Research article

Hematological parameters of hypertensive patients in northeast Ethiopia: A comparative cross-sectional study

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A B S T R A C T

Introduction: Hypertension has emerged as a significant public health concern, ranking among the leading causes of mortality in low- and middle-income countries. Moreover, it is closely associated with structural and functional alterations in hematopoietic cells. Therefore, this study aimed to evaluate the hematological parameters of hypertensive patients in Northeast Ethiopia.

Methods: A comparative cross-sectional study was conducted from January to March 2023, involving 248 participants. This included 124 hypertensive patients and 124 apparently healthy controls selected using a systematic random sampling technique. Socio-demographic and clinical data were collected through a structured questionnaire, and anthropometric measurements were obtained following established guidelines. Ethical approval was obtained from the Ethical Review Committee of the College of Medicine and Health Sciences at Wollo University. After obtaining informed consent, approximately 5 ml of venous blood was drawn from each participant for complete blood count and fasting blood glucose analysis, performed using the Mindray BC-3000 Plus hematology analyzer and the DIRUI CS-T240 automated clinical chemistry analyzer, respectively. Data analysis involved independent t-tests, Mann-Whitney U-tests, correlation tests, and logistic regression. A p-value of <0.05 was considered statistically significant.

Results: The study found that white blood cell count, platelet count, platelet distribution width, red cell distribution width, and mean platelet volume were significantly higher in hypertensive patients compared to the control group ($p < 0.05$). Conversely, red blood cell count, hematocrit, and hemoglobin levels were significantly higher in the control group than in hypertensive patients ($p < 0.05$). Additionally, white blood cells and platelets exhibited a positive correlation with systolic and diastolic blood pressure ($p < 0.05$), while red blood cell count, hematocrit, and hemoglobin demonstrated a negative correlation with blood pressure indices and body mass

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index. Anemia was observed in 20.2 % of hypertensive patients. Notably, an abnormal body mass index (AOR: 3.5, 95 % CI: 1.3–9.6, $p = 0.011$) and high systolic blood pressure (AOR: 4.6, 95 % CI: 1.3–15.5, $p = 0.013$) were significantly associated with anemia among hypertensive patients. *Conclusion:* This study identified significant differences in various hematological parameters between hypertensive patients and the control group. Routine assessments of hematological parameters should be considered to effectively manage hypertension-related complications in hypertensive patients.

1. Introduction

Hypertension (HTN) is a condition where systemic arterial pressure is increased above the predefined value (systolic BP $\geq$ 140 mmHg and/or diastolic BP $\geq$ 90 mmHg). Worldwide, an estimated 1.28 billion adults (30–79 years of age) have HTN, with the majority (two-thirds) living in low- and middle-income countries [1]. It is a significant cause of cardiovascular diseases (CVDs) and premature death; more than 10 million people die from HTN each year [2]. In 2019, there were 10.8 million deaths globally resulting from complications of hypertension, accounting for more than half of all CVD-related fatalities [3]. Ethiopia is also undergoing an epidemiological transformation, with infectious diseases giving way to non-communicable diseases (NCDs). The prevalence of HTN, in particular, is rising at an unprecedented rate [4], [5]. It is one of the top causes of hospital admissions, morbidity, and mortality in health care facilities across the country [6].

Hypertension has the potential to induce life-threatening problems in vital organs such as the heart, blood vessels, kidneys, and brain, resulting in premature impairment and death [7]. It is intimately linked to structural and functional problems in hematopoietic organs [8]. Sympathetic overactivity affects hematological parameters such as hematocrit, blood viscosity, and hypercoagulability, forming part of the complex pathogenesis of HTN [9], [10]. These variables alter blood flow dynamics, increasing the risk of thromboembolism, stroke, and coronary artery disease [10].

There are several disagreements in studies regarding hematological parameters in hypertensive and normotensive individuals. Recent studies showed that white blood cells (WBC), red blood cells (RBC), platelets (PLT), hemoglobin (Hgb), hematocrit (Hct), and red cell distribution width (RDW) were higher in hypertensive patients than in normotensive individuals [11], [12], [13]. However, other studies have reported discordant results regarding these parameters [14], [15]. The relationship between hematological parameters and HTN is poorly understood, but several hematological parameters are connected with HTN due to vascular dysfunction in hypertensive individuals. This dysfunction promotes increased cytokine production, such as tumor necrosis factor-alpha, interleukin-6 (IL-6), IL-17, IL-18, and IL-1 beta, encouraging hematopoietic cells to differentiate and proliferate to accelerate the repair of endothelial injury [16], [17].

Furthermore, very little research has been conducted in Ethiopia on the hematological parameters of HTN patients. Studies have revealed changes in hematological parameters associated with HTN, and further research into these parameters may aid in the earlier detection, prompt therapy, and monitoring of complications like CVD that are related to HTN. Therefore, this study aimed to provide documented evidence about the hematological parameters of hypertensive patients in Northeast Ethiopia.
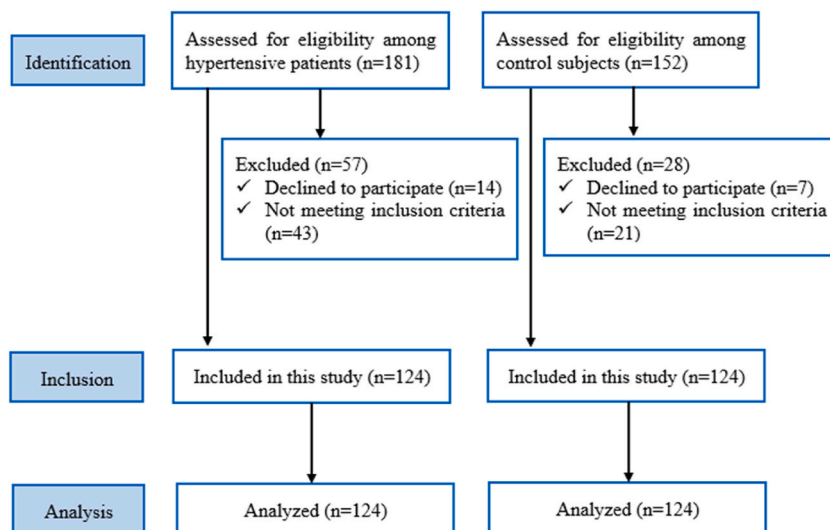

Fig. 1. Strengthening the Reporting of Observational studies in Epidemiology (STROBE) flow chart of study participants.

2. Materials and methods

2.1. Study design, period, and area

A comparative cross-sectional study was conducted in Northeast Ethiopia at Dessie Comprehensive Specialized Hospital (DCSH) and Kombolcha General Hospital (KGH) from January to March 2023. Both hospitals, named after their respective cities, are situated in the Amhara Regional State of Northeast Ethiopia. The study adhered to the guidelines outlined in the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement [18], as illustrated through a flow chart presented in Fig. 1.

2.2. Study participants

The study included adult hypertensive patients attending follow-up appointments at DCSH and KGH for the HTN group, and blood donors visiting Dessie Blood Bank for blood donation for the control group. Participants aged 18 and above, willing to provide written consent and meeting eligibility criteria, were included. Hypertensive patients and healthy controls were matched for age and gender.

Control group individuals underwent screening for infectious diseases transmissible via blood transfusion and other chronic disorders (e.g., hypertension, as per WHO guidelines). Only those with blood deemed safe for transfusion were selected. Additionally, hypertensive patients were identified based on their medical records and clinical history. Individuals who had been diagnosed with hypertension according to WHO guidelines [19] were included. Conversely, hypertensive patients with a history of infectious diseases, alcoholism, smoking, antibiotic use, ongoing anemia treatment, systemic diseases (such as epilepsy, diabetes, cancer, heart disease, stroke, HIV, and asthma), pregnancy, and secondary hypertension were excluded. Exclusion criteria were applied after a thorough review of medical records and a face-to-face interview.

2.3. Study outcomes

The primary outcomes of our study focused on comparing hematological parameters between hypertensive patients and apparently healthy blood donors. Additionally, we determined the prevalence of common hematological abnormalities among hypertensive patients.

2.4. Sample size determination and sampling technique

The sample size was calculated using the formula for two population means of identical sample size, based on the following assumptions: margin of error (d) = 5 %, confidence level = 95 % (two-sided) (corresponding to Z $\alpha/2$ = 1.96), and power of 80 % (β = 0.85). Mean and standard deviation of mean corpuscular hemoglobin concentration (MCHC) in hypertensive patients (34.27 $\pm$ 1.17) and control subjects (34.7 $\pm$ 1.13) were extracted from a prior study conducted in Gondar [12]. After adding a 10 % non-response rate, a total of 248 participants (comprising 124 hypertensive patients and 124 apparently healthy blood donors) were recruited. Participants were proportionally allocated from each hospital, with 80 from DCSH and 44 from KGH. A systematic random sampling technique was employed to select study participants.

2.5. Operational definitions

Anemia was defined by the WHO as Hgb levels <12.0 g/dL for women and <13.0 g/dL for men. According to WHO standards, high waist circumference (WC) values were considered to be > 94 cm for men and >80 cm for women [20]. Leukocytosis was defined as a total WBC count >10,000/µL [21]. Similarly, thrombocytopenia and thrombocytosis were defined as PLT count <150,000/µL and >400,000/µL, respectively [21]. Body mass index (BMI) values of <18.5 kg/m^2, 18.5–24.9 kg/m^2, 25–29.9 kg/m^2, and ≥30 kg/m^2 were categorized as underweight, normal weight, overweight, and obese, respectively [22]. Additionally, HTN indicators included SBP ≥140 mmHg, DBP ≥90 mmHg, and/or self-reported concurrent use of antihypertensive drugs. Pre-HTN was defined as having an SBP between 120 and 139 mmHg and/or a DBP between 80 and 89 mmHg. Stage 1 HTN was characterized by an SBP of 140–159 mmHg or a DBP of 90–99 mmHg, while Stage 2 HTN was defined as having an SBP ≥160 mmHg or a DBP ≥100 mmHg [19]. "Duration of hypertension" referred to the time since an individual received their HTN diagnosis from a healthcare professional.

2.6. Data collection and laboratory methods

2.6.1. Socio-demographic and clinical variables

A structured interviewer-administered questionnaire was used to collect socio-demographic and clinical information from study participants following their provision of written informed consent.

2.6.2. Anthropometric measurements

Anthropometric measurements, including BP, WC, hip circumference (HC), height, and weight, were collected from hypertensive patients and control subjects by clinical nurses. BP was measured using a mercury sphygmomanometer and stethoscope while participants were seated, with readings taken on the right arm. Three measurements of SBP and DBP were recorded at 5-min intervals, and the average of the last two readings was calculated. Height was measured using a stadiometer, with participants standing barefoot on a

flat surface. Weight was measured using a calibrated weighing scale, with participants wearing light clothing and no shoes. BMI was then calculated by dividing weight (in kilograms) by height squared (in meters).

Waist circumference was measured using an elastic-plastic tape at the approximate midpoint between the lower margin of the last palpable rib and the top of the iliac crest. HC was measured around the widest point of the buttocks, with participants wearing non-restrictive pants. The waist-to-hip ratio (WHR) was calculated by dividing WC by HC. Following an interview and a thorough review of medical records, the study subjects were sent to a laboratory where blood was drawn to determine the total blood cell count and fasting blood glucose.

2.6.3. Blood sample collection, processing and laboratory determination

Five milliliters of venous blood were collected from both hypertensive and control subjects, with specimens from control subjects obtained at the time of blood donation. Blood specimens were transferred into ethylenediaminetetraacetic acid (EDTA) and serum separator test tubes for analysis of hematological parameters and fasting blood glucose levels, respectively. Samples in the serum separator test tube were centrifuged at 3500 rpm for 5 min after a 30-min clotting time to obtain serum.

Complete blood count (CBC) measurements were performed using the Mindray BC-3000 plus hematology analyzer (Mindray Corporation, Kobe, China). Hematological parameters, including white blood cells (WBC), red blood cells (RBC), hemoglobin (Hgb), hematocrit (Hct), mean cell volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width-coefficient of variation (RDW-CV), red cell distribution width-standard deviation (RDW-SD), platelet (PLT), mean platelet volume (MPV), and platelet distribution width (PDW), were measured in both hypertensive and control subjects. The machine used the electrical impedance principle for WBC, RBC, and PLT measurements, and the colorimetric approach for Hgb measurement. Subsequently, serum samples were analyzed using the DIRUI CS-T240 automated clinical chemistry analyzer (DIRUI CS-T240, China) to determine fasting blood glucose levels using the glucose oxidase method. All laboratory measurements for both hypertensive individuals and blood donors were conducted at the DCSH laboratory.

2.7. Data quality assurance and management

The questionnaire was back-translated into English by different individuals after being translated into the local language (Amharic) to ensure the accuracy of the data. It was also pretested on 5 % of the study participants at Borumeda General Hospital. Training was provided to data collectors. Anthropometric measurements were repeated twice, with the average value used. A standard protocol for sample collection, processing, transport, and storage was rigorously followed. Additionally, three levels of commercial quality control materials (low, normal, and high) were used to monitor the instrument's and reagents' performance. Every step of data collection was evaluated and checked for accuracy, completeness, timeliness, and other aspects of quality.

2.8. Statistical analysis and interpretation

Data were entered into Epidata version 3.1 software (Epidata Association, Odense, Denmark) and then exported to SPSS (Statistical Package for Social Sciences) version 23 software (IBM Corporation, USA) for analysis. The normality of data distribution was assessed using histograms and the Kolmogorov-Smirnov test, while Levene's test determined variance homogeneity. The results were presented as mean ± standard deviation and median with interquartile range. Independent t-tests and Mann-Whitney U tests were utilized to compare hematological parameters between hypertensive individuals and apparently healthy controls for normally distributed and non-normally distributed data, respectively. Pearson's correlation was used to evaluate the correlation of hematological parameters with independent variables for normally distributed data, while Spearman's correlation (rho) was applied for non-normally distributed data. The relationship between independent variables and anemia was assessed using bivariable and multivariable logistic regression models. The Hosmer-Lemeshow test was used to determine the model's fitness ($p > 0.05$). A *p-value* of <0.05 was considered statistically significant.

2.9. Ethical considerations

The study adhered to the ethical guidelines outlined in the Declaration of Helsinki. Ethical clearance was obtained from the ethical review committee of the College of Medicine and Health Sciences, Wollo University, with reference number CMHC-2169/20/2022. Each participant provided written informed consent after receiving comprehensive information about the study's purpose, procedure, benefits, and potential discomfort. All ethical principles, including privacy and confidentiality, were strictly maintained throughout the study. For ethical reasons, control group participants were screened at the Dessie Blood Bank. Participants with abnormal results were referred to the outpatient clinic department at DCSH and KGH for further management and treatment.

3. Results

3.1. Socio-demographic characteristics of study participants

A total of 248 study participants, including 124 hypertensive patients and 124 apparently healthy individuals, were recruited for this study. The mean age and standard deviation of hypertensive patients and the control group were 50.50 (±8.7) and 49.19 (±5.3) years, respectively. The age ranges for hypertensive individuals and the control group were 31–71 and 28–65 years, respectively. There

were no significant differences in mean age or sex between the two groups ($p > 0.05$). Regarding sex, 81 (65.3 %) of the study participants in both groups were female. Among the total study participants, 92 (74.2 %) hypertensive patients and 104 (83.9 %) apparently healthy individuals were urban dwellers. The majority of hypertensive patients, 98 (79.0 %), and control participants, 106 (85.5 %), were married (Table 1).

3.2. Anthropometrics and clinical characteristics of study participants

The mean $\pm$ SD of BMI, WHR, FBG, SBP, DBP, and duration of illness among hypertensive patients were 23.99 ($\pm$3.46) kg/m^2, 0.90 ($\pm$0.05), 109.33 ($\pm$15.93) mg/dL, 139.64 ($\pm$16.08) mmHg, 86.17 ($\pm$10.16) mmHg, and 6.11 ($\pm$3.59) years, respectively. The majority of the study participants, comprising 82 (66.1 %) hypertensive patients and 107 (86.3 %) apparently healthy individuals, had a BMI falling within the range of 18.5–24.9 kg/m^2 (Table 2).

3.3. Comparison of hematological parameters of hypertensive patients and apparently healthy controls

The findings revealed that the mean $\pm$ SD levels of total WBC (6.46 $\pm$ 2.19), PLT (283.12 $\pm$ 80.68), PDW (16.21 $\pm$ 3.15), RDW-SD (42.55 $\pm$ 3.62), as well as the median (IQR) levels of RDW-CV (13.65 [12.90–14.40]) and MPV (9.54 [8.76–10.40]), were significantly higher in hypertensive patients than in the control group ($p < 0.05$). Conversely, hypertensive patients exhibited significantly lower mean $\pm$ SD levels of RBC (5.09 $\pm$ 0.58), Hct (44.47 $\pm$ 5.31), and median (IQR) levels of Hgb (14.80 [13.70–15.93]) than the control group. However, there were no statistically significant differences ($p > 0.05$) in the levels of other hematological parameters between the two groups (Table 3).

3.4. Correlations of hematological parameters with anthropometric and clinical variables among hypertensive patients

In the bivariate correlation analysis, total WBC and PLT counts exhibited a positive correlation with both SBP and DBP ($p < 0.05$). Conversely, RBC count, Hgb, and Hct demonstrated a negative correlation with SBP and DBP ($p < 0.05$). Among hypertensive patients, total WBC count and MPV were positively correlated with BMI ($p < 0.001$), while RBC, Hgb, and Hct showed negative correlations with BMI ($p = 0.016, 0.027$, and 0.005, respectively). Additionally, WHR displayed negative correlations with MCV and Hct levels ($p = 0.019$ and 0.012, respectively), whereas it exhibited a positive correlation with MPV ($p = 0.004$). The duration of illness showed negative correlations with RBC count, Hgb, and Hct ($p < 0.001, 0.001$, and 0.001, respectively), while displaying positive correlations with PLT count and MPV ($p < 0.001$ and 0.036, respectively) (Table 4).

3.5. Prevalence of common hematological abnormalities among hypertensive patients

The overall prevalence of anemia, leukocytosis, thrombocytopenia, and thrombocytosis among hypertensive patients in this study was 20.2 % (95 % CI 13.7–27.4), 6.5 % (95 % CI 2.4–11.3), 4 % (95 % CI 0.8–8.1), and 10.5 % (95 % CI 5.6–16.1), respectively (Fig. 2).

Table 1
Socio-demographic characteristics of study participants at DCSH and KGH, Northeast Ethiopia, 2023 (n = 124).

Variables	Categories	hypertensive patients Number (%)	Controls Number (%)
Age	Mean $\pm$ SD	50.50 $\pm$ 8.7	49.19 $\pm$ 5.3
	<45	33 (26.6)	48 (38.7)
	$\geq$45	91 (73.4)	76 (61.3)
Sex	Male	43 (34.7)	43 (34.7)
	Female	81 (65.3)	81 (65.3)
Residence	Urban	92 (74.2)	104 (83.9)
	Rural	32 (25.8)	20 (16.1)
Marital status	Single	8 (6.5)	8 (6.5)
	Married	98 (79.0)	106 (85.5)
	Divorced	6 (4.8)	7 (5.6)
	Widowed	12 (9.7)	3 (2.4)
Educational status	Unable to read and write	35 (28.2)	6 (4.8)
	Primary school	32 (25.8)	30 (24.2)
	Secondary school	22 (17.7)	31 (25.0)
	College and above	35 (28.2)	57 (46.0)
Occupational status	Gov't employees	33 (26.6)	43 (34.7)
	Daily laborer	4 (3.2)	4 (3.2)
	Farmer	11 (8.9)	7 (5.6)
	Merchant	16 (12.9)	15 (12.1)
	Housewives	47 (37.9)	24 (19.4)
	Others	13 (10.5)	31 (25.0)

Table 2
Anthropometrics and clinical characteristics of study participants at DCSH and KGH, Northeast Ethiopia, 2023 (n = 248).

Variables	Categories	Hypertensive patients	Controls	*p-value*
BMI (kg/m^2)	Mean ± SD	23.99 ± 3.46	23.13 ± 1.69	0.014*
	<18.5	2 (1.6)	0 (0)	NA
	18.5–24.9	82 (66.1)	107(86.3)	
	25–29.9	29 (23.4)	17 (13.7)	
	≥30	11 (8.9)	0 (0)	
WHR	Mean ± SD	0.90 ± 0.05	–	NA
FBS (mg/dL)	Mean ± SD	109.33 ± 15.93	88.02 ± 8.52	<0.001*
	≤126	104 (83.9)	124 (100)	NA
	>126	20 (16.1)	0 (0)	
SBP (mmHg)	Mean ± SD	139.64 ± 16.08	121.06 ± 3.36	<0.001*
	<120	5 (4.1)	13 (10.5)	NA
	120–139	51 (41.1)	111 (89.5)	
	≥140	68 (54.8)	0 (0)	
DBP (mmHg)	Mean ± SD	86.17 ± 10.16	79.79 ± 2.15	<0.001*
	<80	13 (10.5)	14 (11.3)	NA
	80–89	59 (47.6)	110 (88.7)	
	≥90	52 (41.9)	0 (0)	
Duration of the illness (years)	Mean ± SD	6.11 ± 3.59	–	NA
	<5 years	48 (38.7)	–	
	5–10 years	58 (46.8)	–	
	>10 years	18 (14.5)	–	

Note: BMI: body max index; WHR: waist to hip ratio; FBG: fasting blood glucose; SBP: systolic blood pressure; DBP: diastolic blood pressure; NA: not available; *: statistically significant association.

Table 3
Comparison of hematological parameters of hypertensive patients and apparently healthy controls at DCSH and KGH, Northeast Ethiopia, 2023 (n = 248).

Hematological parameters	Hypertensive patients	Apparently healthy controls	*p-value*
WBC (10^3/μl), mean ± SD	6.46 ± 2.19	5.82 ± 0.94	0.003*
RBC (10^6/μl), mean ± SD	5.09 ± 0.58	5.33 ± 0.35	<0.001*
Hgb (g/dl), median (IQR)	14.80 (13.70–15.93)	15.66 (14.28–16.43)	0.003**
Hct (%), mean ± SD	44.47 ± 5.31	46.04 ± 3.39	0.006*
MCV (fl), mean ± SD	86.72 ± 5.35	86.55 ± 6.32	0.813
MCH (Pg), median (IQR)	29.47 (28.00–30.40)	29.20 (27.30–30.20)	0.899
MCHC (%), median (IQR)	33.50 (32.12–34.67)	32.90 (32.40–34.40)	0.990
RDW-CV (%), median (IQR)	13.65 (12.90–14.40)	13.15 (12.70–13.50)	<0.001**
RDW-SD (fl), mean ± SD	42.55 ± 3.62	41.79 ± 2.02	0.043*
PLT (10^9/μl), mean ± SD	283.12 ± 80.68	257.43 ± 51.23	0.003*
MPV (fl), median (IQR)	9.54 (8.76–10.40)	9.10 (8.70–9.77)	<0.001**
PDW (fl), mean ± SD	16.21 ± 3.15	15.32 ± 1.76	0.006*

Note: **: *p-value* is determined using the Mann-Whitney *U* test; *: *p-value* is determined using the independent T test; *p-value* < 0.05 is considered as statistically significant.

Table 4
Correlations of hematological parameters of hypertensive patients with anthropometric and clinical variables at DCSH and KGH, Northeast Ethiopia, 2023 (n = 124).

Hematological parameters		SBP	DBP	FBG	BMI	WHR	Duration of HTN
WBC	**r (p)**	0.236 (0.008) *	0.250 (0.005) *	−0.084 (0.355)	0.326 (<0.001) *	0.070 (0.440)	0.006 (0.943)
RBC	**r (p)**	−0.266 (0.003) *	−0.217 (0.016) *	−0.056 (0.533)	−0.215 (0.016) *	−0.149 (0.099)	−0.315 (<0.001) *
Hgb	**rho (p)**	−0.304 (0.001) **	−0.218 (0.015) **	−0.009 (0.922)	−0.199 (0.027) **	−0.164 (0.068)	−0.307 (0.001) **
Hct	**r (p)**	−0.315 (<0.001) *	−0.242 (0.007) *	0.032 (0.724)	−0.252 (0.005) *	−0.224 (0.012) *	−0.306 (0.001) *
MCV	**r (p)**	−0.100 (0.267)	−0.033 (0.712)	0.112 (0.080)	−0.188 (0.037)	−0.210 (0.019) *	−0.071 (0.432)
MCH	**rho (p)**	−0.174 (0.053)	−0.120 (0.184)	−0.144 (0.112)	−0.133 (0.141)	−0.160 (0.075)	−0.067 (0.462)
MCHC	**rho (p)**	−0.083 (0.359)	−0.038 (0.675)	−0.082 (0.365)	0.010 (0.909)	−0.018 (0.842)	−0.078 (0.387)
RDW-CV	**rho (p)**	−0.066 (0.469)	0.080 (0.378)	−0.071 (0.436)	0.072 (0.424)	−0.131 (0.148)	0.018 (0.845)
RDW-SD	**r (p)**	0.003 (0.972)	0.111 (0.221)	0.101 (0.264)	0.010 (0.912)	0.010 (0.908)	−0.005 (0.957)
PLT	**r (p)**	0.258 (0.004) *	0.249 (0.005) *	−0.162 (0.073)	0.037 (0.684)	0.052 (0.566)	0.450 (<0.001) *
MPV	**rho (p)**	0.084 (0.356)	0.049 (0.589)	0.058 (0.360)	0.541 (<0.001) **	0.255 (0.004) * *	0.188 (0.036) **
PDW	**r (p)**	−0.102 (0.258)	−0.166 (0.066)	0.053 (0.560)	0.129 (0.153)	0.006 (0.951)	−0.017 (0.850)

Note: **: *p-value* is determined using the Spearman correlation test; *: *p-value* is determined using the Pearson correlation test; *p-value* < 0.05 is considered as statistically significant.
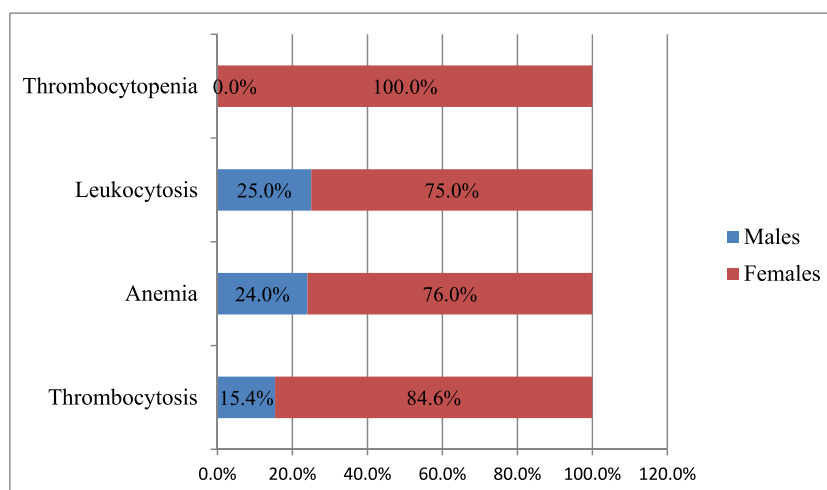
Fig. 2. The prevalence of common hematological abnormalities based on sex in hypertensive patients from the total positive cases.

3.6. Factors associated with anemia among hypertensive patients

In the bivariable logistic regression analysis, gender, residence, abnormal WC, abnormal BMI, high SBP, high DBP, and duration of illness were associated with anemia ($p < 0.25$). The multivariable logistic regression model included variables with a *p-value* of less than 0.25. Ultimately, it revealed that having an abnormal BMI (AOR: 3.5, 95 % CI, 1.3–9.6, $p = 0.011$) and high SBP (AOR: 4.6, 95 % CI, 1.3–15.5, $p = 0.013$) were significantly associated with anemia among hypertensive patients (Table 5).

4. Discussion

Hypertension has emerged as a major public health concern and is a risk factor for various CVDs. It is also closely linked to structural and functional issues in hematopoietic organs. In this study, hypertensive patients and the control group showed statistically significant differences in total WBC count, RBC count, Hgb, Hct, RDW-CV, PLT count, and MPV.

In this study, hypertensive patients exhibited a significantly higher mean total WBC count (6.46 ± 2.19) compared to the control group (5.82 ± 0.94), consistent with findings from Ethiopia [12], [13], India [23], Iran [11], and Saudi Arabia [10]. Conversely, a study in Nigeria [14] reported a lower total WBC count in hypertensive patients than in the control group. Our study also found a positive correlation between total WBC count and both SBP and DBP ($p < 0.05$) consistent with previous research in Ethiopia [12]. The

Table 5
Factors associated with anemia among hypertensive patients at DCSH and KGH, Northeast Ethiopia, 2023 (n = 124).

Variables	Categories	Anemia		COR (95 % CI)	*p-value*	AOR (95 % CI)	*p-value*
		Yes (%)	No (%)				
Age	<45	6 (18.2)	27 (81.8)	1			
	≥45	19 (20.9)	72 (79.1)	1.187 (0.429–3.289)	0.741		
Gender	Male	6 (14.0)	37 (86.0)	1		1	
	Female	19 (23.5)	62 (76.5)	0.293 (0.93–0.919)	0.214*	2.554 (0.805–8.106)	0.112
Residence	Urban	16 (17.4)	76 (82.6)	1		1	
	Rural	9 (28.1)	23 (71.9)	1.859 (0.726–4.760)	0.196*	2.514 (0.846–7.466)	0.097
Education	≥High school	13 (19.4)	54 (80.6)	1			
	<High school	12 (21.1)	45 (78.9)	0.903 (0.375–2.174)	0.820		
WC	Normal	11 (16.2)	57 (83.8)	1		1	
	High	14 (25.0)	42 (75.0)	1.727 (0.713–4.183)	0.226*	0.852 (0.270–2.686)	0.784
BMI	Normal	10 (11.9)	74 (88.1)	1		1	
	High	15 (37.5)	25 (62.5)	4.440 (1.770–11.138)	0.001*	3.596 (1.336–9.680)	0.011*
SBP	<140	4 (7.1)	52 (92.9)	1		1	
	≥140	21 (30.9)	47 (69.1)	5.809 (1.858–18.156)	0.002*	4.640 (1.387–15.520)	0.013*
DBP	<90	8 (11.1)	64 (88.9)	1		1	
	≥90	17 (32.7)	35 (67.3)	3.886 (1.524–9.907)	0.004*	2.241 (0.595–8.450)	0.233
FBG	<126	22 (21.2)	82 (78.8)	1			
	≥126	3 (15.0)	17 (85.0)	0.658 (0.177–2.449)	0.532		
Duration of HTN	<5years	4 (8.3)	41 (91.7)	1		1	
	≥5 years	21 (27.6)	55 (72.4)	4.200 (1.343–13.137)	0.014*	2.754 (0.781–9.715)	0.115

Note: COR: crud odds ratio, AOR: adjusted odds ratio, CI: confidence interval, *: statistically significant association.

observed increase in WBC count and its correlation with blood pressure indices in hypertensive patients may be attributed to vascular dysfunction, leading to cytokine system activation [16], [24]. Cytokines like steam cell factor (SCF) are produced to aid in endothelium recovery [25], leading to leukocyte activation and attachment to vascular endothelium, ultimately increasing vascular resistance and BP [26].

The study found that hypertensive patients had a significantly lower mean RBC count (5.09 ± 0.58) compared to the control group (5.33 ± 0.35). This contrasts with studies from Iran [11], Ethiopia [12], and Nigeria [14], which reported a higher RBC count in hypertensive patients, while another study from Ethiopia [13] found no significant difference. Additionally, our correlation analysis revealed a negative correlation between RBC count and both SBP and DBP ($p < 0.05$), contradicting findings from Ethiopia [12]. The decreased RBC count in hypertensive patients may be attributed to the use of certain antihypertensive drugs, particularly those inhibiting the angiotensin-converting enzyme (ACE) [27], [28]. ACE inhibitors can restrict erythropoiesis by lowering circulating levels of insulin-like growth factor 1 [27], [28] and increasing plasma concentrations of N-acetyl-seryl-aspartyl-lysylproline, which inhibits hematopoietic stem cell recruitment [29]. Another possible mechanism could involve decreased erythropoietin synthesis and bone marrow resistance to erythropoietin stimulation [30].

Similarly, the study found significantly lower median Hgb levels and mean Hct levels in hypertensive patients compared to the control group, consistent with findings from Nigeria [14], and India [15]. However, discordant findings were reported in Ethiopia [12], [13], India [23], and Iran [11], where hypertensive patients exhibited higher Hgb and HCT levels. In bivariate correlation analysis, Hgb and Hct levels were negatively correlated with both SBP and DBP ($p < 0.05$), contrary to findings from Ethiopia [12] and France [31]. This relationship may be attributed to renal arteriolar constriction induced by sympathetic activity, leading to increased renin and aldosterone secretion, resulting in sodium and water retention and subsequent hemodilution [32], [33]. Additionally, leptin, a hormone produced by the human obesity gene, may influence erythrocyte rheology and microcirculation in hypertension [34].

Both the mean and median levels of RDW-SD and RDW-CV were significantly higher in hypertensive patients compared to the control group, consistent with findings from studies in Ethiopia [12], [13] and Turkey [35], [36]. However, contradictory results were reported in studies conducted in Iran [11] and Nigeria [14]. The association between RDW and hypertension is attributed to inflammatory reactions and stimulation of the renin-angiotensin-aldosterone system (RAAS). Angiotensin II, a known factor in hypertension, regulates neurohumoral processes through the RAAS system [37], leading to increased erythropoietin secretion and the production of immature red blood cells, consequently elevating RDW levels [38], [39]. Additionally, increased production of inflammatory cytokines alters iron metabolism and bone marrow function, leading to greater RBC size inequality and higher RDW levels [40]. Higher RDW levels contribute to decreased blood flow, hypoxia, endothelial dysfunction, and ultimately elevated BP [41], [42].

Regarding platelet indices, hypertensive patients exhibited a significantly higher mean PLT count compared to the control group, consistent with findings from India [23]. However, studies in Nigeria [14], Iran [11], Ethiopia [12], [13], and India [15] reported increased PLT count in hypertensive patients without statistical significance. Our correlational analysis revealed a significant positive correlation between PLT count and both SBP and DBP, aligning with a study in Ethiopia [12] but contradicting another in the same country [13]. Similarly, hypertensive patients showed significantly higher mean PDW and median MPV compared to controls, consistent with studies in Ethiopia [12], India [23], and Turkey [43], but inconsistent with those in Iran [11] and another in Ethiopia [13]. These associations may be attributed to hypertension-induced endothelial damage, leading to increased platelet activation and clot formation [43]. The over-activated sympathetic nervous system stimulates platelet activation via alpha-2 adrenoreceptors, altering platelet morphology and increasing MPV. Elevated adrenaline levels contribute to an increase in PDW, prompting the release of larger activated platelets stored in the spleen into circulation. This process may be the primary mechanism for the elevation of MPV levels [44].

In correlation analysis, the study revealed a positive correlation between total WBC count and BMI ($r = 0.326$, $p < 0.001$), consistent with findings from Ethiopia [13]. This correlation may be attributed to elevated fatty acid levels associated with excess adipose tissue, which trigger the immune system through the release of antigens from adipocyte cell death. This process leads to the secretion of inflammatory cytokines like interleukin (IL)-6 and IL-8, enhancing the recruitment and activation of lymphocytes, monocytes, and macrophages [45], [46]. Similarly, MPV exhibited a positive correlation with BMI ($r = 0.241$, $p = 0.007$) and WHR ($r = 0.255$, $p = 0.004$). Vascular dysfunction in insulin resistance may heighten platelet reactivity due to reduced prostacyclin and nitric oxide synthesis, alongside endothelial dysfunction-triggered cytokine production [47]. This can lead to larger platelet formation in the bone marrow [48], potentially elevating MPV and PDW [49].

Conversely, RBC count, Hgb, and Hct showed negative correlations with BMI ($r = -0.215$, $p = 0.016$), ($r = -0.199$, $p = 0.027$), and ($r = -0.252$, $p = 0.005$), respectively. Similarly, Hct and MCV were significantly negatively correlated with WHR ($r = -0.224$, $p = 0.012$) and ($r = -0.210$, $p = 0.019$), respectively. This negative correlation might be attributed to oxidative stress-induced free radicals and pro-inflammatory cytokines released by adipocytes. Elevated free radicals can disrupt RBC membrane proteins, altering their structure, fragility, and survival, leading to an increased fraction of circulating premature erythrocytes and resulting in anisocytosis [50].

Regarding the correlation of hematological parameters with duration of illness, RBC count, Hgb, and Hct showed negative correlations ($r = -0.315$, $p < 0.001$), ($r = -0.307$, $p = 0.001$), and ($r = -0.306$, $p = 0.001$), respectively. This may be attributed to the prolonged use of antihypertensive medication [51]. Additionally, PLT count showed a significant positive correlation ($r = 0.450$, $p < 0.001$), along with MPV ($r = 0.188$, $p = 0.036$). This suggests that vascular complications in hypertensive patients worsen over time, leading to vascular injury and subsequent platelet activation, causing larger PLTs to be released from the bone marrow, resulting in an increased platelet count and high MPV [49].

In the present study, the overall prevalence of anemia in hypertensive patients was found to be 20.2 % (95 % CI 13.7–27.4). Normocytic anemia is common among hypertensive patients, with those having uncontrolled blood pressure exhibiting lower

hemoglobin concentrations, indicating an elevated risk for CVD [52]. Multivariate analysis revealed that hypertensive patients with high SBP had higher odds of anemia (AOR: 4.6, 95 % CI, 1.3–15.5, $p = 0.013$). Those with high SBP were 4.6 times more likely to have anemia compared to those with normal SBP. This association may be linked to hypertension-driven inflammatory activation, leading to increased production of pro-inflammatory cytokines like tumor necrosis factor and IL-6. These cytokines can directly inhibit bone marrow function, thereby contributing to anemia by suppressing erythropoiesis [53], [54], [55].

Likewise, the odds of anemia were higher in hypertensive patients with an abnormal BMI (AOR: 3.5, 95 % CI, 1.3–9.6, $p = 0.011$). Individuals with an abnormal BMI were found to be 3.5 times more likely to have anemia compared to those with a normal BMI. This association may be attributed to chronic inflammation associated with adiposity, leading to increased production of hepcidin. Elevated hepcidin levels can result in anemia of inflammation, characterized by low serum iron levels, elevated serum ferritin, and low hemoglobin [56]. Our study has several limitations. Firstly, due to the cross-sectional nature of our study design, we were unable to establish a cause-and-effect relationship. Therefore, longitudinal studies are necessary to address this gap in understanding. Secondly, we did not assess morphological or coagulation profiles, which could provide further insights into the hematological characteristics of hypertensive patients. Additionally, we did not conduct cell-free hemoglobin analysis, which could have added valuable information to our findings.

5. Conclusion and recommendations

In the current study, hypertensive patients had higher levels of total WBC count, PLT count, PDW, RDW-SD, RDW-CV, and MPV, and lower levels of RBC count, Hct, and Hgb than normotensive individuals. This indicates that hypertension can cause derangements in hematological parameters. Furthermore, hematological parameters were found to be positively and negatively correlated with different clinical and anthropometric variables, showcasing their prompt impact on hypertension management.

Moreover, hematological abnormalities, especially anemia, are common among hypertensive patients, with those having high BMI and SBP being more likely to have anemia. Therefore, assessing the hematological alterations in hypertensive patients is crucial for physicians to develop an efficient and timely therapeutic response to prevent serious consequences. To manage hypertensive patients effectively, routine hematological parameter screening should be considered. Additionally, with regard to hematological abnormalities, close attention should be paid to abnormal blood pressure and BMI. Finally, for an accurate assessment of the issue, a longitudinal study with a larger sample size is preferable.

Data availability statement

The data associated with our study are not deposited in a publicly available repository. The data sets used and analyzed during the current study are available from corresponding author on a reasonable request.

CRediT authorship contribution statement

Ermiyas Alemayehu: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Ousman Mohammed:** Writing – review & editing, Visualization, Validation, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation. **Habtu Debash:** Writing – review & editing, Visualization, Validation, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation. **Melaku Ashagrie Belete:** Writing – review & editing, Visualization, Validation, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation. **Daniel Gebretsadik Weldehanna:** Writing – review & editing, Visualization, Validation, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation. **Mihret Tilahun:** Writing – review & editing, Visualization, Validation, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation. **Alemu Gedefie:** Writing – review & editing, Visualization, Validation, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation. **Hussen Ebrahim:** Writing – review & editing, Visualization, Validation, Supervision, Software, Project administration, Methodology, Funding acquisition, Formal analysis, Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e34069.

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