm \\ 5.7 \\ (91.8 \pm \\ 4.9) \end{gathered}$ | $\begin{gathered} 336.9 \pm \\ 8.7 \\ (337.0 \pm \\ 9.0) \end{gathered}$ | $\begin{gathered} 30.6 \pm \\ 2.4 \\ (31.0 \pm \\ 2.0) \end{gathered}$ | $\begin{gathered} \hline 13.4 \pm \\ 1.2 \\ (13.1 \pm \\ 0.9) \\ \hline \end{gathered}$ | $\begin{gathered} 8.9 \pm \\ 1.1 \\ (8.8 \pm \\ 1.3) \\ \hline \end{gathered}$ | $\begin{gathered} 239.4 \pm \\ 56.8 \\ (237.0 \pm \\ 79.3) \\ \hline \end{gathered}$ |
|  | PHTN |  |  |  |  |  |  |  |  |  |  |
|  | $\begin{aligned} & \text { Mean } \pm \text { SD } \\ & (\mathrm{Q} 2 \pm \mathrm{IQR}) \end{aligned}$ | $\begin{gathered} 4.5 \pm \\ 0.3 \\ (4.5 \pm \\ 0.4) \\ \hline \end{gathered}$ | $\begin{gathered} \hline 5.7 \pm \\ 1.6 \\ (5.6 \pm \\ 1.7) \end{gathered}$ | $\begin{gathered} 40.6 \pm \\ 2.9 \\ (40.8 \pm \\ 3.7) \end{gathered}$ | $\begin{gathered} 136.5 \pm \\ 11.3 \\ (138.0 \pm \\ 13.0) \end{gathered}$ | $\begin{gathered} 89.9 \pm \\ 6.2 \\ (91.1 \pm \\ 5.6) \end{gathered}$ | $\begin{gathered} 336.3 \pm \\ 9.4 \\ (336.5 \pm \\ 11.0) \end{gathered}$ | $\begin{gathered} 30.3 \pm \\ 2.6 \\ (30.9 \pm \\ 2.2) \\ \hline \end{gathered}$ | $\begin{gathered} 13.4 \pm \\ 1.2 \\ (13.1 \pm \\ 0.8) \\ \hline \end{gathered}$ | $\begin{gathered} 8.8 \pm \\ 1.0 \\ (8.7 \pm \\ 1.2) \end{gathered}$ | $\begin{gathered} 246.9 \pm \\ 56.4 \\ (243.0 \pm \\ 71.5) \end{gathered}$ |
|  | HTN |  |  |  |  |  |  |  |  |  |  |
|  | $\begin{aligned} & \text { Mean } \pm \text { SD } \\ & (\mathrm{Q} 2 \pm \mathrm{IQR}) \end{aligned}$ | $\begin{gathered} \hline 4.7 \pm \\ 0.4 \\ (4.6 \pm \\ 0.5) \end{gathered}$ | $\begin{gathered} 6.2 \pm \\ 1.5 \\ (6.0 \pm \\ 1.9) \\ \hline \end{gathered}$ | $\begin{gathered} \hline 41.6 \pm \\ 3.1 \\ (41.6 \pm \\ 3.8) \\ \hline \end{gathered}$ | $\begin{gathered} 137.6 \pm \\ 11.3 \\ (138.0 \pm \\ 13.0) \end{gathered}$ | $\begin{gathered} 89.3 \pm \\ 5.2 \\ (89.8 \pm \\ 5.0) \\ \hline \end{gathered}$ | $\begin{gathered} 330.4 \pm \\ 8.3 \\ (331.5 \pm \\ 10) \\ \hline \end{gathered}$ | $\begin{gathered} 29.5 \pm \\ 2.0 \\ (29.8 \pm \\ 1.9) \\ \hline \end{gathered}$ | $\begin{gathered} 13.3 \pm \\ 1.1 \\ (13.2 \pm \\ 0.9) \\ \hline \end{gathered}$ | $\begin{gathered} 10.0 \pm \\ 1.5 \\ (10.0 \pm \\ 2.2) \\ \hline \end{gathered}$ | $\begin{gathered} 239.1 \pm \\ 60.8 \\ (237.0 \pm \\ 78.3) \\ \hline \end{gathered}$ |
| Female |  |  |  |  |  |  |  |  |  |  |  |
|  | NTN |  |  |  |  |  |  |  |  |  |  |
|  | $\begin{aligned} & \text { Mean } \pm \text { SD } \\ & (\mathrm{Q} 2 \pm \mathrm{IQR}) \end{aligned}$ | $\begin{gathered} 4.9 \pm \\ 0.5 \\ (4.9 \pm \\ 0.4) \end{gathered}$ | $\begin{gathered} 6.1 \pm \\ 1.6 \\ (5.9 \pm \\ 1.9) \end{gathered}$ | $\begin{gathered} 45.0 \pm \\ 5.3 \\ (45.5 \pm \\ 3.4) \end{gathered}$ | $\begin{gathered} 154.9 \pm \\ 9.0 \\ (155.0 \pm \\ 11.0) \end{gathered}$ | $\begin{gathered} 92.3 \pm \\ 4.3 \\ (92.2 \pm \\ 5.1) \end{gathered}$ | $\begin{gathered} 340.8 \pm \\ 10.6 \\ (340.0 \pm \\ 9.0) \end{gathered}$ | $\begin{gathered} 31.5 \pm \\ 1.8 \\ (31.5 \pm \\ 1.9) \end{gathered}$ | $\begin{gathered} 13.2 \pm \\ 0.6 \\ (13.1 \pm \\ 0.6) \\ \hline \end{gathered}$ | $\begin{gathered} 8.8 \pm \\ 1.1 \\ (8.7 \pm \\ 1.4) \end{gathered}$ | $\begin{gathered} 222.9 \pm \\ 50.3 \\ (219.0 \pm \\ 67.7) \end{gathered}$ |
|  | PHTN |  |  |  |  |  |  |  |  |  |  |
|  | $\begin{aligned} & \text { Mean } \pm \text { SD } \\ & (\mathrm{Q} 2 \pm \mathrm{IQR}) \end{aligned}$ | $\begin{gathered} 5.0 \pm \\ 0.3 \\ (5.0 \pm \\ 0.4) \end{gathered}$ | $\begin{gathered} 6.7 \pm \\ 1.5 \\ (6.6 \pm \\ 1.9) \\ \hline \end{gathered}$ | $\begin{gathered} 45.8 \pm \\ 4.5 \\ (46.2 \pm \\ 3.4) \\ \hline \end{gathered}$ | $\begin{gathered} 157.3 \pm \\ 9.5 \\ (158 \pm \\ 12.0) \end{gathered}$ | $\begin{gathered} 92.1 \pm \\ 4.4 \\ (92.0 \pm \\ 4.7) \end{gathered}$ | $\begin{gathered} 341.0 \pm \\ 7.5 \\ (341.0 \pm \\ 10.0) \end{gathered}$ | $\begin{gathered} 31.4 \pm \\ 1.7 \\ (31.4 \pm \\ 1.8) \end{gathered}$ | $\begin{gathered} 13.2 \pm \\ 0.6 \\ (13.1 \pm \\ 0.4) \end{gathered}$ | $\begin{gathered} 8.8 \pm \\ 1.0 \\ (8.7 \pm \\ 1.2) \\ \hline \end{gathered}$ | $\begin{gathered} 225.4 \pm \\ 51.4 \\ (220.0 \pm \\ 62.0) \end{gathered}$ |
|  | HTN |  |  |  |  |  |  |  |  |  |  |
|  | $\begin{aligned} & \text { Mean } \pm \text { SD } \\ & (\mathrm{Q} 2 \pm \mathrm{IQR}) \end{aligned}$ | $\begin{gathered} 4.90 \pm \\ 0.4 \\ (4.9 \pm \\ 0.6) \end{gathered}$ | $\begin{gathered} 6.2 \pm \\ 1.6 \\ (6.0 \pm \\ 2.0) \\ \hline \end{gathered}$ | $\begin{gathered} 46.8 \pm \\ 3.9 \\ (47.0 \pm \\ 3.9) \\ \hline \end{gathered}$ | $\begin{gathered} 157.3 \pm \\ 10.7 \\ (157.0 \pm \\ 13.0) \end{gathered}$ | $\begin{gathered} 91.1 \pm \\ 4.1 \\ (90.6 \pm \\ 5.2) \\ \hline \end{gathered}$ | $\begin{gathered} 335.4 \pm \\ 7.6 \\ (30.5 \pm \\ 1.9) \\ \hline \end{gathered}$ | $\begin{gathered} 30.5 \pm \\ 1.5 \\ (30.5 \pm \\ 1.9) \end{gathered}$ | $\begin{gathered} 13.1 \pm \\ 0.7 \\ (13.1 \pm \\ 0.8) \end{gathered}$ | $\begin{gathered} \hline 9.9 \pm \\ 1.4 \\ (9.9 \pm \\ 2.2) \\ \hline \end{gathered}$ | $\begin{gathered} 224.4 \pm \\ 58.1 \\ (219.5 \pm \\ 73.8) \\ \hline \end{gathered}$ |

RBC: red blood cell; WBC: white blood cell; HGB: hemoglobin; HCT: hematocrit; MCV: mean corpuscular volume; MEHC: mean erythrocyte hemoglobin concentration; MCHC: mean corpuscular hemoglobin concentration; RDW: red cell distribution width; PDW: platelet distribution width; PLT: platelet count; NTN: normotensive, PHTN: prehypertensive, HTN: hypertensive; Q2: median; IQR: interquartile range
Table 3: Comparison of hematological factors by sex across BP category

It was evident that the mean and median values of hematological factors increased across the BP category (progression from NTN to HTN). The median $\pm$ IQR of hematological factors was predominantly higher in males than in females across the BP category. For instance, the median $\pm \mathrm{IQR}$ of HCT in female was $40.0 \pm 3.1(\mathrm{~g} / \mathrm{dl})$ for NTN, $40.8 \pm 3.7(\mathrm{~g} / \mathrm{dl})$ for PHTN and $41.6 \pm 3.8(\mathrm{~g} / \mathrm{dl})$ for HTN, respectively while in males it was $45.5 \pm 3.4(\mathrm{~g} / \mathrm{dl})$ for NTN, $46.8 \pm 3.7(\mathrm{~g} / \mathrm{dl})$ for PHTN and $41.6 \pm 3.8(\mathrm{~g} / \mathrm{dl})$ for HTN, respectively. In this study, the hemoglobin mean levels of females were higher than that of males in that, there were 978/1339 males who were 50 years and above. Metabolism slows with age. Also, older people are more likely to have low iron diets, and hematopoietic defects (reduced hamtopoeisis in illness or have an iron absorption problem) (Table 3).

A Kruskal-Wallis test was conducted to evaluate differences between NTN ( $\mathrm{n}=1000$ ), PHTN ( $\mathrm{n}=1000$ ), and HTN ( $\mathrm{n}=1000$ ) on median change in hematological factors. There was a statistically significant ( $P<0.001$ ) difference of hematological factors between the BP category (NTN, PHTN, and HTN), except for RDW and PLT with $P=0.150$ and 0.357 , respectively. Following Mann-Whitney U tests were conducted to evaluate pairwise differences among three groups, controlling the Type I errors using the Bonferroni correction approach. These tests indicated a significant difference between RBC, WBC, HCT, MEHC, and the pairwise comparison of the BP category. However, MCV ( $P=0.885$ ), MCHC ( $P=0.153$ ), and MPV ( $P=0.188$ ) showed no statistically significant difference between NTN and PHTN groups. Also, $\mathrm{Hgb}(P=0.055)$ did not show a statistically significant difference between PHTN and HTN (Table 4).

| Variable | Kruskal-Wallis Test |  | Mann-Whitney U Test |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | $\begin{aligned} & \text { Mean } \pm \text { SD } \\ & (\mathrm{Q} 2 \pm \mathrm{IQR}) \end{aligned}$ | $\begin{gathered} \mathrm{P} \\ \text { Value } \end{gathered}$ | $\begin{gathered} \text { NTN vs PHTN } \\ \text { Mean } \pm \text { SD } \\ (\mathrm{Q} 2 \pm \mathrm{IQR}) \end{gathered}$ | P <br> value | $\begin{gathered} \text { NTN vs HTN } \\ \text { Mean } \pm \text { SD } \\ (\mathrm{Q} 2 \pm \mathrm{IQR}) \end{gathered}$ | $\begin{gathered} \text { P } \\ \text { Value } \end{gathered}$ | $\begin{gathered} \text { PHTN vs HTN } \\ \text { Mean } \pm \text { SD } \\ (\mathrm{Q} 2 \pm \mathrm{IQR}) \end{gathered}$ | P value |
| $\begin{gathered} \text { RBC } \\ (1012 / \mathrm{L}) \end{gathered}$ | $\begin{gathered} 4.9 \pm 0.4 \\ (4.9 \pm 0.6) \end{gathered}$ | <0.001 | $\begin{gathered} 4.9 \pm 0.4 \\ (4.9 \pm 0.6) \end{gathered}$ | <0.001 | $\begin{gathered} 4.9 \pm 0.4 \\ (4.9 \pm 0.6) \end{gathered}$ | <0.001 | $\begin{gathered} 4.9 \pm 0.4 \\ (4.9 \pm 0.6) \end{gathered}$ | <0.001 |
| $\begin{gathered} \text { WBC } \\ (109 / L) \end{gathered}$ | $\begin{gathered} 6.2 \pm 1.6 \\ (6.0 \pm 2.0) \end{gathered}$ | <0.001 | $\begin{gathered} 6.2 \pm 1.6 \\ (6.0 \pm 2.0) \end{gathered}$ | <0.001 | $\begin{gathered} 6.2 \pm 1.6 \\ (6.0 \pm 2.0) \end{gathered}$ | <0.001 | $\begin{gathered} 6.2 \pm 1.6 \\ (6.0 \pm 2.0) \end{gathered}$ | <0.001 |
| $\begin{aligned} & \mathrm{HCT} \\ & (\mathrm{~g} / \mathrm{dl}) \end{aligned}$ | $\begin{gathered} 44.1 \pm 5.0 \\ (44.7 \pm 5.6) \end{gathered}$ | $<0.001$ | $\begin{gathered} 44.1 \pm 5.0 \\ (44.7 \pm 5.6) \end{gathered}$ | <0.001 | $\begin{gathered} 44.1 \pm 5.1 \\ (44.7 \pm 5.6) \end{gathered}$ | <0.001 | $\begin{gathered} 44.1 \pm 5.0 \\ (44.7 \pm 5.6) \end{gathered}$ | <0.001 |
| $\begin{gathered} \text { HGB } \\ (\mathrm{g} / \mathrm{l}) \\ \hline \end{gathered}$ | $\begin{gathered} 149.7 \pm 14.4 \\ (151.0 \pm 20.0) \end{gathered}$ | $<0.001$ | $\begin{gathered} 149.7 \pm 14.4 \\ (151.0 \pm 20.0) \end{gathered}$ | <0.001 | $\begin{gathered} 149.7 \pm 14.3 \\ (151.0 \pm 20.0) \end{gathered}$ | <0.001 | $\begin{gathered} 149.7 \pm 14.4 \\ (151.0 \pm 20.0) \end{gathered}$ | 0.055 |
| MCV <br> (fl) | $\begin{gathered} 91.3 \pm 4.9 \\ (91.5 \pm 5.0) \end{gathered}$ | <0.001 | $\begin{gathered} \hline 91.3 \pm 4.9 \\ (91.5 \pm 5.0) \end{gathered}$ | <0.885 | $\begin{gathered} \hline 91.3 \pm 4.9 \\ (91.5 \pm 5.0) \end{gathered}$ | <0.001 | $\begin{gathered} \hline 91.3 \pm 4.9 \\ (91.5 \pm 5.0) \end{gathered}$ | <0.001 |
| MEHC <br> (pg) | $\begin{gathered} 337.6 \pm 9.1 \\ (338.0 \pm 10.0) \end{gathered}$ | <0.001 | $\begin{gathered} \hline 337.6 \pm 9.1 \\ (338.0 \pm 10.0) \end{gathered}$ | <0.001 | $\begin{gathered} \hline 337.6 \pm 9.1 \\ (338.0 \pm 10.0) \end{gathered}$ | <0.001 | $\begin{gathered} 337.6 \pm 9.1 \\ (338.0 \pm 10.0) \end{gathered}$ | <0.001 |
| MCHC <br> (g/dl) | $\begin{gathered} 30.8 \pm 2.0 \\ (31.0 \pm 2.0) \end{gathered}$ | <0.001 | $\begin{gathered} 30.8 \pm 2.0 \\ (31.0 \pm 2.0) \end{gathered}$ | <0.153 | $\begin{gathered} 30.8 \pm 2.0 \\ (31.0 \pm 2.0) \\ \hline \end{gathered}$ | <0.001 | $\begin{gathered} 30.8 \pm 2.0 \\ (31.0 \pm 2.0) \end{gathered}$ | <0.001 |
| RDW | $\begin{gathered} 13.2 \pm 0.9 \\ (13.1 \pm 0.8) \end{gathered}$ | 0.150 | $\begin{gathered} 13.2 \pm 0.9 \\ (13.1 \pm 0.8) \end{gathered}$ | 0.772 | $\begin{gathered} 13.2 \pm 0.9 \\ (13.1 \pm 0.8) \\ \hline \end{gathered}$ | 0.165 | $\begin{gathered} 13.2 \pm 0.9 \\ (13.1 \pm 0.8) \end{gathered}$ | 0.251 |
| MPV | $\begin{gathered} 9.2 \pm 1.3 \\ (8.9 \pm 1.7) \end{gathered}$ | 0.001 | $\begin{gathered} \hline 9.2 \pm 1.3 \\ (8.9 \pm 1.7) \end{gathered}$ | 0.188 | $\begin{gathered} \hline 9.2 \pm 1.3 \\ (8.9 \pm 1.7) \end{gathered}$ | <0.001 | $\begin{gathered} \hline 9.2 \pm 1.3 \\ (8.9 \pm 1.7) \end{gathered}$ | <0.001 |
| PLT | $\begin{gathered} 229.9 \pm 55.6 \\ (226.0 \pm 70.0) \end{gathered}$ | 0.357 | $\begin{gathered} 229.9 \pm 55.6 \\ (226.0 \pm 70.0) \end{gathered}$ | 0.313 | $\begin{gathered} 229.9 \pm 55.6 \\ (226.0 \pm 70.0) \end{gathered}$ | 0.115 | $\begin{gathered} 229.9 \pm 55.6 \\ (226.0 \pm 70.0) \end{gathered}$ | 0.499 |

RBC: red blood cell; WBC: white blood cell; HGB: hemoglobin; HCT: hematocrit; MCV: mean corpuscular volume; MEHC: mean erythrocyte hemoglobin concentration; MCHC: mean corpuscular hemoglobin concentration; RDW: red cell distribution width; PDW: platelet distribution width; PLT: platelet count; NTN: normotensive, PHTN: prehypertensive, HTN: hypertensive; Q2: Median Table 4: Pairwise comparison of hematological factors across BP category

## Discussion

We performed a non-parametric test and found a statistically significant association between sex, age group, BMI, smoking status, FPG, and BP category. There was a high prevalence of increased BMI and FPG levels in the PHTN and HTN category as compared to the NTN category. The levels of RBC, WBC, HCT, MEHC, MCHC, MCV, and MPV were significantly increased in PHTN and HTN individuals with some similarities compared to the normotensive group. RDW ( $P=0.150$ ) and PLT ( $P=0.357$ ) showed no statistically significant differences in median $\pm \mathrm{IQR}$ across the BP category.

Hematocrit as a determinant of blood viscosity affects the peripheral resistance to blood flow which may, in turn, affect blood pressure. A study showed an association between HCT and incidence of PHTN in a large cross-sectional study in the Chinese population [5,11]. HCT within the normal range was independently associated with the incidence of hyperuricemia [14]. An increase in HCT is usually accompanied by high blood viscosity. An increase in RBC count in HTN increases blood pressure which may result in CVD complications [15]. Hgb levels were elevated in PHTN and HTN groups than the NTN population [9,16]. These were similar to the findings in this study.

A decrease in MCV is an adaptive mechanism to decrease RBC-induced hypertension and viscosity without compromising blood flow. MCV is a hypertension-related risk factor [17]. However, one study showed no relationship between MCV and hypertension [18]. In our research, the post hoc analysis showed a significant difference in mean corpuscular hemoglobin concentration (MCHC) between pairwise BP categories.

WBC count as an inflammatory marker increases the risk of cardiovascular diseases in HTN individuals [1,19]. This study showed an increase in WBC count across the BP category (progression from NTN to HTN). WBC count is higher in PHTN and HTN individuals [20,21]. WBC count is a risk factor for hypertension and an independent predictor of cardiovascular morbidity in hypertensive patients [22].

Elevated RDW has adverse clinical outcomes in patients with HTN, coronary heart disease pulmonary HTN and serves as a potential predictor of mortality and morbidity in cardiovascular disease complications [23]. Increased levels of RDW may act as a marker of systemic inflammation and oxidative stress, which are critical biological mechanisms in both initiation and progression of hypertension. Higher RDW values are strongly correlated with higher systolic and diastolic blood pressure [24]. Platelet activation and p-selectin may participate in the accelerated target organ injury in high-risk hypertensive patients. MPV may predict hypertensive microvascular end-organ damage, diabetic microvascular complications, including nephropathy and microvascular injury in coronary vessels [25].

Platelets play a pivotal role in the development of atherosclerotic lesions, plaque destabilization, and atherothrombosis. Mean platelet volume levels were associated with severity of end-organ damage, including carotid atherosclerosis, left ventricular hypertrophy, and renal impairment [26]. In our study, the level of RDW and PLT did not show any statistically significant difference across the BP category.

Knowledge of the structural and functional disorders of the hematological factors in PHTN and HTN patients will help regulate the mechanism involved in the pathophysiology of hypertension and cardiovascular disease. This will, in turn, control and prevent hypertension health-related complications. This study has several limitations. Firstly it was cross-sectional and therefore had no comparable control group. Secondly, other hematological blood count parameters, including the neutrophil-to-lymphocyte ratio of the patients, could be investigated in further studies. Thirdly, this study was only conducted in adults aged 35 years and above.

## Conclusion

Hematological disorders in RBC, WBC, HCT, MEHC, and MPV, may cause hypertensive end-organ damage in PHTN and HTN patients. Early detection and treatment of hematological disorders in PHTN and HTN patients will control and prevent CVD and its associated diseases. Further studies on the role of hematological factors in the pathophysiologic mechanism of PHTN and HTN are warranted.

## Data availability

All data generated or analyzed during this study are included in this published article.

## Authors' contributions

Conceptualization: AL, XL, and JW; methodology: AL, XL, ZL, BT, PL, and HS; software: AL, XL, ZL, BT, PL, MLS, RG and HS; validation: JW; formal analysis: AL , XL, ZL, BT, PL, and HS; investigation: XL, ZL, BT, PL, HS, MLS, RG and JW; resources: XL and JW; data curation: XL and JW; writing-original draft preparation: AL and XL; writing-review and editing: JW; visualization: AL, XL and JW; supervision: JW; project administration: XL and JW; funding acquisition: JW. All authors have agreed on the journal to which the article has been submitted and agreed to be accountable for all aspects of the work.

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## Conflict of interest

The authors declare no conflict of interest.

## Ethical approval

This study was approved by the ethics committee of Nanjing Medical University. The study was conducted in accordance with the Declaration of Helsinki.

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