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EFFECT OF CIGARETTE SMOKING ON RED BLOOD CELL INDICES IN HEALTHY ADULT MALE POPULATION

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ABSTRACT

Cigarette smoking is a modifiable major risk factor that induces systemic physiological changes, including alterations in hematological profiles. This study evaluated how cigarette consumption affected platelet levels, white blood cell (WBC) counts, and red blood cell (RBC) indices, and associated lifestyle behaviors among healthy adult males. A cross-sectional comparative study was carried out on 100 healthy male blood donors, ages 18 to 52, who were divided into two groups: 29 smokers and 71 non-smokers. Data on demographics, anthropometry, and lifestyle were collected via structured questionnaires. Complete blood counts were analyzed using automated hematology analyzers. Statistical analysis was conducted using independent t-tests and chi-square, with a significance level of $p < 0.05$. The two groups did not differ significantly in terms of age, height, weight, physical activity, or dietary habits. However, alcohol consumption ($p = 0.002$) and pan chewing ($p = 0.004$) were significantly more prevalent among smokers. Hemoglobin ($p = 0.234$), RBC count ($p = 0.832$), and packed cell volume ($p = 0.245$) were slightly higher in smokers; however, these variations did not reach statistical significance. Among RBC indices, mean corpuscular hemoglobin (MCH) was significantly elevated in smokers ($p = 0.038$), while mean corpuscular volume (MCV) showed a non-significant increase ($p = 0.10$). MCHC, WBC counts, leukocyte differentials, and platelet levels remained comparable. Smoking is significantly associated with specific alterations in red cell morphology, particularly increased MCH. These hematological changes may represent early subclinical responses to tobacco-induced hypoxia and oxidative stress.

Keywords: Cigarette smoking, Red blood cell indices, Hematological changes, Oxidative stress, Hypoxia, Pan chewing

INTRODUCTION

Cigarette smoking is among the most preventable morbidity and mortality and has an impeccable effect on almost all physiological systems of the body. The most affected system is the hematopoietic system, which is highly responsive to the systemic inflammatory effects of the smoke and hence hypoxic effects. In tobacco smoke, over 7,000 chemicals have been identified, among them carbon monoxide, nicotine, and reactive oxidants, many of which affect the red blood cell production, turn over as well as morphology, via oxidative stress, hypoxia, and abnormal cytokine signalling pathways [1]. Red blood cells (RBCs) provide oxygen delivery and, as a result, the overall tissue oxygenation, which is why they are of special interest to the pathophysiological studies of smoking influence. Bonding of carbon monoxide with haemoglobin (through cigarette tar) leads to the covalent combination of carboxyhemoglobin forming thus reducing the oxygen carrying capacity of RBCs, and this causes compensatory erythropoiesis [2]. Such an adaptation mechanism usually occurs in the form of elevated hemoglobin, high hematocrit, and progression in RBC count in long-time cigarette smokers, which strives to provide tissues with oxygenation in a hypoxic condition that is chronic [3,4]. In addition, a long-term exposure to nicotine and other toxins has been documented to induce changes in the structure of erythrocyte membranes and changes in RBC indices as mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and red blood cell distribution width (RDW) [5].

The studies have reported that smoking can increase hematological values of hemoglobin, RBC count, and packed cell volume, that usually regarded as secondary polycythemia, which can further lead to blood viscosity and cardiovascular vulnerability [6]. Anemia affects more than the red cell mass, however. It has been shown that the process of oxidative damage to the membrane of erythrocytes is more thoroughly conducted in smokers, which reduces the viability of these cells and their deformability [7]. A deterioration of the erythrocyte membrane structure has the potential to affect the process of oxygen delivery and has been noted in smokers as well as those with comorbidities [8]. The hematologic changes that occur in smokers also tend to be age, nutritional, and co-morbid status dependent, as the effects of smoking in conjunction with other lifestyle choices may further add to the developing influences of the inflammatory or hypoxic conditions of smoking [9]. Notably, previous research has frequently depended on hospital-based or cross-gender ones, which reduces the applicability of its results. Conversely, studying healthy male donors who are young adults with special emphasis on those of voluntary donation centers enables one to study the toxic changes related to smoking in a rather homogeneous group of individuals that are not complicated by disease or drugs [10]. Moreover, the examination of people in their most productive donation years acts as a virtual representation of the subclinical disruptions in hematology, which can be viewed as a foretelling sign of pathology at the systemic level. A potential cause-effect relationship between smoking and anatomy and pathophysiology of hematological changes is also being confirmed by emerging evidence using genomic investigations and large-scale databases of biobanking, because in Mendelian randomization studies, the increment in the average number of RBC and hemoglobin has been confirmed as genetically profiled consequences of the smoking habit [11]. Equally, an expanding literature base has also seen a connection between smoking and alterations in RDW, another index that continues to gain recognition as a prognostic indicator in cardiovascular and inflammatory diseases [12,13]. Nevertheless, despite increasing evidence on the hematologic effects of smoking, there has been an absence of finer population-level data of specific demographic subpopulations, like that of the healthy Indian male, where regional lifestyle, dietary, and environmental factors might modify hematologic response. Additionally, the bystander effect of the correlated risk behaviors, such as the use of alcohol and the consumption of betel nut, needs a complex evaluation model that factors in several determining behaviors and lifeways covariates [14].

The current research aims to cover the gap in the existing knowledge and examine the red blood cell indices within a clearly defined group of healthy adult male blood donors. The nature of the study

also makes the comparison between the smokers and the non-smokers easier since they exclude those with prior medical conditions, history of infection, and those on any kind of medications that may affect the hematologic values.

Research Objectives

1. To compare the red blood cell indices of healthy adult males who smoke and those who do not
2. To assess the impact of smoking on hematological values alongside lifestyle factors
3. To identify early hematological changes linked to smoking in asymptomatic individuals

METHODOLOGY

Study Design and Setting

A cross-sectional comparative study was utilized to examine the effect of cigarette smoking on RBC indices along with other related parameters, among healthy adult male blood donors. The research was done in the Blood Bank of PIMS & RC (Prathima Institute of Medical Sciences and Research Centre). The key purpose of the research was to evaluate the outcome of smoking cigarettes on diverse hematological parameters and demographic, lifestyle, anthropometric, and dietary factors.

Sample Selection

The 100 volunteer male blood donors in the research had a mean age of 30.3 + 7.1 years and ranged in age from 18 to 52. The participants were recruited sequentially during their attendance at the blood donation center and registered into the study through informed consent. Normal eligibility standards were used to donate blood. The participants who were older patients with identified acute or chronic medical conditions, recent infections, or taking medications that might influence hematological parameters were excluded on the basis of homogeneity in the baseline health status.

Variables and Data Collection

Data were collected using a structured, interview-based schedule along with standard hematological laboratory reports. Variables were grouped into six categories: demographic and occupational characteristics, anthropometric measurements, physical activity metrics, dietary habits, substance use patterns, and hematological indices.

Demographic and Occupational Variables

The demographic characteristics were age (completed in years) and the place of residence (urban/semi-urban/rural). The occupational details were also identified and distributed into physical activities needed, like sedentary occupations, slightly sedentary, heavy physical labor, or occupations that require frequent travel.

Anthropometric Measurements

Both height (in centimeters) and weight (in kilograms) were recorded for each participant as key indicators of body composition and general health status.

Physical Activity Metrics

The participants were told to answer the question of whether they engage with exercise regularly, frequently, and with intensity. Exercise type and classification were categorized in this manner. Along with exercise, the data was provided on the use of walking, sporting activities, and yoga, which was also provided with specific groupings (walking group, sports group, and yoga group) to stratify the level of activity.

Dietary Habits

Information obtained from the diet was based on non-vegetarian consumption of food. The participants were categorized depending on their non-vegetarian versus vegetarian status and further ranked depending on the status of frequency and regularity of non-vegetarian food consumption.

Substance Use Patterns

There was a thorough evaluation of substance use behaviors. Questionnaires were used to determine the cigarette smoking status of the participants, the frequency of smoking, and to categorize them categorized into groups (e.g., daily smokers, occasional smokers, non-smokers). Consumption of alcohol was also estimated and categorized in term of frequency considered. Pan chewing (the use of areca nut or betel leaf products) was also recorded and pooled.

Hematological Indices

An automated hematological analyzer was used to examine venous blood samples. The parameters measured included hemoglobin (g/dL), red blood cell count ($\times 10^6/\mu L$), packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC). In addition, there were the platelet count, neutrophils (N), lymphocytes (L), mixed white cells (Mxd), and total white blood cell count (WBC).

Statistical Analysis

Descriptive statistics, such as means, standard deviations and ranges, were used to characterize continuous variables, while frequencies and percentages were used to summarize categorical data. In inferential comparisons, people were stratified in such a way that there were smokers and non-smokers. Most of the continuous variables appeared to have a non-parametric distribution; hence, the differences between the two groups were examined using the Mann-Whitney U test. Whenever feasible, the chi-square or Fisher's exact test was applied to categorical variables. Every comparison was considered statistically significant if the p-value was less than 0.05.

RESULTS

Overview of Participant Characteristics

A total of 100 healthy adult male blood donors, aged between 18 and 52 years (mean ± SD: 30.3 ± 7.1 years), participated in the study. Based on smoking history, participants were categorized into Smokers (n = 29) and Non-Smokers (n = 71). The distribution showed that 71% of participants were non-smokers, while 29% were smokers (Fig.1).

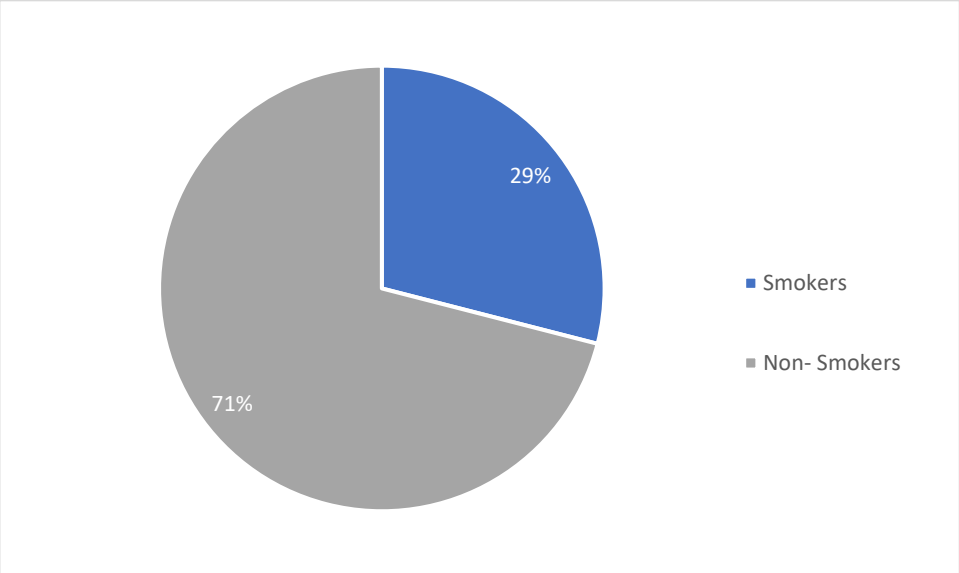

Figure 1. Percentage distribution of smokers and non-smokers

Smokers' mean age (32.55 ± 7.91 years) was marginally older than non-smokers' (29.42 ± 6.60 years) although the difference was not statistically significant (p = 0.382). Anthropometric measurements also showed no discernible variation as shown in Table 1:

Table 1. Demographic and Anthropometric Profile by Smoking Status

Variable	Smokers (Mean ± SD)	Non-Smokers (Mean ± SD)	p-value
Age (years)	32.55 ± 7.91	29.42 ± 6.60	0.382
Height (cm)	165.86 ± 8.40	166.51 ± 9.14	0.483
Weight (kg)	70.90 ± 11.02	69.28 ± 11.18	0.553

These findings confirm that the baseline demographic and physical parameters were statistically comparable between smokers and non-smokers, ruling out confounding due to age or body habitus. A comparative bar chart of these variables is presented in Figure 2, highlighting the visual similarity in age, height, and weight between the two groups.

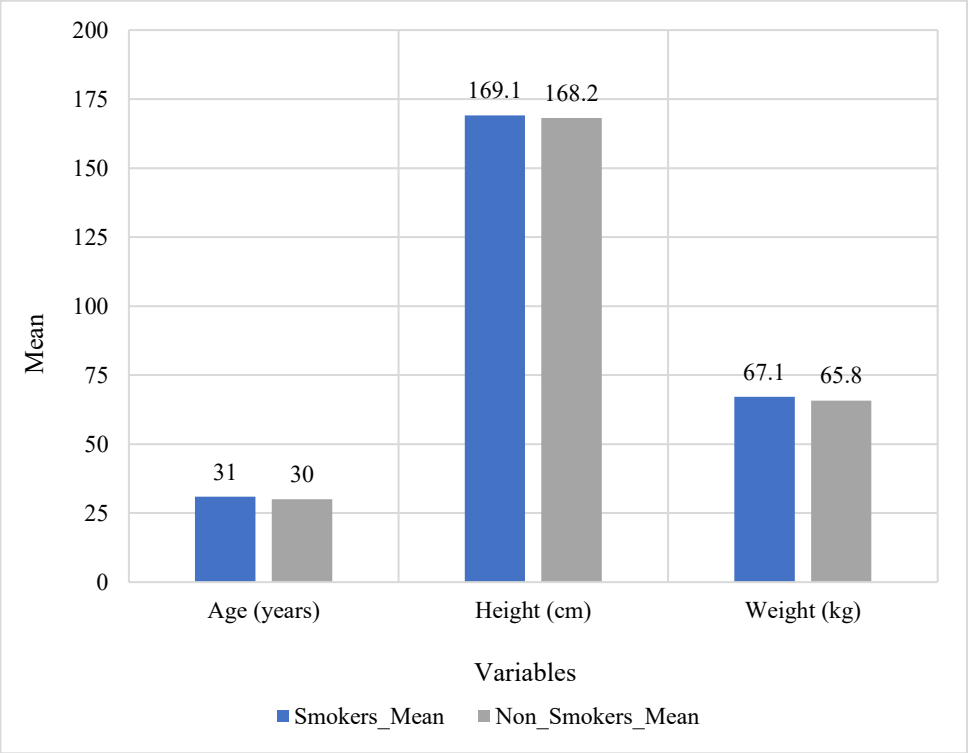

Figure 2. Comparison of age, height, and weight between smokers and non-smokers

Physical Activity and Lifestyle Patterns

Physical activity participation, including regular exercise, walking, sports, and yoga, was comparable among smokers and non-smokers. These lifestyle factors did not significantly differ and were evenly distributed across groups. Table 2 summarizes the statistical test results for each variable:

Table 2. Physical Activity Distribution by Smoking Status

Physical Activity	Test Statistic	*p*-value
Regular Exercise	0.270	0.603
Walking Habit	0.002	0.961
Sports Participation	0.010	0.922
Yoga Practice	0.390	0.532

These results are visually represented in Figure 3, which shows a bar chart of the p-values for each activity compared against the standard threshold of significance (0.05). None of the bars fall below the red threshold line, reinforcing the conclusion of non-significance across the variables assessed.

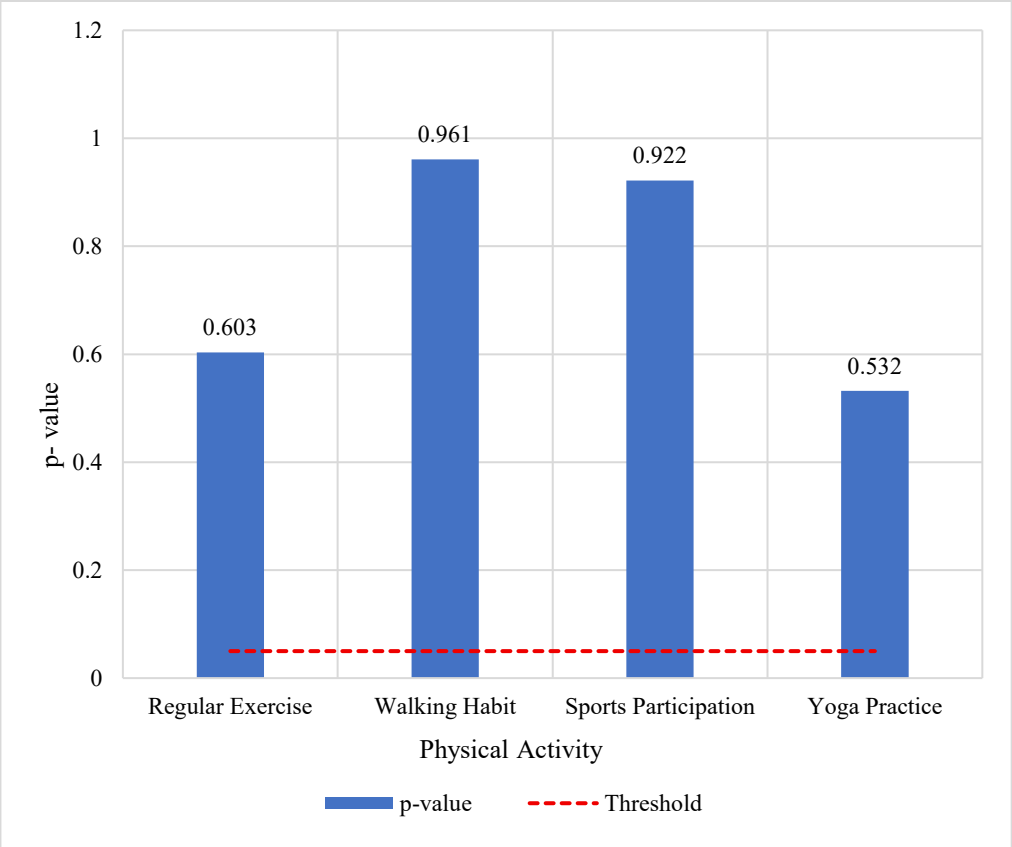

Figure 3. Physical activity behavior comparison between smokers and non-smokers, represented by p-values

Dietary and Substance Use Patterns

Dietary patterns showed no significant difference in non-vegetarian food consumption between the two groups. However, alcohol consumption and pan chewing were significantly more frequent among smokers, indicating clustering of multiple risk behaviors. Table 3 summarizes the p-values for each behavioral parameter, showing that while dietary habits are comparable, substance use patterns differ meaningfully between the groups.

Table 3. Dietary and Substance Use Patterns

Behavior	**Test Statistic**	***p*-value**
Non-Vegetarian Diet	0.011	0.918
Alcohol Use	9.244	0.002 **
Pan Chewing	8.493	0.004 **

There was no significant difference in non-vegetarian dietary habits between smokers and non-smokers, and the p-value was 0.918. However, alcohol use and pan chewing were significantly more prevalent among smokers, as indicated by their low p-values ($p = 0.002$ and $p = 0.004$, respectively).

These conclusions suggest a clustering of multiple risk behaviors among individuals who smoke. Figure 4 visually demonstrates the comparative p-values for these lifestyle behaviors, with alcohol consumption and pan chewing crossing the threshold for statistical significance.

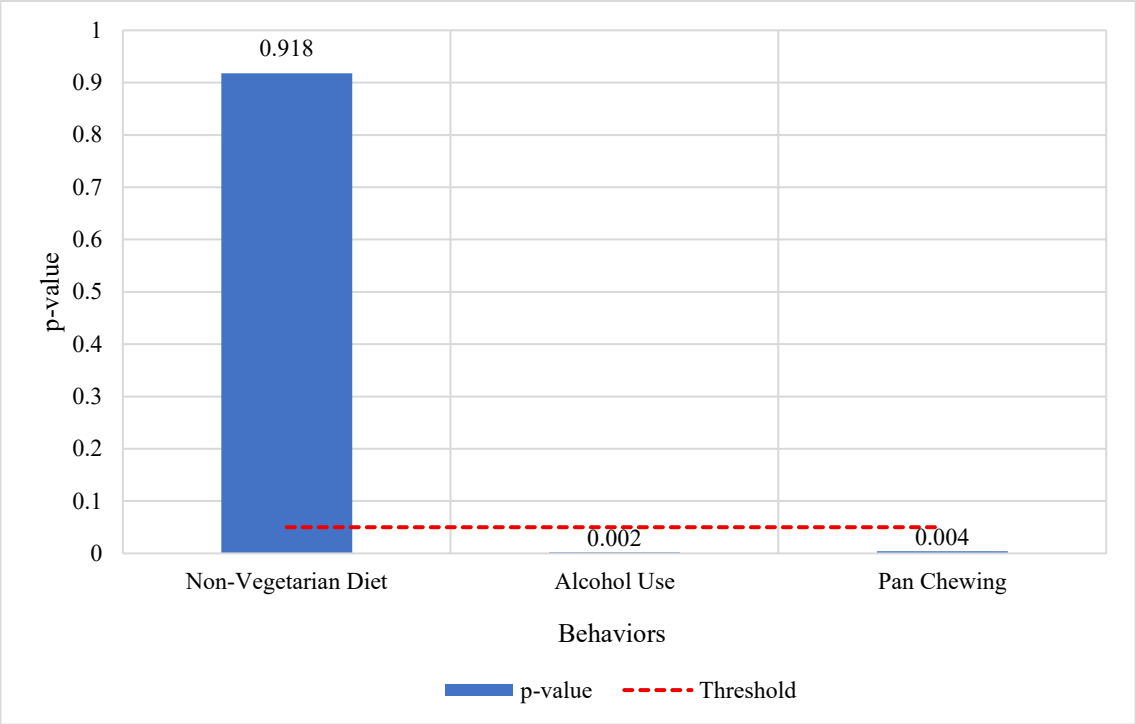

Figure 4. Comparison of Dietary and Substance Use Patterns by Smoking Status

Figure 4 displays the statistical comparison of lifestyle behaviors among smokers and non-smokers. While the bar representing non-vegetarian diet rises above the red threshold line, indicating no significant difference, both alcohol use and pan chewing bars fall well below this threshold. This visual representation confirms that smokers are significantly more likely to engage in alcohol consumption and pan chewing compared to non-smokers, reinforcing the clustering of behavioral risk factors in this population.

Red Blood Cell (RBC) Indices

This section examines how smoking affects red blood cell (RBC) properties in healthy adult male volunteers. The study evaluated potential smoking-related differences in erythrocyte profiles by comparing hemoglobin parameters among smokers and non-smokers (Table 4).

Table 4. Red Blood Cell Indices by Smoking Status

RBC Parameter	Smokers (Mean ± SD)	Non-Smokers (Mean ± SD)	p-value
Hemoglobin (g/dL)	15.56 ± 1.36	15.14 ± 1.00	0.234
RBC Count (×10⁶/µL)	5.28 ± 0.50	5.29 ± 0.43	0.832
Packed Cell Volume (%)	48.02 ± 4.87	46.81 ± 3.40	0.245
Mean Corpuscular Volume (MCV) (fL)	91.05 ± 4.05	88.60 ± 4.41	0.10
Mean Corpuscular Hemoglobin (MCH) (pg)	29.56 ± 1.54	28.69 ± 1.77	0.038 *
Mean Corpuscular Hb Conc. (MCHC) (%)	32.45 ± 1.53	32.45 ± 1.40	0.580

*Note: **p < 0.05 indicates statistical significance.*

The results in Table 4 indicate that while hemoglobin concentration, RBC count, and packed cell volume were marginally higher in smokers, the differences did not reach statistical significance (Fig. 5). This suggests that the overall red cell mass and oxygen-carrying capacity were comparable across the two groups.

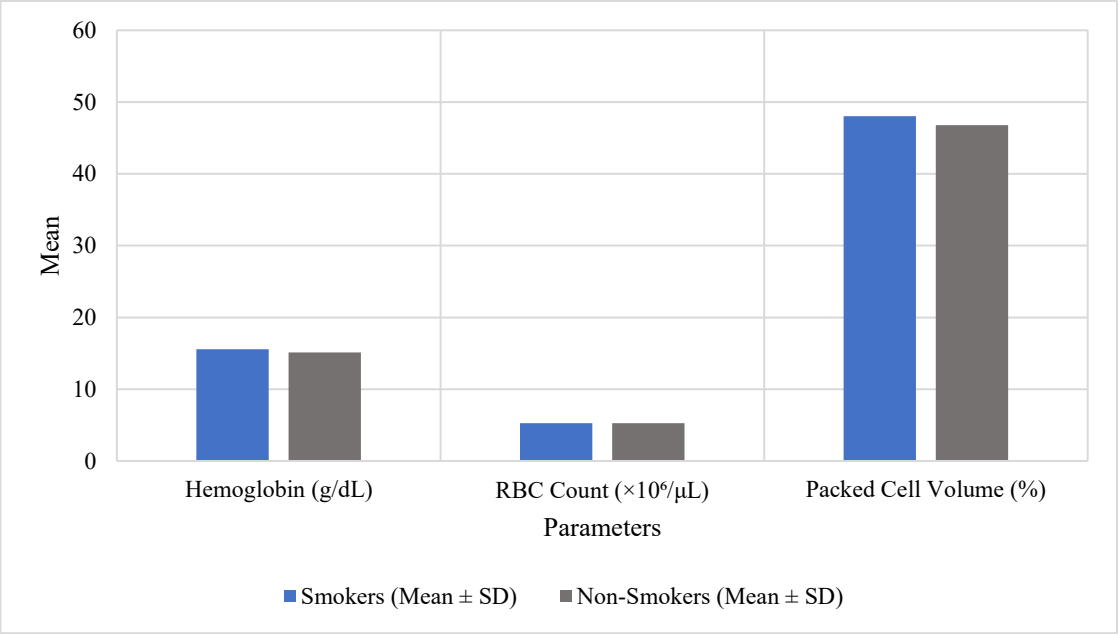

Figure 5. Hemoglobin, RBC Count, and Packed Cell Volume in Smokers and Non-Smokers

Three red blood cell indicators are compared between smokers and non-smokers in this clustered bar chart: hemoglobin, RBC count, and packed cell volume. Visual similarities reflect the absence of statistical significance in these parameters.

Regarding red cell morphology, only MCH showed a statistically significant elevation among smokers ($p = 0.038$), while MCV showed a higher mean value but did not reach statistical significance ($p = 0.10$) (Fig.6). This suggests a partial morphological alteration in erythrocytes, possibly as a physiological response to chronic hypoxia and oxidative stress from smoking exposure. MCHC levels remained stable between groups, indicating that hemoglobin content relative to cell volume was unaffected.

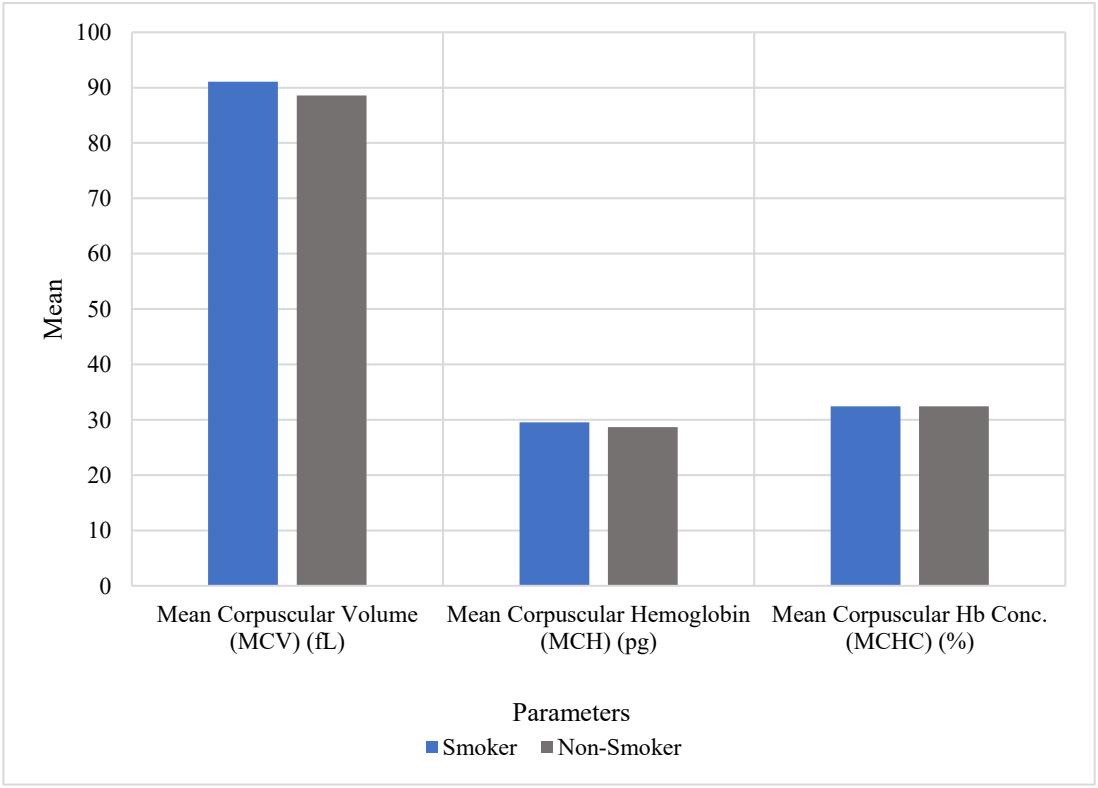

Figure 6. MCV, MCH, and MCHC in Smokers vs Non-Smokers

This grouped bar chart displays the distribution of MCV, MCH, and MCHC between smokers and non-smokers. While MCH values are significantly much in smokers, MCV shows a mild elevation that does not achieve significance. MCHC remains unchanged across groups, highlighting a selective impact of smoking on red cell morphology.

In summary, smoking appears to influence red blood cell morphology, particularly through elevated MCH, though not all indices reach statistical significance. The significance of taking smoking status into account when analyzing erythrocyte indices especially those that include hemoglobin content, is highlighted by these findings.

White Blood Cell and Platelet Indices

White blood cell counts (WBC), differential leukocyte percentages, and platelet counts did not show statistically substantial variations between smokers and non-smokers, according to the investigation. This implies that red blood cell characteristics are the main effects of smoking and does not induce notable alterations in leukocyte or thrombocyte indices among otherwise healthy individuals. These observations are presented in Table 5, which summarizes the comparative values and associated p-values for WBC subtypes and platelet count.

Table 5. WBC and Platelet Indices by Smoking Status

Parameter	Smokers (Mean ± SD)	Non-Smokers (Mean ± SD)	*p*-value
WBC Count (×10³/μL)	6.88 ± 1.97	6.52 ± 1.85	0.337
Lymphocyte %	28.63 ± 7.15	29.48 ± 6.50	0.486
Neutrophil %	60.48 ± 7.87	59.31 ± 7.65	0.426
Mixed WBC %	10.90 ± 2.89	11.21 ± 2.76	0.623
Platelet Count (×10³/μL)	234.2 ± 64.1	229.4 ± 61.8	0.702

To visually interpret these findings, Figure 7 illustrates the grouped mean values for total and differential WBCs, along with platelet counts.

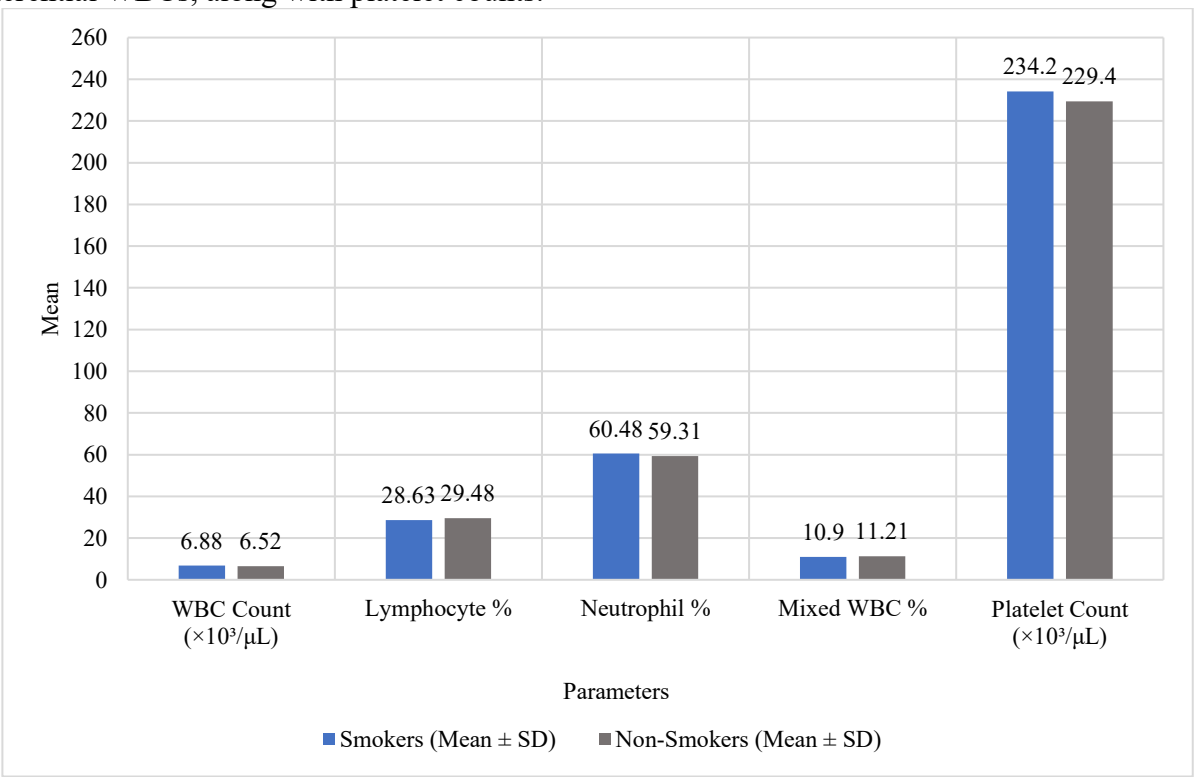

Figure 7. WBC and Platelet Indices

The bar chart presents a side-by-side comparison of mean WBC, lymphocyte, neutrophil, mixed WBC percentages, and platelet count for both groups. The bars show proximity in height, reflecting minimal

variation between smokers and non-smokers across all white cell and platelet parameters. The visual supports the statistical conclusion of non-significance, reinforcing that smoking's hematological impact is limited to red cell indices.

DISCUSSION

Red blood cell indices were the primary focus of the current investigation, which examined the hematologic effects of smoking on normal adult men. White blood cell and platelet profiles, along with behavioral and lifestyle characteristics, were also included in the analysis. Demographic and anthropometric traits, namely age, height and weight, were not observed to differ significantly between smokers and non-smokers, reducing the possibility that age-related or physiological differences could influence the study's findings. The degree of physical activity, such as performing regular exercises, walking, sports, and yoga, was also not statistically different among the groups, implying that both cohorts were equally physically active [15]. The consistency adds to the internal validity of the hematological comparisons. Nevertheless, smokers recorded a considerably increased rate of alcohol use and chewing of pan compared to the rates of non-smokers. These results align with other literature that defines clustering of the risk behaviors when it comes to smokers, as there are always other bad habits tied to tobacco smoking, which increase the cumulative physiological stress [16]. Although they were numerically greater in smokers due to an anti-plasma impact of smoking, hemoglobin ($p = 0.234$), RBC count ($p = 0.832$), and packed cell volume (PCV) ($p = 0.245$) did not significantly vary between those who smoke and those who don't in red blood cell indices. This implies that in this group, smoking did not change the general erythrocyte mass and oxygen transport capacity [7]. However, smokers had a significantly greater mean corpuscular hemoglobin (MCH) ($p = 0.038$), implying a higher hemoglobin concentration per red cell. It might be a compensatory response to chronic hypoxic stress resulting state of carbon monoxide exposure in smoking cigarettes [17].

Smokers also showed a trend towards higher mean corpuscular volume (MCV); however, it fell short of statistical significance ($p = 0.10$). This finding may indicate a possible subclinical macrocytic shift, although the study may not have had sufficient power to detect a definitive morphological difference [18]. The unchanged MCHC levels between the groups indicated hemoglobin saturation per unit volume of red cell was maintained irrespective of hemoglobin content, thus confirming the theory of controlled erythrocytic homeostasis during oxidative conditions [19]. The overall number of white blood cells did not significantly change, both in the comparison of the leukocyte differentials, as well as the number of platelets, between the groups. These findings are contrary to those of other earlier reports, which have associated smoking with both leukocytosis and thrombocytosis, which may be a marker of the sample population, the extent of smoking, or the duration of use [14]. The fact that participants were on a relatively healthy level and at a reasonable age can have reduced inflammatory or hematopoietic alterations characteristic of chronic or intensive smokers [20]. The very strong relation between smoking and co-occurring behaviors, i.e., alcohol and pan use, is crucial. Together, these might augment oxidative and cytotoxic strain within the hematopoietic tissues, notwithstanding normal outward arrangements of hematological parameters [12].

The obtained increase in MCH, in this regard, can be regarded as an initial indicator of systemic adaptation or distress. Clinically, more moderate changes in the hematological parameters may have faint antecedents like an increase in MCH. As early as macrocytosis, it has been reported to be linked with lower red cell deformability and poor microcirculation, which leads to subsequent cardiovascular risk [21]. The result points towards the necessity to incorporate detailed erythrocyte indices along with the total counts in the health monitoring programmes of smokers. Furthermore, recent research highlights the role that red blood cells play in maintaining vascular homeostasis and controlling immunity. The effect of the structural or functional alterations in erythrocytes can thus be both systemic in the context of oxygen transportation [22]. Examination of this study shows that the total red cell count, WBCs, and platelet numbers in healthy males were not significantly impacted by cigarette smoking, but there was a statistically significant rise in MCH and an approaching significant rise in MCV, indicating morphologic changes in the erythrocytes. Such results indicate that there may

be subclinical hematological alterations that have implications since smoking may have hematological implications, and routine monitoring of red cell indices, particularly in at-risk populations, cannot be underestimated.

CONCLUSION

This study shows that among healthy adult males, smoking cigarettes is substantially linked to specific changes in red blood cell morphology, particularly an increase in mean corpuscular hemoglobin (MCH), with a borderline elevation in mean corpuscular volume (MCV). While other hematological parameters, including total hemoglobin, packed cell volume, WBC count, leukocyte differentials, RBC count, and platelet indices, remained statistically comparable between those who smoke and those who don't. The observed morphological changes in erythrocytes suggest early physiological responses to smoking-induced oxidative and hypoxic stress. Moreover, the clustering of harmful behaviors such as increased alcohol consumption and pan chewing among smokers underscores a compounded risk profile, likely to amplify systemic stress on hematopoietic and vascular systems. These findings highlight the importance of including red blood cell morphology in routine hematological evaluations, even among clinically healthy individuals with a history of smoking. The study calls for greater awareness regarding the subtle yet measurable effects of tobacco exposure on hematological health. Public health interventions should not only focus on tobacco cessation but also address associated risk behaviors to mitigate early subclinical changes that may predispose individuals to long-term health complications.

REFERENCES

1. Mohammed, Z. J., Sharba, M. M., & Mohammed, A. A. (2022). The effect of cigarette smoking on haematological parameters in healthy college students in the capital, baghdad. *European Journal of Molecular & Clinical Medicine*, 9(3), 11013–11022.
2. Pedersen, K. M., Çolak, Y., Ellervik, C., Hasselbalch, H. C., Bojesen, S. E., & Nordestgaard, B. G. (2019). Smoking and increased white and red blood cells: a mendelian randomization approach in the copenhagen general population study. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 39(5), 965–977.
3. Elisia, I., Lam, V., Cho, B., Hay, M., Li, M. Y., Yeung, M., ... & Krystal, G. (2020). The effect of smoking on chronic inflammation, immune function and blood cell composition. *Scientific Reports*, 10(1), 19480.
4. Nah, E. H., Kim, S., Cho, S., & Cho, H. I. (2018). Complete blood count reference intervals and patterns of changes across pediatric, adult, and geriatric ages in Korea. *Annals of Laboratory Medicine*, 38(6), 503.
5. Hartl, S., Breyer, M. K., Burghuber, O. C., Ofenheimer, A., Schrott, A., Urban, M. H., ... & Breyer-Kohansal, R. (2020). Blood eosinophil count in the general population: typical values and potential confounders. *European Respiratory Journal*, 55(5).
6. Azimi, S., Faramarzi, E., Sarbakhsh, P., Ostadrahimi, A., Somi, M. H., & Ghayour, M. (2019). Folate and vitamin B12 status and their relation to hematological indices in healthy adults of Iranians: Azar cohort study. *Nutrition and Health*, 25(1), 29–36.
7. Poz, D., De Falco, E., Pisano, C., Madonna, R., Ferdinandy, P., & Balistreri, C. R. (2019). Diagnostic and prognostic relevance of red blood cell distribution width for vascular aging and cardiovascular diseases. *Rejuvenation Research*, 22(2), 146–162.
8. Wirth, M. D., Sevoyan, M., Hofseth, L., Shivappa, N., Hurley, T. G., & Hébert, J. R. (2018). The Dietary Inflammatory Index is associated with elevated white blood cell counts in the National Health and Nutrition Examination Survey. *Brain, Behavior, and Immunity*, 69, 296–303.
9. Hu, Y., Stilp, A. M., McHugh, C. P., Rao, S., Jain, D., Zheng, X., ... & Reiner, A. P. (2021). Whole-genome sequencing association analysis of quantitative red blood cell phenotypes: The NHLBI TOPMed program. *The American Journal of Human Genetics*, 108(5), 874–893.
10. Roubinian, N. H., Plimier, C., Woo, J. P., Lee, C., Bruhn, R., Liu, V. X., ... & Busch, M. P. (2019). Effect of donor, component, and recipient characteristics on hemoglobin increments following

red blood cell transfusion. *Blood, The Journal of the American Society of Hematology*, 134(13), 1003–1013.
11. Purdy, J. C., & Shatzel, J. J. (2021). The hematologic consequences of obesity. *European Journal of Haematology*, 106(3), 306–319.
12. Mohamed, S. E., Eid, H. A., Moazen, E. M., & Abd El-Fattah, D. A. (2023). Impact of chronic cigarette smoking on blood count indices, erythrocyte sedimentation rate and C-reactive protein as inflammatory markers in healthy individuals. *Journal of Recent Advances in Medicine*, 4(1), 74–85.
13. Arkew, M., Gemechu, K., Haile, K., & Asmerom, H. (2022). Red blood cell distribution width as novel biomarker in cardiovascular diseases: a literature review. *Journal of Blood Medicine*, 413–424.
14. Fest, J., Ruiter, R., Ikram, M. A., Voortman, T., Van Eijck, C. H., & Stricker, B. H. (2018). Reference values for white blood-cell-based inflammatory markers in the Rotterdam Study: a population-based prospective cohort study. *Scientific Reports*, 8(1), 10566.
15. Thomas, T., Stefanoni, D., Dzieciatkowska, M., Issaian, A., Nemkov, T., Hill, R. C., ... & D'Alessandro, A. (2020). Evidence of structural protein damage and membrane lipid remodeling in red blood cells from COVID-19 patients. *Journal of Proteome Research*, 19(11), 4455–4469.
16. Mazer, C. D., Hare, G. M., Connelly, P. W., Gilbert, R. E., Shehata, N., Quan, A., ... & Verma, S. (2020). Effect of empagliflozin on erythropoietin levels, iron stores, and red blood cell morphology in patients with type 2 diabetes mellitus and coronary artery disease. *Circulation*, 141(8), 704–707.
17. Foy BH, Carlson JC, Reinertsen E, Valls RP, Lopez RP, Palanques-Tost E, Mow C, Westover MB, Aguirre AD, Higgins JM. Association of red blood cell distribution width with mortality risk in hospitalized adults with SARS-CoV-2 infection. JAMA network open. 2020 Sep 1;3(9):e2022058-.
18. Amézaga, J., Arranz, S., Urruticoechea, A., Ugartemendia, G., Larraioz, A., Louka, M., ... & Tueros, I. (2018). Altered red blood cell membrane fatty acid profile in cancer patients. *Nutrients*, 10(12), 1853.
19. Bain, B. J., & Leach, M. (2025). *Blood Cells: A Practical Guide*. John Wiley & Sons.
20. Aher, S. M. (2020). Early versus late erythropoietin for preventing red blood cell transfusion in preterm and/or low birth weight infants. *Cochrane Database of Systematic Reviews*, (2).
21. Remy, K. E., Hall, M. W., Cholette, J., Juffermans, N. P., Nicol, K., Doctor, A., ... & Pediatric Critical Care Blood Research Network (Blood Net). (2018). Mechanisms of red blood cell transfusion-related immunomodulation. *Transfusion*, 58(3), 804–815.
22. Anderson, H. L., Brodsky, I. E., & Mangalmurti, N. S. (2018). The evolving erythrocyte: red blood cells as modulators of innate immunity. *The Journal of Immunology*, 201(5), 1343–1351.