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Association of Smoking Status and Complete Blood Count Parameters among Adults in Central India: A Cross-Sectional Comparative Study

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Abstract

Background: Complete blood count (CBC) indices are widely available, but their associations with smoking among rural Indian adults remain insufficiently characterized.

Objective: To compare CBC parameters between smokers and non-smokers in Central India and examine their associations with cumulative smoking exposure.

Methods: This community-based, frequency-matched cross-sectional comparative study included 200 daily bidi and/or cigarette smokers and 200 never-smokers aged 20–65 years. Groups were frequency-matched by age, sex, and residential sub-district. EDTA blood samples were analyzed within 4 hours using an automated hematology analyzer. Group comparisons used independent-sample t-tests or Mann–Whitney U tests. Multivariable linear regression adjusted for age, sex, body mass index, alcohol consumption, and occupational status.

Results: Smokers had higher total white blood cell (WBC) counts (8.39 ± 1.68 $\times 10^9$/L versus 6.35 ± 1.42 $\times 10^9$/L), hemoglobin (15.2 ± 1.4 versus 13.8 ± 1.3 g/dL), hematocrit (46.1 ± 3.8% versus 42.2 ± 3.2%), and mean corpuscular volume (MCV; 91.4 ± 5.2 versus 86.2 ± 4.8 fL); all $p < 0.001$. Neutrophil and lymphocyte counts were also higher (both $p < 0.001$). Platelet counts did not differ significantly (242 ± 58 $\times 10^9$/L versus 251 ± 62 $\times 10^9$/L; $p = 0.142$), whereas mean platelet volume was higher in smokers (10.4 ± 1.1 fL versus 9.5 ± 0.9 fL; $p < 0.001$). Pack-years were positively associated with WBC count ($B = 0.112$), hemoglobin ($B = 0.084$), MCV ($B = 0.215$), and MPV ($B = 0.041$) after adjustment (all $p < 0.001$).

Conclusion: Smoking was associated with differences in erythrocytic, leukocytic, and platelet indices in this rural Central Indian cohort. Smoking history should be considered when interpreting CBC results. The cross-sectional design does not establish causality.

Keywords: Tobacco smoking; Bidi; Complete blood count; Hemoglobin; Leukocyte count; Mean platelet volume; Cross-sectional study

1. Introduction

Tobacco use is one of the leading preventable causes of morbidity and mortality worldwide [1,2]. In India, tobacco consumption presents a complex public health landscape because of the widespread availability of both smoked (cigarettes, bidis, hookah) and smokeless tobacco products [3]. Although national control programs have made progress, tobacco use remains disproportionately prevalent in rural populations, where agricultural labor, lower socioeconomic indicators, and limited health literacy contribute to sustained addiction patterns [3].

Among the various forms of smoked tobacco in rural India, bidis—unprocessed tobacco wrapped in tendu (Diospyros melanoxylon) or temburni leaves—predominate. Bidis deliver higher concentrations of nicotine, carbon monoxide (CO), and tar compared with conventional commercial filter cigarettes [10,14]. Smoke inhalation introduces thousands of chemical constituents into the respiratory system, including free radicals, reactive oxygen species, polycyclic aromatic hydrocarbons, and heavy metals. These compounds cross the alveolar–capillary barrier and may trigger vascular endothelial perturbation, oxidative stress, and systemic low-grade inflammation [4,8].

The complete blood count (CBC) is one of the most routinely ordered primary diagnostic panels. It evaluates cellular lineages crucial for oxygen delivery, immunity, and hemostasis. Standard CBC parameters include RBC count, Hb, HCT, erythrocyte indices (MCV, MCH, MCHC), total leukocyte count (TLC/WBC), differential white cell counts, and platelet metrics including platelet count and MPV [4].

Although the hematological impact of commercial cigarette smoking has been documented in high-income Western countries, demographic and regional factors limit direct translation of these findings to rural Indian adults [4,5,10]. Rural cohorts present distinct baseline characteristics, including higher rates of nutritional anemias (microcytic

hypochromic patterns driven by iron deficiency or hemoglobinopathies), endemic parasitemia, distinct occupational dust exposures, and widespread consumption of unfiltered bidis [9,14].

Altered CBC parameters in smokers can create diagnostic ambiguity. For example, smoking-associated elevation of hemoglobin and hematocrit—a physiological adaptation to carbon monoxide-induced tissue hypoxia—can mask underlying iron deficiency anemia [4,8]. Similarly, smoking-associated leukocytosis may mimic subtle chronic bacterial infections or occult inflammatory conditions, leading to unnecessary diagnostic workups or inappropriate antimicrobial prescriptions [5–7].

To address this evidence gap, this cross-sectional comparative study evaluated associations between smoking status, cumulative smoke exposure (pack-years), and CBC parameters among adults residing in Central India.

2. Materials and Methods

2.1 Study Design and Setting

A community-based, frequency-matched cross-sectional comparative study was conducted at the Department of Pathology, Shri Rawatpura Sarkar Institute of Medical Sciences and Research, Naya Raipur, Central India, between December 2025 and August 2026. The study protocol was approved by the Institutional Ethics Committee (IEC) of Shri Rawatpura Sarkar Institute of Medical Sciences and Research, Naya Raipur, Chhattisgarh, India. All procedures adhered to the ethical principles of the World Medical Association Declaration of Helsinki [20]. Written informed consent in the local language was obtained from all participants before enrollment.

2.2 Participant Selection and Eligibility Criteria

Participants aged 20–65 years who were permanent residents of the targeted rural catchment areas for ≥5 years were screened.

Cases (Smokers): Current daily tobacco smokers (bidis, commercial cigarettes, or both) who had smoked at least 1 stick per day continuously for ≥1 year before recruitment.

Controls (Non-smokers): Individuals who had never smoked tobacco in any form in their lifetime and lived in households free from indoor tobacco smoke. Controls were frequency-matched to cases at the group level with an overall target ratio of 1:1. Matching strata were defined by age (±3 years), biological sex, and residential sub-district. This approach ensured comparable distributions of these variables across the two groups without requiring exact individual one-to-one pairing, thereby permitting minor variations in stratum-specific counts while maintaining overall balance.

Exclusion Criteria:

- Known chronic systemic medical conditions (e.g., chronic kidney disease stage 3–5, chronic heart failure, overt COPD requiring long-term oxygen therapy, active tuberculosis, malignancy, autoimmune connective tissue diseases).
- Acute inflammatory or infectious illness within the preceding 4 weeks.
- History of blood transfusion or active hematinic therapy (iron, vitamin B12, or folate) within the past 3 months.
- Concurrent use of medications known to alter bone marrow kinetics or leukocyte counts (e.g., corticosteroids, immunosuppressive agents, disease-modifying antirheumatic drugs).
- Known history of hematological disorders (e.g., sickle cell trait/disease, thalassemia major/intermedia, leukemia, aplastic anemia).
- Pregnancy or lactation within the past 6 months.
- Regular consumption of smokeless tobacco products (e.g., gutkha, khaini, zarda) among controls, or exclusive smokeless tobacco use.

Exclusion criteria were established through a combination of structured participant self-report, review of available medical records during screening, and clinical evaluation. Routine laboratory testing was not performed to confirm all exclusionary diagnoses (e.g., hemoglobinopathies or renal function). Among the smoker cohort, concurrent smokeless tobacco use was assessed via questionnaire; exclusive smokeless tobacco users were excluded, but dual users of smoked and smokeless products were permitted, and their smokeless tobacco consumption was recorded. Alcohol consumption was measured via self-report and quantified as grams per week. Occupational exposure to biomass, agricultural dust, and pesticides was assessed through self-report and categorized based on primary occupation (agricultural field labor vs. non-agricultural labor/trade). We acknowledge that reliance on self-report and the lack of comprehensive medical records may introduce information bias and limit the precision of exposure assessment, and that objective biomarkers for nutritional status or tobacco exposure were not measured.

2.3 Sample Size Determination

Sample size was calculated using G*Power version 3.1.9.7 (Heinrich-Heine-Universität Düsseldorf, Germany) for an independent two-sample t-test using a non-central t-distribution. Based on pilot data from 20 smokers and 20 non-smokers at our institution, the mean difference in total leukocyte count was 0.8×10^9/L with a pooled standard deviation of 2.1×10^9/L. With $\alpha=0.05$ (two-tailed) and power $(1-\beta)=0.90$, the minimum required sample size was 146 per group. To account for an anticipated 25% loss due to hemolyzed specimens, incomplete questionnaires, or participant

withdrawal, the target was inflated to 195 per group (146 / 0.75 = 194.67, rounded up). Ultimately, 200 cases and 200 controls were recruited, yielding N=400.

2.4 Data Collection and Smoking Assessment

Trained research staff administered a structured face-to-face questionnaire covering:

- Socio-demographics: Age, sex, occupation, educational level, income category.
- Lifestyle and clinical antecedents: Alcohol consumption (grams/week), physical activity, medical history, concurrent medication use.
- Smoking profile: Product type (bidi, commercial cigarette, dual), duration of smoking (years), average number of sticks consumed daily.

Cumulative smoking intensity was quantified using pack-years:

Pack-years = (sticks smoked per day ÷ 20) × years of active smoking

For bidi smokers, 1 bidi was treated as equivalent to 1 conventional cigarette stick as a count-based proxy. It is acknowledged that treating 1 bidi as equivalent to 1 conventional cigarette is a count-based proxy and may not accurately reflect actual nicotine, tar, or carbon monoxide delivery. Bidis are typically smaller and often lack filters, but require more frequent and deeper puffs to maintain combustion, which may alter the effective dose of toxicants. Consequently, pack-years calculated using this equivalence may misclassify true exposure and attenuate or exaggerate dose-response associations. This limitation should be considered when interpreting the cumulative smoking intensity categories.

Participants were categorized as:

- Light Smokers: <10 pack-years
- Moderate Smokers: 10–19.9 pack-years
- Heavy Smokers: ≥20 pack-years

Anthropometric parameters—height (cm) and weight (kg)—were measured using standard protocols. BMI was computed as weight (kg) / height (m^2).

2.5 Blood Sample Collection and Hematological Analysis

A 3 mL venous blood sample was collected from the antecubital vein of each morning-fasted participant under strict aseptic precautions using K_2EDTA tubes. Venipuncture was performed promptly after applying light venous stasis (<1 minute) to avoid tourniquet-induced hemoconcentration.

Samples were transported in temperature-monitored cold boxes (4–8°C) to the central laboratory within 2 hours of collection. Analyses were performed within 4 hours using a Nihon Kohden Celltac G (MEK-9100) automated hematology analyzer (Nihon Kohden Corporation, Tokyo, Japan). Daily internal quality control was performed using low, normal, and high commercial control materials (e-Check) to monitor precision. Instrument calibration was performed independently every six months using manufacturer-provided calibrators, distinct from the daily internal QC process. Specimens were rejected if visible clots, hemolysis, or insufficient volume were present, and a repeat venipuncture was requested.

Analyzed CBC parameters included:

- Erythrocytic lineage: RBC count ($\times 10^{12}$/L), Hb (g/dL), HCT (%), MCV (fL), MCH (pg), MCHC (g/dL), RDW-CV (%).
- Leukocytic lineage: TLC/WBC ($\times 10^9$/L), absolute neutrophil count ($\times 10^9$/L), absolute lymphocyte count ($\times 10^9$/L), absolute monocyte count ($\times 10^9$/L), absolute eosinophil count ($\times 10^9$/L), absolute basophil count ($\times 10^9$/L).
- Thrombocytic lineage: Platelet count ($\times 10^9$/L), Mean Platelet Volume (MPV, fL), and Platelet Distribution Width (PDW, %). PDW was measured directly by the impedance method and reflects the heterogeneity of platelet size.

2.6 Statistical Analysis

Data entry was conducted via EpiData, and statistical processing was performed using IBM SPSS Statistics (Version 28.0) and R (Version 4.3).

Continuous variables were evaluated for distributional normality using the Shapiro–Wilk test and visual histogram inspection. Normally distributed parameters were reported as mean ± SD; non-normally distributed metrics as median with interquartile range (IQR). Categorical variables were presented as absolute counts and percentages.

Bivariable comparisons between cases and controls used:

- Student's independent t-test for normally distributed continuous variables.
- Mann–Whitney U test for non-parametric continuous variables.
- Pearson's chi-square test or Fisher's exact test for categorical parameters.

Differences across smoking intensity categories (non-smokers, light, moderate, and heavy smokers) were evaluated using Welch's ANOVA when variances were unequal, followed by Games–Howell pairwise comparisons.

To evaluate independent associations between cumulative smoking exposure (pack-years) and specific CBC markers (TLC, Hb, MCV, MPV), multivariable linear regression models were constructed. Standardized beta coefficients (β), unstandardized coefficients (B) with 95% confidence intervals (CI), and adjusted R^2 values were derived. Covariates included age, biological sex, BMI, alcohol consumption (g/week), and primary occupational status (agricultural field exposure vs. non-field labor). Statistical significance was defined at two-tailed $p < 0.05$.

All multivariable linear regression models included 400 participants. Complete-case analysis was used because there were no missing data for the primary outcomes or covariates included in the models. Male sex and agricultural occupation were coded as 1, with female sex and non-agricultural occupation coded as 0. Pack-years and alcohol consumption (g/week) were treated as continuous variables. Model diagnostics indicated no violations of linearity or homoscedasticity, variance inflation factors were <2.0, and residuals were approximately normally distributed. The WBC, hemoglobin, MCV, and MPV models are presented in Table 6.

3. Results

3.1 Demographic and Clinical Profile

The study included 400 rural adult participants divided equally into cases (n = 200) and controls (n = 200). Matching protocols maintained balance between groups for basic demographic variables (Table 1). Mean age was 43.6 ± 10.4 years for cases and 42.9 ± 10.1 years for controls (p = 0.498). Males comprised 88.5% (n = 177) of cases and 87.0% (n = 174) of controls (p = 0.644). Agricultural labor was the primary occupation in both groups (61.0% vs. 58.5%, p = 0.612). BMI was lower in smokers (21.8 ± 3.1 kg/m²) compared with non-smokers (22.6 ± 3.4 kg/m²; p = 0.015). Within the cases group, 64.5% (n = 129) smoked bidis exclusively, 20.5% (n = 41) smoked manufactured cigarettes exclusively, and 15.0% (n = 30) were dual users. Mean duration of smoking was 18.4 ± 9.2 years, with a median daily consumption of 12 sticks (IQR 8–18). Mean cumulative smoke exposure was 13.2 ± 8.6 pack-years.

Table 1. Socio-demographic and clinical characteristics of study participants.

Baseline Parameter	Cases (Smokers, n = 200)	Controls (Non-smokers, n = 200)	Test statistic (χ^2/t)	p-value
Age (years), mean ± SD	43.6 ± 10.4	42.9 ± 10.1	t = 0.680	0.498
Sex (Male/Female), n (%)	177 (88.5%) / 23 (11.5%)	174 (87.0%) / 26 (13.0%)	χ^2=0.213	0.644
BMI (kg/m²), mean ± SD	21.8 ± 3.1	22.6 ± 3.4	t = −2.449	0.015*
Primary Occupation, n (%)			χ^2=0.258	0.612
— Agricultural Field Labor	122 (61.0%)	117 (58.5%)		
— Non-Agricultural Labor/Trade	78 (39.0%)	83 (41.5%)		
Alcohol Consumption, n (%)	64 (32.0%)	52 (26.0%)	χ^2=1.736	0.188
Smoking Product Type, n (%)				
— Bidi Exclusively	129 (64.5%)	—	—	—
— Cigarette Exclusively	41 (20.5%)	—	—	—
— Dual Users (Bidi + Cigarette)	30 (15.0%)	—	—	—
Pack-Years, mean ± SD	13.2 ± 8.6	0.0 ± 0.0	—	—

Values are mean ± SD or n (%). Dashes indicate not applicable. *p < 0.05. BMI, body mass index; SD, standard deviation. Cases and controls were frequency-matched by age (±3 years), sex, and residential sub-district. Agricultural field labor involved crop cultivation or livestock handling for ≥6 months per year. Alcohol use was self-reported; intake was quantified as grams of ethanol per week. No missing data were reported for the variables shown.

3.2 Comparison of Erythrocytic Indices

Evaluation of red blood cell parameters revealed statistically significant elevations in cases compared with controls across several key metrics (Table 2).

Mean RBC count was significantly higher in smokers (5.18 ± 0.48 ×10¹²/L) than in non-smokers (4.72 ± 0.42 ×10¹²/L; p < 0.001). Mean hemoglobin was elevated by 1.4 g/dL in smokers (15.2 ± 1.4 g/dL vs. 13.8 ± 1.3 g/dL; p < 0.001). Hematocrit followed a similar pattern (46.1 ± 3.8% vs. 42.2 ± 3.2%; p < 0.001).

Mean erythrocyte volume was higher among smokers. MCV was significantly higher in smokers (91.4 ± 5.2 fL) than in controls (86.2 ± 4.8 fL; p < 0.001). MCH was similarly elevated (30.2 ± 2.1 pg vs. 28.4 ± 1.9 pg; p < 0.001). Median MCHC was slightly higher in smokers [33.5 g/dL (IQR 32.9–34.2)] than in non-smokers [33.0 g/dL (IQR 32.4–33.7)]; Mann–Whitney U = 16,450, p = 0.003. RDW-CV was higher among smokers (14.6 ± 1.4% vs. 13.8 ± 1.1%; p < 0.001), indicating greater heterogeneity in erythrocyte size.

Table 2. Comparison of erythrocytic parameters between cases and controls.

Erythrocytic Parameter	Cases (n = 200)	Controls (n = 200)	Mean difference (95% CI)	Test Statistic	p-value
RBC Count (×10¹²/L)	5.18 ± 0.48	4.72 ± 0.42	0.46 (0.37, 0.55)	t = 10.11	<0.001*
Hemoglobin (g/dL)	15.2 ± 1.4	13.8 ± 1.3	1.40 (1.13, 1.67)	t = 10.44	<0.001*

Erythrocytic Parameter	Cases (n = 200)	Controls (n = 200)	Mean difference (95% CI)	Test Statistic	p-value
Hematocrit (%)	46.1 ± 3.8	42.2 ± 3.2	3.90 (3.21, 4.59)	t = 11.13	<0.001*
MCV (fL)	91.4 ± 5.2	86.2 ± 4.8	5.20 (4.21, 6.19)	t = 10.33	<0.001*
MCH (pg)	30.2 ± 2.1	28.4 ± 1.9	1.80 (1.40, 2.20)	t = 9.10	<0.001*
MCHC (g/dL), median (IQR)	33.5 (32.9–34.2)	33.0 (32.4–33.7)	—	U = 16,450	0.003*
RDW-CV (%)	14.6 ± 1.4	13.8 ± 1.1	0.80 (0.55, 1.05)	t = 5.98	<0.001*

Values are mean ± SD except MCHC, which is presented as median (IQR). *p < 0.05. Mean differences are smokers minus non-smokers. RBC, red blood cell; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; RDW-CV, red cell distribution width coefficient of variation; CI, confidence interval. Independent-sample t-tests were used except for MCHC, which was analyzed using the Mann–Whitney U test.

3.3 Comparison of Leukocytic Indices

Leukocyte profiles demonstrated marked elevations across total and differential white cell lineages in the smoker cohort (Table 3).

TLC was markedly higher in cases (8.39 ± 1.68 $\times 10^9$/L) compared with controls (6.35 ± 1.42 $\times 10^9$/L; $p < 0.001$), representing a 32.1% mean increase. Absolute neutrophil counts were significantly elevated in smokers (5.12 ± 1.22 $\times 10^9$/L vs. 3.78 ± 0.98 $\times 10^9$/L; $p < 0.001$). Absolute lymphocyte counts were also significantly higher in cases (2.38 ± 0.61 $\times 10^9$/L vs. 1.92 ± 0.49 $\times 10^9$/L; $p < 0.001$).

Monocyte counts were elevated in smokers (0.54 ± 0.16 $\times 10^9$/L vs. 0.41 ± 0.12 $\times 10^9$/L; $p < 0.001$). Absolute eosinophil counts showed a slight elevation (0.32 ± 0.14 $\times 10^9$/L vs. 0.21 ± 0.10 $\times 10^9$/L; $p < 0.001$). Basophil counts remained comparable between groups (0.06 ± 0.02 $\times 10^9$/L vs. 0.05 ± 0.02 $\times 10^9$/L; $p = 0.081$).

Table 3. Comparison of leukocytic lineage parameters between cases and controls.

Leukocytic Parameter	Cases (n = 200)	Controls (n = 200)	Mean difference (95% CI)	p-value
Total WBC ($\times 10^9$/L)	8.39 ± 1.68	6.35 ± 1.42	2.04 (1.73, 2.35)	<0.001*
Absolute Neutrophils ($\times 10^9$/L)	5.12 ± 1.22	3.78 ± 0.98	1.34 (1.12, 1.56)	<0.001*
Absolute Lymphocytes ($\times 10^9$/L)	2.38 ± 0.61	1.92 ± 0.49	0.46 (0.35, 0.57)	<0.001*
Absolute Monocytes ($\times 10^9$/L)	0.54 ± 0.16	0.41 ± 0.12	0.13 (0.10, 0.16)	<0.001*
Absolute Eosinophils ($\times 10^9$/L)	0.32 ± 0.14	0.21 ± 0.10	0.11 (0.08, 0.14)	<0.001*
Absolute Basophils ($\times 10^9$/L)	0.06 ± 0.02	0.05 ± 0.02	0.01 (0.00, 0.02)	0.081

Values are mean ± SD. *p < 0.05. Mean differences are smokers minus non-smokers. All leukocyte counts are expressed as $\times 10^9$/L. WBC, white blood cell; CI, confidence interval.

3.4 Comparison of Thrombocytic Indices

Total platelet counts did not show a statistically significant difference between smokers (242 ± 58 $\times 10^9$/L) and non-smokers (251 ± 62 $\times 10^9$/L; $p = 0.142$) (Table 4). However, MPV—a metric reflecting platelet size and enzymatic activity—was significantly higher in cases (10.4 ± 1.1 fL) than in controls (9.5 ± 0.9 fL; $p < 0.001$). PDW was also higher in smokers (15.2 ± 1.8% vs. 13.8 ± 1.4%; $p < 0.001$).

Table 4. Comparison of thrombocytic parameters between cases and controls.

Thrombocytic Parameter	Cases (n = 200)	Controls (n = 200)	Mean difference (95% CI)	t-statistic	p-value
Platelet Count ($\times 10^9$/L)	242 ± 58	251 ± 62	-9.00 (-20.8, 2.8)	-1.47	0.142
Mean Platelet Volume (fL)	10.4 ± 1.1	9.5 ± 0.9	0.90 (0.70, 1.10)	8.91	<0.001*
Platelet Distribution Width (%)	15.2 ± 1.8	13.8 ± 1.4	1.40 (1.08, 1.72)	8.51	<0.001*

Values are mean ± SD. *p < 0.05. Mean differences are smokers minus non-smokers. CI, confidence interval. Independent-sample t-tests were used.

3.5 CBC Parameters Across Smoking Intensity Categories

Subgroup comparisons across non-smokers, light smokers (<10 pack-years), moderate smokers (10–19.9 pack-years), and heavy smokers (≥20 pack-years) showed increasing mean values for several hematological metrics (Table 5).

Hemoglobin levels increased from non-smokers (13.8 ± 1.3 g/dL) to light smokers (14.6 ± 1.2 g/dL), moderate smokers (15.4 ± 1.3 g/dL), and heavy smokers (16.1 ± 1.2 g/dL; Welch's ANOVA $F = 42.18$, $p < 0.001$). Post-hoc Games–Howell comparisons were reported to show significant differences between all hemoglobin groups ($p < 0.05$).

Similarly, TLC increased across non-smokers (6.35 ± 1.42 $\times 10^9$/L), light smokers (7.48 ± 1.35 $\times 10^9$/L), moderate smokers (8.64 ± 1.52 $\times 10^9$/L), and heavy smokers (9.38 ± 1.62 $\times 10^9$/L; Welch's ANOVA $F = 68.34$, $p < 0.001$). MCV values followed a similar upward trajectory, peaking in the heavy smoker subgroup (94.2 ± 4.8 fL).

Table 5. CBC parameters by cumulative smoking exposure.

CBC parameter	Non-smokers (n = 200)	Light smokers (n = 72)	Moderate smokers (n = 84)	Heavy smokers (n = 44)	F statistic	p-value
Hemoglobin (g/dL)	13.8 ± 1.3[a]	14.6 ± 1.2[b]	15.4 ± 1.3[c]	16.1 ± 1.2[d]	42.18	<0.001*
Total WBC (×10⁹/L)	6.35 ± 1.42[a]	7.48 ± 1.35[b]	8.64 ± 1.52[c]	9.38 ± 1.62[d]	68.34	<0.001*
MCV (fL)	86.2 ± 4.8[a]	88.9 ± 4.6[b]	92.1 ± 4.9[c]	94.2 ± 4.8[d]	51.12	<0.001*
MPV (fL)	9.5 ± 0.9[a]	9.9 ± 1.0[b]	10.5 ± 1.1[c]	10.9 ± 1.0[d]	28.76	<0.001*

Values are mean ± SD. Smoking categories: light, <10 pack-years; moderate, 10–19.9 pack-years; heavy, ≥20 pack-years. *p < 0.05. Welch's ANOVA was used because of unequal variances, with Games–Howell post-hoc comparisons. Within each row, groups with different superscript letters differ significantly at p < 0.05. CBC, complete blood count; WBC, white blood cell; MCV, mean corpuscular volume; MPV, mean platelet volume.

3.6 Multivariable Linear Regression Models

Multivariable linear regression analyses were conducted to assess independent associations between cumulative smoking exposure (pack-years) and four hematological outcomes: total WBC count, hemoglobin, MCV, and MPV (Table 6).

After adjusting for age, biological sex, BMI, alcohol consumption, and agricultural occupational status:

- Total Leukocyte Count: Significantly associated with pack-years (B = 0.112, 95% CI 0.088–0.136, p < 0.001; standardized β = 0.482). Each 10 pack-year increment was associated with an estimated increase of 1.12 ×10⁹/L in total white cell count.
- Hemoglobin: Positively associated with pack-years (B = 0.084, 95% CI 0.058–0.110, p < 0.001; standardized β = 0.364).
- MCV: Positively associated with pack-years (B = 0.215, 95% CI 0.154–0.276, p < 0.001; standardized β = 0.412).
- Mean Platelet Volume: Positively associated with pack-years (B = 0.041, 95% CI 0.025–0.057, p < 0.001; standardized β = 0.198).

Table 6. Multivariable linear regression models assessing associations between cumulative pack-years and select CBC parameters (N = 400).

Dependent Variable	Explanatory Variable	B	SE	95% CI for B	Standardized β	p-value
Total WBC (R^2adj = 0.342)	(Constant)	4.512	0.895	2.754 to 6.270	—	<0.001*
	Pack-Years	0.112	0.012	0.088 to 0.136	0.482	<0.001*
	Age (years)	0.008	0.007	-0.006 to 0.022	0.048	0.254
	Sex (Male=1)	0.214	0.182	-0.144 to 0.572	0.046	0.241
	BMI (kg/m²)	-0.022	0.018	-0.057 to 0.013	-0.044	0.221
	Alcohol intake (g/week)	0.003	0.004	-0.005 to 0.011	0.032	0.412
	Agricultural Occupation (Yes=1)	0.156	0.142	-0.123 to 0.435	0.038	0.274
Hemoglobin (R^2adj = 0.315)	(Constant)	11.245	0.752	9.768 to 12.722	—	<0.001*
	Pack-Years	0.084	0.013	0.058 to 0.110	0.364	<0.001*
	Age (years)	-0.004	0.008	-0.020 to 0.012	-0.021	0.612
	Sex (Male=1)	1.412	0.198	1.022 to 1.802	0.285	<0.001*
	BMI (kg/m²)	0.038	0.020	-0.001 to 0.077	0.072	0.058
	Alcohol intake (g/week)	0.002	0.005	-0.008 to 0.012	0.018	0.658
	Agricultural Occupation (Yes=1)	-0.082	0.156	-0.388 to 0.224	-0.020	0.598
MCV (R^2adj = 0.288)	(Constant)	82.110	1.803	78.570 to 85.650	—	<0.001*
	Pack-Years	0.215	0.031	0.154 to 0.276	0.412	<0.001*
	Age (years)	0.042	0.019	0.005 to 0.079	0.088	0.028*
	Sex (Male=1)	0.512	0.465	-0.403 to 1.427	0.041	0.272
	BMI (kg/m²)	-0.081	0.048	-0.175 to 0.013	-0.064	0.092
	Alcohol intake (g/week)	0.006	0.011	-0.016 to 0.028	0.022	0.584
	Agricultural Occupation (Yes=1)	0.324	0.372	-0.406 to 1.054	0.034	0.384
MPV (R^2adj = 0.198)	(Constant)	8.450	0.450	7.566 to 9.334	—	<0.001*
	Pack-Years	0.041	0.008	0.025 to 0.057	0.198	<0.001*
	Age (years)	0.008	0.005	-0.002 to 0.018	0.045	0.312

Dependent Variable	Explanatory Variable	B	SE	95% CI for B	Standardized β	p-value
	Sex (Male=1)	0.112	0.115	-0.114 to 0.338	0.028	0.412
	BMI (kg/m²)	-0.010	0.012	-0.034 to 0.014	-0.022	0.521
	Alcohol intake (g/week)	0.001	0.003	-0.005 to 0.007	0.012	0.742
	Agricultural Occupation (Yes=1)	0.085	0.090	-0.091 to 0.261	0.032	0.345

B, unstandardized coefficient; β, standardized coefficient; SE, standard error; CI, confidence interval; R^2, coefficient of determination; WBC, white blood cell; MCV, mean corpuscular volume; MPV, mean platelet volume; BMI, body mass index. *p < 0.05. All models included 400 participants. Non-smokers were coded as 0 pack-years. Male sex and agricultural occupation were coded as 1; female sex and non-agricultural occupation as 0. Model diagnostics indicated no material violations of linearity or homoscedasticity, variance inflation factors were <2.0, and residuals were approximately normally distributed.

4. Discussion

This community-based cross-sectional comparative study provides data on associations between tobacco smoking status, cumulative smoke exposure, and CBC parameters in a rural adult Indian cohort. The findings demonstrate elevations associated with greater smoking intensity across erythrocyte, leukocyte, and thrombocytic indices among smokers, in a cohort in which bidi smoking predominated.

4.1 Erythrocytic Alterations and Secondary Erythropoietic Responses

Our results show significant increases in RBC count, hemoglobin, hematocrit, MCV, MCH, and RDW-CV among smokers compared with frequency-matched non-smoking controls. The observed mean hemoglobin elevation of 1.4 g/dL in smokers is consistent with a compensatory erythropoietic response to smoke exposure described in the literature [4,8,10], although these group-level mean values do not establish a clinical diagnosis of erythrocytosis in individual participants.

A hypothesized mechanism for the observed erythrocytic changes involves inhaled carbon monoxide (CO). CO has an affinity for human hemoglobin approximately 200–250 times greater than that of molecular oxygen, yielding carboxyhemoglobin (COHb). COHb shifts the oxyhemoglobin dissociation curve to the left, reducing peripheral tissue oxygen unloading. Unfiltered bidis may produce high CO concentrations due to incomplete combustion of coarse tobacco wrapped in non-porous tendu leaves. Consequently, rural bidi smokers may experience persistent functional hypoxia [10,14].

The concurrent observed increase in MCV—with a higher mean value among smokers (91.4 ± 5.2 fL vs. 86.2 ± 4.8 fL)—presents another relevant physiological pattern. Inhaled tobacco toxins may impair DNA synthesis during erythropoiesis, potentially inducing mild megaloblastoid changes or accelerated reticulocytosis. Reticulocytes possess larger volumes (100–105 fL) than mature erythrocytes, elevating the total erythrocyte population's average volume.

Clinical Implication for Rural Anemia Screening

In Central India, anemia screening programs (e.g., Anemia Mukt Bharat) rely heavily on point-of-care capillary hemoglobin measurements or automated CBC panels. Iron deficiency anemia remains widespread in rural communities. Smoking-associated elevations in mean hemoglobin and hematocrit may elevate baseline hemoglobin in some individuals, which could potentially mask concurrent iron deficiency anemia. A smoker with depleted ferritin stores may present with a "normal" hemoglobin level (e.g., 13.0 g/dL), delaying necessary diagnostic or therapeutic interventions [4,8].

4.2 Leukocytosis and Systemic Inflammation Dynamics

One of the most robust findings in our study is the 32.1% mean elevation in TLC among smokers (8.39 $\times 10^9$/L vs. 6.35 $\times 10^9$/L), accompanied by absolute elevations in neutrophils, lymphocytes, monocytes, and eosinophils.

Smoking-associated leukocytosis may operate through two complementary pathways:

Direct Mucosal and Vascular Irritation: Inhaled particulates, aldehydes, and acrolein cause localized inflammation across bronchial and alveolar epithelia. Activated alveolar macrophages release pro-inflammatory cytokines, including tumor necrosis factor-alpha, interleukin-1 beta, interleukin-6, and interleukin-8. These systemic mediators stimulate bone marrow granulopoiesis and promote demargination of leukocytes from vascular walls into circulating blood [5–7].

Neuroendocrine-Mediated Release: Nicotine inhaled via smoke stimulates the sympathetic nervous system and adrenal medulla, promoting catecholamine secretion. Cortisol and catecholamines mobilize marginal pools of neutrophils into active circulation, elevating peripheral white blood cell counts [5–7].

Persistent leukocytosis may reflect systemic inflammatory activity in smokers. Although inflammatory leukocyte activation has plausible vascular implications, the present study did not measure cardiovascular or thrombotic outcomes; these mechanistic interpretations should therefore be considered hypothesis-generating.

4.3 Thrombocytic Metrics and Mean Platelet Volume

While total platelet counts did not differ significantly between smokers and non-smokers ($p = 0.142$), MPV was significantly elevated in the smoking cohort (10.4 ± 1.1 fL vs. 9.5 ± 0.9 fL; $p < 0.001$).

MPV serves as a proxy marker of platelet size, activity, and dense granule content. Larger platelets are metabolically and enzymatically more active than smaller, older platelets. They express higher surface densities of glycoprotein IIb/IIIa receptors, produce more thromboxane A_2, and possess higher pro-thrombotic potential [17].

Inhaled smoke components may contribute to platelet activation and turnover. Release of younger, larger platelets from the bone marrow provides a plausible explanation for the higher MPV observed in smokers. The finding is consistent with a more reactive platelet phenotype, but the present study did not assess vascular or thrombotic events and does not establish clinical risk at the individual level.

4.4 Strengths and Limitations

This study has several methodological strengths:

- Focus on a rural Indian demographic, addressing a population underrepresented in epidemiological literature.
- Detailed evaluation of bidi-dominant smoking profiles, which present distinct chemical exposure dynamics compared with commercial filter cigarettes.
- Matching for age, sex, and residential sub-district location, combined with exclusion of major medical conditions and adjustment for occupational confounders.

Several limitations should also be considered:

- Study Design: The cross-sectional comparative design demonstrates associations but cannot establish direct causal temporality.
- Exposure Measurement: Tobacco exposure was assessed via structured self-reports (pack-years). Objective biomarkers such as urinary cotinine or exhaled carbon monoxide were not measured due to field logistics.
- Unmeasured Confounders: While major clinical confounders were controlled for, underlying nutritional biomarkers (such as baseline serum ferritin, vitamin B12, or folate levels) were not measured across the cohort.
- Single-Centre Design: Findings may not be generalizable to other regions.
- Residual Confounding: Occupational and environmental exposures were measured broadly; biomass, dust, and pesticide exposures were not quantified in detail.
- No Outcome Ascertainment: Vascular and thrombotic outcomes were not measured; mechanistic statements remain hypothesis-generating.

5. Conclusion

This study demonstrates significant associations between tobacco smoking status and alterations in complete blood count parameters among rural adults in Central India. Smokers had higher RBC count, hemoglobin, hematocrit, MCV, total WBC count, several differential leukocyte counts, and MPV, with multiple parameters showing graded increases across smoking-exposure categories.

These hematological patterns may reflect chronic systemic inflammation, nicotine-related neuroendocrine effects, tissue hypoxia, and compensatory erythropoietic responses. Because the study was cross-sectional and did not measure objective tobacco-exposure biomarkers or longitudinal clinical outcomes, causal and prognostic interpretations should remain cautious.

Healthcare professionals in rural primary-care settings should consider smoking history when interpreting automated CBC results. Awareness of smoking-associated shifts in hemoglobin, leukocyte counts, and platelet indices may improve clinical interpretation and help identify situations in which additional evaluation for anemia, inflammation, or other underlying conditions is warranted.

Declarations

Ethics approval and consent to participate: The study protocol was approved by the Institutional Ethics Committee of Shri Rawatpura Sarkar Institute of Medical Sciences and Research, Naya Raipur, Chhattisgarh, India. Written informed consent was obtained from all participants in Hindi and Chhattisgarhi prior to enrollment. Approval was obtained before participant recruitment, and the original approval letter is available for editorial verification upon request.

Consent for publication: Not applicable.

Data availability: The de-identified participant-level dataset and data dictionary are available from the corresponding author upon reasonable request, subject to institutional data-sharing policies. Because of participant-privacy requirements and the conditions of informed consent, raw data are not publicly deposited.

Competing interests: The authors declare no competing interests.

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Authors' contributions: AS and PCD contributed to the conception and design of the study and were responsible for participant recruitment, data collection, and laboratory analysis. AS performed the statistical analysis and drafted the initial manuscript. PCD critically revised the manuscript for important intellectual content. Both authors read and approved the final version and agree to be accountable for all aspects of the work.

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AI-assisted technology declaration: The authors confirm that no generative AI or AI-assisted technology was used in the conduct, analysis, or interpretation of the original study data. AI-assisted tools were used during editorial revision for language editing, reference checks, and formatting. The authors reviewed and approved the final text and take responsibility for its accuracy and integrity.

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