RESEARCH PAPER

Running Title: *WBC Count and Hypertension Staging*

Correlation of White Blood Cell Count with Hypertension Grading: A Hospital-Based Case-Control Study in Treatment-Naïve Adults

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ABSTRACT

Background: Systemic inflammation has emerged as a contributor to hypertension pathophysiology. White blood cell (WBC) count is a readily available inflammatory marker and may correlate with blood pressure elevation and disease severity. Limited data exists regarding this association in newly diagnosed, treatment-naïve hypertensive adults.

Objectives: To evaluate total WBC count in newly detected hypertensive patients compared with normotensive controls and assess its correlation with hypertension staging per European Society of Hypertension (ESH) 2023 guidelines.

Methods: This case-control study enrolled 180 participants (90 treatment-naïve hypertensive cases, 90 normotensive controls) from a tertiary care center. WBC count was measured using automated hematology analyzers. Hypertension staging followed ESH 2023 criteria. Group comparisons used independent t-tests; correlations were assessed using Pearson and Spearman methods. Age-adjusted analyses included ANCOVA and partial correlations.

Results: WBC count was significantly higher in cases than controls (14.41 ± 2.07 vs $9.24 \pm 1.13 \times 10^3/\mu L$; $p < 0.001$). Strong correlations were observed between WBC and systolic blood pressure ($r = 0.888$) and diastolic blood pressure ($r = 0.807$). After adjusting for age, correlations remained robust (partial $r = 0.857$ and 0.752, respectively). WBC increased progressively across hypertension grades (Grade 1: 12.25; Grade 2: 15.08; Grade 3: $17.98 \times 10^3/\mu L$; ANOVA $p < 0.001$; Spearman $\rho = 0.75$).

Conclusion: Elevated WBC count is independently associated with hypertension and correlates with disease severity in treatment-naïve adults. This accessible marker may support cardiovascular risk stratification in newly diagnosed patients.

Keywords: White blood cell count; Hypertension; Inflammation; Blood pressure staging; Cardiovascular risk.

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INTRODUCTION

Systemic arterial hypertension is a highly prevalent chronic condition affecting over 1.28 billion adults worldwide, with approximately two-thirds residing in

low- and middle-income countries.[1,2] In India, hypertension affects nearly 30% of adults, with higher rates observed in urban populations.[3] The condition remains a leading modifiable risk factor for

cardiovascular disease, stroke, chronic kidney disease and heart failure.[4]

Although traditionally viewed as a hemodynamic disorder, accumulating evidence supports the role of systemic inflammation in hypertension pathophysiology.[5,6] Inflammatory processes contribute to endothelial dysfunction, arterial stiffness and vascular restructuring - all of which are implicated in blood pressure elevation.[7] This recognition has shifted attention toward inflammatory biomarkers as potential indicators of hypertension risk and severity.

White blood cell (WBC) count is a readily available, inexpensive marker of systemic inflammation. Elevated WBC counts have been associated with cardiovascular risk and mortality in several population-based studies.[8,9] Ruggiero et al., in the Baltimore Longitudinal Study of Aging, demonstrated that higher WBC counts were independently associated with increased mortality and cardiovascular complications.[8] Subsequent studies have linked elevated WBC counts to metabolic syndrome components, including hypertension.[10,11]

Despite these associations, limited data exist specifically examining WBC count in newly diagnosed, treatment-naïve hypertensive individuals. Most available studies focus on patients with established cardiovascular disease or examine WBC as part of broader inflammatory panels. Furthermore, the relationship between WBC count and hypertension staging - an important determinant of clinical management is underexplored.

Given this background, we aimed to evaluate total WBC count in newly detected hypertensive patients compared with normotensive controls and assess its correlation with hypertension staging as defined by the European Society of Hypertension (ESH) 2023 guidelines.[12]

MATERIALS AND METHODS

Study Design and Setting

This was a hospital- based case- control study conducted in the Department of General Medicine at a tertiary care teaching hospital in North India from April 2024 to November 2025. The study protocol was approved by the Institutional Ethics Committee and written informed consent was obtained from all participants prior to enlistment.

Study Population

Consecutive adults attending the Medicine outpatient and inpatient departments who met eligibility criteria were screened. Participants were classified as hypertensive cases or normotensive controls based on blood pressure measurements.

Inclusion criteria for cases were: (1) newly diagnosed hypertension per ESH 2023 guideline thresholds (systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg); (2) age ≥18 years; and (3) treatment-naïve status. Controls were normotensive adults with similar age and sex distribution. Exclusion criteria included: current antihypertensive therapy; malignancy; established cardiovascular disease (heart failure, coronary artery disease, stroke, peripheral arterial disease); moderate-to-severe valvular heart disease; diabetes mellitus; chronic kidney disease; inflammatory, thromboembolic, or hematological disorders; thyroid dysfunction; active infections; and pregnancy.

Sample Size

Using the Cochran formula with an estimated hypertension prevalence of 31%, confidence level of 95% and margin of error of 7%, the minimum required sample size was 168 participants. To account for potential non-response and ensure balanced groups - we enlisted 180 participants (90 cases, 90 controls).

Clinical Measurements

Blood pressure was measured using a calibrated mercury sphygmomanometer with participants in the sitting position after at least 5 minutes of rest. Three readings were taken 5 minutes apart and the mean was recorded. Hypertension staging followed ESH 2023 criteria: Grade 1 (140–159/90–99 mmHg), Grade 2 (160–179/100–109 mmHg) and Grade 3 (≥180/≥110 mmHg).[12] Anthropometric measurements included height, weight and body mass index (BMI).

Laboratory Measurements

Venous blood samples was collected from the antecubital vein using standard phlebotomy techniques. Total WBC count was obtained from complete blood count analysis performed using automated hematology analyzers per standard laboratory protocols. Reference intervals for total WBC count were 4.0–11.0 $\times 10^3/\mu L$. Fasting plasma glucose was also measured.

Statistical Analysis

Numerical clinical variables were expressed with their descriptive statistics. Group comparisons were performed using independent samples t-tests. Correlations between WBC count and blood pressure were assessed using Pearson correlation coefficients. Spearman rank correlation was used to evaluate the monotonic relationship between WBC and ordinal hypertension grades. One-way analysis of variance (ANOVA) compared WBC across hypertension stages. To address potential confounding by age - analysis of

covariance (ANCOVA) was performed with age as covariate and partial correlations were calculated controlling for age. A multivariable linear regression model assessed the independent effect of hypertension status on WBC after adjusting for age, sex and BMI. Age-stratified analyses were also conducted. Statistical significance was set at $p < 0.05$ (two-tailed). Analyses were performed using SPSS version 25 and Python (statsmodels).

RESULTS

Participant Characteristics

A total of 180 participants were enrolled, comprising 90 hypertensive cases and 90 normotensive controls. The study flow is presented in Figure 1. Baseline characteristics are shown in Table 1. Cases were significantly older than controls (53.3 ± 5.6 vs 44.8 ± 8.1 years; $p < 0.001$) and had higher BMI (27.1 ± 3.2 vs 25.1 ± 2.4 kg/m²; $p < 0.01$). Among cases, the distribution by ESH 2023 staging was: Grade 1, 26 (28.9%); Grade 2, 59 (65.6%); and Grade 3, 5 (5.6%).

Table 1. Baseline Characteristics of Study Participants

Variable	Cases (n=90)	Controls (n=90)	p-value
Age (years)	53.3 ± 5.6	44.8 ± 8.1	<0.001
Male sex, n (%)	62 (68.9)	45 (50.0)	0.012
BMI (kg/m²)	27.1 ± 3.2	25.1 ± 2.4	<0.01
SBP (mmHg)	164.4 ± 10.9	120.7 ± 3.0	<0.001
DBP (mmHg)	96.2 ± 5.5	78.4 ± 1.5	<0.001
FPG (mg/dL)	113.1 ± 16.8	79.1 ± 3.8	<0.001
Family history HTN, n (%)	30 (33.3)	12 (13.3)	0.002

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HTN, hypertension. Data expressed as mean ± SD or n (%).

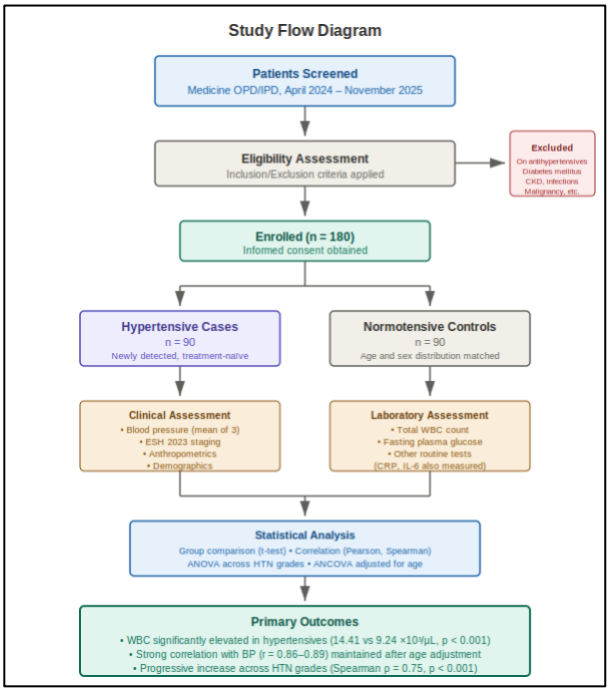

Figure 1. Study Flow Diagram

WBC Count: Group Comparison

Total WBC count was significantly elevated in hypertensive cases compared with normotensive controls (14.41 ± 2.07 vs 9.24 ± 1.13 ×10³/µL; $t = 20.77$; $p < 0.001$), representing a 56% increase (Table 2, Figure 2). The mean WBC in controls was within the upper portion of the normal reference range, while cases demonstrated values above the upper limit of normal (11.0 ×10³/µL).

Table 2. WBC Count Comparison Between Groups

Parameter	Cases (n=89)	Controls (n=90)	t-statistic	p-value
WBC (×10³/µL)	14.41 ± 2.07	9.24 ± 1.13	20.77	<0.001
Range	11.20 – 19.50	6.80 – 10.70	-	-

WBC, white blood cell count. Data expressed as mean ± SD. One case had missing WBC data.

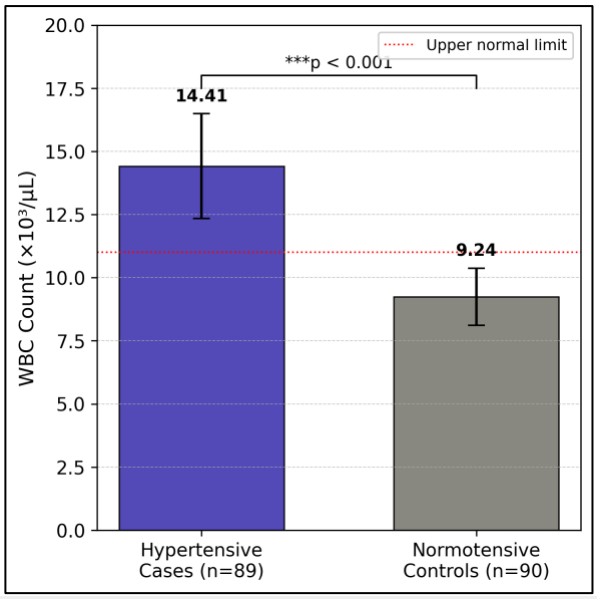

Figure 2: WBC comparison between groups

Correlation with Blood Pressure

WBC count demonstrated strong positive correlations with both systolic blood pressure (r = 0.888, p < 0.001) and diastolic blood pressure (r = 0.807, p < 0.001) across all participants (Table 3, Figure 3). These correlations indicated that higher WBC counts were consistently associated with higher blood pressure levels.

Table 3. Correlation of WBC Count with Blood Pressure: Unadjusted and Age-Adjusted

Correlation	Unadjusted r	p-value	Age-adjusted r	p-value
WBC vs SBP	0.888	<0.001		
WBC vs DBP	0.807	<0.001		

WBC, white blood cell count; SBP, systolic blood pressure; DBP, diastolic blood pressure. Age-adjusted values represent partial correlations controlling for age.

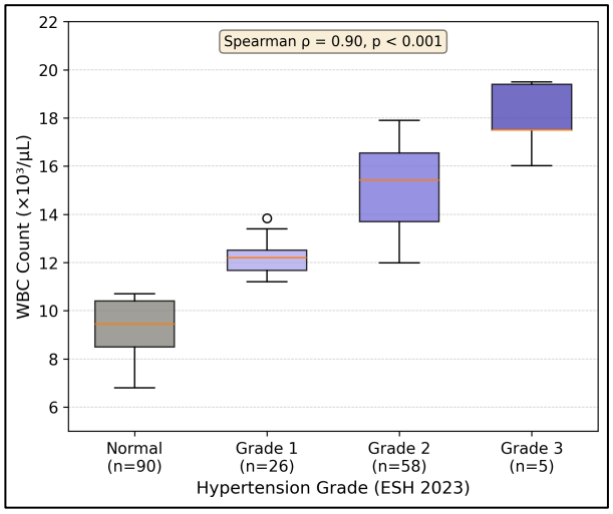

Figure 3: Scatter plot of WBC vs SBP with regression line

WBC Count Across Hypertension Stages

Among hypertensive cases, WBC count demonstrated a progressive increase across ESH 2023 hypertension grades (Table 4, Figure 4). Mean WBC was 12.25 ± 0.74 ×10³/μL in Grade 1, 15.08 ± 1.59 ×10³/μL in Grade 2 and 17.98 ± 1.47 ×10³/μL in Grade 3 (ANOVA F = 54.31, p < 0.001). Spearman correlation between WBC and hypertension grade was strong (ρ = 0.750, p < 0.001), confirming a monotonic relationship between inflammatory burden and disease severity.

Table 4. WBC Count by Hypertension Grade (Cases Only)

HTN Grade	n	WBC (×10³/μL)	Min	Max
Grade 1	26	12.25 ± 0.74	11.20	13.84
Grade 2	58	15.08 ± 1.59	11.98	17.90
Grade 3	5	17.98 ± 1.47	16.02	19.50
ANOVA F = 54.31, p < 0.001; Spearman ρ = 0.750, p < 0.001				

HTN, hypertension; WBC, white blood cell count. Data expressed as mean ± S.D.

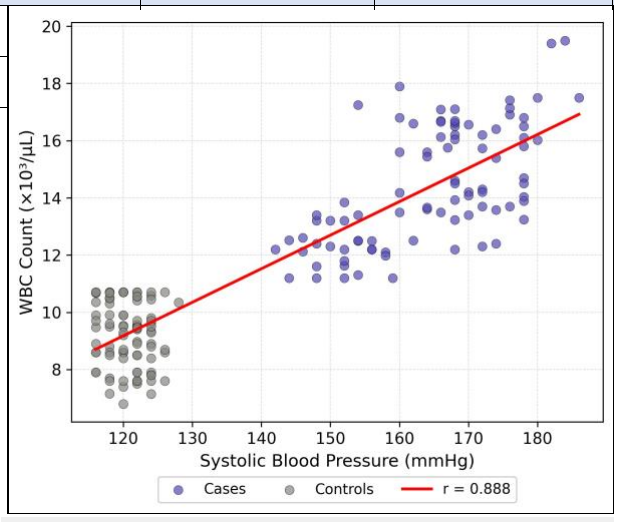

Figure 4: Box plot of WBC across hypertension grades

Analysis performed for age adjustments to assess it as a confounder

Given the significant age difference between groups, we performed several analyses to assess potential confounding. ANCOVA with age as covariate confirmed

that the group difference in WBC was highly significant (adjusted coefficient for hypertensive status: +5.12 $\times 10^3/\mu L$, $p < 0.001$), while age itself was not a significant predictor (coefficient: +0.007/year, $p = 0.70$). Partial correlations controlling for age showed minimal attenuation: WBC-SBP decreased from $r = 0.888$ to $r = 0.857$; WBC-DBP decreased from $r = 0.807$ to $r = 0.752$ (both $p < 0.001$; Table 3, Figure 5).

In a multivariable model that included age, sex and BMI - only hypertension status was clearly noted as a significant predictor of WBC (coefficient: +4.99, $p < 0.001$); age ($p = 0.69$), sex ($p = 0.31$) and BMI ($p = 0.64$) were not significant (Table 5). Age-stratified analyses demonstrated consistent elevations in WBC among cases across all age groups: 30–45 years (14.00 vs 9.30 $\times 10^3/\mu L$, $p < 0.001$), 46–55 years (14.44 vs 9.19 $\times 10^3/\mu L$, $p < 0.001$) and 56–65 years (14.47 vs 9.05 $\times 10^3/\mu L$, $p < 0.001$).

Table 5. Multivariable Linear Regression: Predictors of WBC Count

Variable	Coefficient	Std. Error	t	p-value
Hypertension (Case vs Control)	+4.99	0.33	15.23	<0.001
Age (per year)	+0.007	0.018	0.40	0.69
Sex (Male vs Female)	-0.28	0.27	-1.03	0.31
BMI (per kg/m²)	+0.03	0.07	0.47	0.64

Dependent variable: WBC count ($\times 10^3/\mu L$). Model $R^2 = 0.58$.

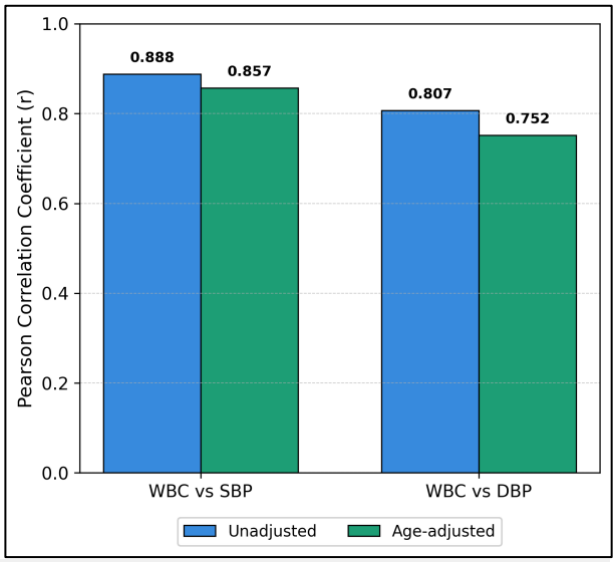

Figure 5: Unadjusted vs age-adjusted correlations comparison

DISCUSSION

The present study demonstrated that total WBC count was significantly elevated in newly detected, treatment-naïve hypertensive adults compared with normotensive controls. WBC count showed strong positive correlations with both systolic and diastolic blood pressure and increased progressively across hypertension grades. Importantly, these associations persisted after adjustment for age, sex and BMI, supporting an independent relationship between systemic inflammation - as reflected by WBC elevation - and hypertension severity. Our findings align with and extend previous observations linking WBC count to cardiovascular risk. Ruggiero et al., in the Baltimore Longitudinal Study of Aging, demonstrated that elevated WBC counts were independently associated with mortality and cardiovascular complications.[8] Kim et al. identified significant associations between WBC differential profiles and metabolic syndrome components, including elevated blood pressure.[10] Dzieża-Grudnik et al. reported that WBC counts were significantly higher in newly diagnosed hypertensives than controls (8.6 ± 1.9 vs 7.1 ± 1.4 $\times 10^3/\mu L$, $p < 0.01$), with positive correlations to blood pressure.[13] Our study extends these findings by demonstrating strong effect sizes in a treatment-naïve population and providing detailed stage-wise analyses.

The correlation coefficients observed in our study ($r = 0.866–0.89$) exceed those typically reported in the literature ($r = 0.29–0.51$).[13,14] Several factors may explain this discrepancy. First, our population was entirely treatment-naïve, eliminating potential confounding by antihypertensive medications that may modulate inflammatory markers. Second, our sample included participants across a wide range of hypertension severity (Grades 1–3), enhancing the ability to detect correlations. Third, the relatively homogeneous population from a single center may have reduced measurement variability.

The mechanistic basis for the WBC-hypertension association is well-established. Chronic low-grade inflammation contributes to endothelial dysfunction, arterial stiffness and vascular remodelling - all implicated in hypertension pathophysiology.[5,6] Elevated WBC counts reflect immune system activation and increased production of pro-inflammatory cytokines, which impair nitric oxide bioavailability and promote vasoconstriction.[7] The progressive increase in WBC across hypertension grades observed in our study supports a biological gradient linking inflammatory burden to disease severity.

A notable strength of our study was the rigorous assessment of age confounding. Although cases were significantly older than controls (53.3 vs 44.8 years), multiple analytical approaches demonstrated that age did not explain the observed associations. Age was not correlated with WBC within either group (cases: r = 0.086, p = 0.42; controls: r = -0.034, p = 0.75) and age-adjusted analyses showed minimal attenuation of effect sizes. The consistency of findings across age-stratified subgroups further supports an age-independent association.

Our study has several limitations. Ours was a single centre setting and hence it could limit it's generalization to other populations. The small number of Grade 3 cases (n = 5) limits statistical power for this subgroup. We measured only total WBC count; differential leukocyte analysis or neutrophil-to-lymphocyte ratio might provide additional mechanistic insights. Other inflammatory markers (C-reactive protein, interleukin-6) were measured but not included in this focused analysis.

Clinical implications of our findings warrant consideration. WBC count is a routinely available, inexpensive test that may support cardiovascular risk stratification in newly diagnosed hypertensive patients. The strong correlation with hypertension severity suggests potential utility in identifying individuals who may benefit from more aggressive management. Future longitudinal studies should assess whether WBC count predicts hypertension progression or cardiovascular events and whether anti-inflammatory interventions modify this relationship.

CONCLUSION

In conclusion - our study demonstrates that total WBC count is significantly elevated in newly detected, treatment-naïve hypertensive adults and shows strong, age-independent correlations with blood pressure levels and hypertension staging. The progressive increase in WBC across disease grades supports a biological gradient linking systemic inflammation to hypertension severity. These findings suggest that WBC count - a readily available inflammatory marker - may have utility in cardiovascular risk assessment of newly diagnosed hypertensive patients. Longitudinal studies are warranted to evaluate the prognostic value of WBC elevation and the potential role of anti-inflammatory strategies in hypertension management.

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FIGURE LEGENDS

Figure 1. Study flow diagram showing participant screening, enrollment and outcomes. A total of 180 participants were enrolled (90 hypertensive cases and 90 normotensive controls). Primary outcomes included comparison of WBC counts between groups and correlation with hypertension staging.

Figure 2. Comparison of white blood cell (WBC) count between hypertensive cases and normotensive controls. Bar heights represent mean values; error bars represent standard deviation. The horizontal dashed line indicates the upper limit of normal ($11.0 \times 10^3/\mu L$). ***$p < 0.001$ by independent t-test.

Figure 3. Scatter plot showing the correlation between WBC count and systolic blood pressure (SBP). Purple circles represent hypertensive cases; gray circles represent normotensive controls. The solid red line represents the linear regression line ($r = 0.888$, $p < 0.001$).

Figure 4. Box plot showing WBC count distribution across hypertension grades (ESH 2023 classification). Normal = normotensive controls; Grades 1–3 = hypertensive cases stratified by severity. Boxes represent interquartile range with median line; whiskers extend to 1.5× IQR. The annotation shows Spearman correlation across the full range including controls.

Figure 5. Comparison of unadjusted and age-adjusted Pearson correlation coefficients for WBC count versus systolic blood pressure (SBP) and diastolic blood pressure (DBP). Minimal attenuation after age adjustment confirms age-independent associations.