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IMPACT OF SMOKELESS TOBACCO USE ON HEMATOLOGICAL PARAMETERS AND ANEMIA-RELATED INDICES IN ADULT MALES

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Abstract

Background: Smokeless tobacco (SLT) is widely consumed in South Asia and has been linked to several systemic health effects. Evidence regarding its influence on hematological parameters and anemia-related indices remains inconsistent.

Methodology: A cross-sectional study was conducted among 234 adult males, including 59 smokeless tobacco users and 175 non-users. Hematological parameters including hemoglobin (Hb), red blood cell count (RBC), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), white blood cell count (WBC), platelet count (PLT), mean platelet volume (MPV), lymphocyte percentage, and neutrophil percentage were compared between groups.

Results: Smokeless tobacco users demonstrated lower mean hemoglobin, RBC count, hematocrit, and MCH values than non-users. Users also exhibited slightly higher platelet counts, MPV, and lymphocyte percentages. However, none of the observed differences reached statistical significance ($p>0.05$). The pattern nevertheless suggested a tendency toward less favorable anemia-related indicesamong smokeless tobacco users.

Conclusion: Smokeless tobacco use was associated with lower hemoglobin-related indices, although statistically significant differences were not observed. Larger prospective studies are required to clarify the potential contribution of smokeless tobacco to anemia and hematological alterations.

Key Words: Smokeless tobacco, anemia, hemoglobin, hematological parameters, red blood cell indices.

Introduction

Tobacco consumption remains a major public health challenge worldwide. Although cigarette smoking has received considerable attention, smokeless tobacco products such as naswar, gutka, snuff, and chewing tobacco continue to be widely used, particularly in South Asian countries. These products are often perceived as safer alternatives to smoking despite containing nicotine and numerous toxic compounds.1

Smokeless tobacco contains tobacco-specific nitrosamines, heavy metals, and oxidant-generating substances that may adversely affect human health. Chronic exposure to these compounds can induce oxidative stress, inflammation, endothelial dysfunction, and metabolic disturbances. Such mechanisms may interfere with normal hematopoiesis and contribute to alterations in blood cell production and function.2

SLT products deliver nicotine through the oral mucosa and contain more than 3,000 chemical constituents, including alkaloids, heavy metals, nitrosamines, and polycyclic aromatic hydrocarbons.[3] These constituents are bioactive and can exert systemic effects far beyond the oral cavity. There is growing evidence that regular SLT use is associated with cardiovascular disease, metabolic dysfunction, and oral malignancy.4-5 However, SLT effects on haematological homeostasis a domain of critical importance for overall physiological function remain incompletely understood.

The complete blood count (CBC) is one of the most commonly performed clinical investigations and serves as an integrated marker of bone marrow function, haematopoiesis, oxygen-carrying capacity, immunological competence, and haemostatic potential. Alterations in red cell parameters such as haemoglobin, haematocrit, and red cell distribution width (RDW), or in platelet parameters such as platelet count and mean platelet volume (MPV), may signal subclinical pathology well before overt disease manifests. Nicotine, a principal active component of SLT, is known to stimulate erythropoietin secretion, influence platelet aggregation, and modulate leucocyte function; yet evidence from population-based studies in low- and middle-income countries (LMICs), where SLT prevalence is highest, remains sparse.3-4 Several studies have suggested that tobacco exposure may affect erythrocyte survival, iron metabolism, and bone marrow function, potentially increasing the risk of anemia.3-6

Anemia is a common health problem in developing countries and is associated with fatigue, reduced physical performance, impaired cognition, and diminished quality of life. Identification of modifiable risk factors for anemia remains an important public health objective. While the relationship between cigarette smoking and hematological changes has been extensively investigated, comparatively limited information is available regarding the effects of smokeless tobacco.

The present study therefore aimed to determine whether current SLT consumption is associated with measurable differences in CBC parameters including red cell indices, platelet parameters, and leucocyte counts compared with non-tobacco-using controls

Methodology

This cross-sectional study was conducted on a total of 234 males, aged 23–40 years. Participants were categorised into two groups based on tobacco use history: SLT users (n = 59), defined as individuals with current and regular use of any smokeless tobacco product (principally naswar) for at least six months; and non-users (controls, n = 175), defined as individuals with no history of tobacco use in any form. Individuals with a known haematological disorder, chronic systemic illness (diabetes, renal disease, hepatic disease), current or recent (within four weeks) infection, use of haematinics or anticoagulants, or concurrent cigarette smoking were excluded to minimise confounding. Smokers and dual users were similarly excluded. The study was conducted after ethical clearance from the institutional ethics committee. Written informed consent was obtained from all of the study participants before the start of the study.

Sociodemographic information including age, area of residence (rural/urban), family structure (nuclear/combined), educational attainment (years), and monthly household income (PKR) was obtained through a structured face-to-face interview administered by trained research assistants. Tobacco use status and type of product used were ascertained through direct questioning. Five millilitres of venous blood were drawn under aseptic conditions by venepuncture into EDTA-anticoagulated vacutainer tubes. Samples were processed within two hours of collection using an automated haematology analyser. The following CBC parameters were measured: total white blood cell count (WBC), haemoglobin (Hb), red blood cell count (RBC), haematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), red cell distribution width standard deviation (RDW-SD), red cell distribution width coefficient of variation (RDW-CV), platelet count (PLT), mean platelet volume (MPV), lymphocyte percentage (LYM%), and neutrophil percentage (NEUT%). Data were entered and managed in IBM SPSS Statistics version 25. Continuous variables are presented as mean ± standard deviation (SD) for normally distributed data. A two-tailed p-value of less than 0.05 was considered statistically significant

Results

The study enrolled 234 males, comprising 59 SLT users and 175 non-users. The two groups were well matched across all sociodemographic parameters. Mean age was 31.37 ± 4.69 years in non-users and 32.46 ± 4.74 years in SLT users, with no significant difference between groups ($p = 0.126$). Educational attainment (mean years of schooling: 8.35 ± 4.55 vs. 8.90 ± 3.58, $p = 0.400$) and monthly household income (PKR 36,749 ± 60,856 vs. PKR 36,322 ± 62,112, $p = 0.963$) were comparable. The distribution of rural versus urban residence, family type, and age group also did not differ significantly between groups.

Among 234 participants, 25.2% were smokeless tobacco users and 74.8% were non-users. The mean age of users was 32.46 ± 4.74 years compared with 31.37 ± 4.69 years among non-users. Users demonstrated lower mean hemoglobin (12.27 vs 12.52 g/dL), lower RBC count (5.11 vs 5.13), lower hematocrit (37.59% vs 37.78%), and lower MCH (26.15 vs 27.07 pg) compared with non-users. These findings indicate a trend toward less favorable anemia-related indices among smokeless tobacco users. Platelet count (274.17 vs 269.28 $\times 10^3/\mu L$), MPV (10.12 vs 9.83 fL), and lymphocyte percentage (35.75% vs 33.42%) were slightly higher among users. However, all comparisons yielded p-values greater than 0.05, indicating that the differences were not statistically significant. Overall, the pattern of results suggests that smokeless tobacco users may exhibit subtle hematological alterations and lower hemoglobin-related indices, although the current study lacked sufficient evidence to establish a statistically significant association.

Table I: Mean difference of hematological parameters among smokeless tobacco users and non-smokeless tobacco users.

Variable	Smokeless tobacco users (Mean ± SD) n = 59	Non Smokeless tobacco users (Mean ± SD) n = 175	p-Value
Age (Years)	32.46 ± 4.74	31.37 ± 4.69	.131
Haemoglobin (g/dl)	12.25 ± 1.9	12.72 ± 1.41	.102
RBC's (million/mm3)	5.11 ±.74	5.13 ± .61	.897
Haematocrit (%)	37.59 ± 5.08	37.78 ± 4.12	.181
MCH (pg)	26.15 ± 12.26	27.78 ± 13.32	.470
Platelets (109/L)	274 ± 84.30	269 ± 77.88	.313
WBC's (per mm3)	7.74 ± 2.09	7.51 ± 2.40	.461
Lymphocytes (%)	34.75 ± 7.93	33.42 ± 8.96	.264
Neutrophils (%)	52.69 ± 10.76	54.49 ± 10.12	.208

Discussion

The present study explored smokeless tobacco use and its impact on hematological parameters among adult males. Smokeless tobacco users exhibited lower hemoglobin concentration, RBC count, hematocrit, and MCH compared with non-users. Although these differences were not statistically significant, the consistent direction of change may suggest early hematological effects associated with chronic tobacco exposure.

At first glance, this finding may appear surprising given the known pharmacological activity of nicotine and other SLT constituents on haematopoietic tissue. Nicotine stimulates the release of catecholamines, which in turn can mobilise marginated leucocytes and transiently elevate WBC counts; it also modulates platelet reactivity, erythropoietin release, and, over longer periods, red cell production.[7-8] Several studies from neighbouring South Asian countries have reported haematological differences in tobacco users. A study from Nepal found significantly higher haemoglobin and haematocrit values among male SLT users, attributed to nicotine-driven erythropoietin stimulation, while a study from India documented elevated WBC and platelet counts in gutka users.[9-10]

A number of explanations may account for our null finding. First, the participants in the current study were relatively young (mean age approximately 31–32 years), and many may have been early in their SLT exposure history. Haematological derangements attributable to tobacco use may require prolonged, cumulative exposure to become detectable by routine CBC analysis. Second, the SLT product predominantly used in District Kech is naswar a mixture of tobacco, lime, and indigo typically retained in the oral vestibule which differs from combusted tobacco in its mode of nicotine delivery, systemic bioavailability, and co-constituent profile. Its haematological impact may therefore differ from that of cigarettes or even other SLT products.[11] Third, given the rural and resource-limited setting, it is plausible that both SLT users and non-users may have shared background exposures nutritional insufficiencies, subclinical infections, or occupational factors that could attenuate between-group differences in haematological parameters.

Regarding specific parameters, the absence of a difference in haemoglobin and haematocrit is consistent with some prior literature showing that short-term nicotine exposure does not uniformly produce polycythaemia in non-smokers.[12] The comparable platelet counts and MPV across groups are particularly noteworthy, as MPV is an emerging marker of platelet activation and cardiovascular risk. Studies involving cigarette smokers have generally found elevated MPV, but comparable data for SLT users are limited, and some authors have suggested that the route of administration critically modulates platelet biology.[13] The present study adds to this emerging evidence base by demonstrating that SLT use in this demographic and geographic context is not accompanied by the platelet activation signal that might be anticipated from combusted tobacco.

The leucocyte findings also merit comment. A consistently reported effect of cigarette smoking is chronic, low-grade leucocytosis reflective of systemic inflammation; this has been attributed to combustion products, particularly carbon monoxide and tar constituents.[14] SLT, lacking a combustion phase, may not replicate this inflammatory stimulus to the same degree. The absence of a leucocyte differential alteration in the current study aligns with this mechanistic reasoning, though definitive conclusions would require measurement of inflammatory cytokines or high-sensitivity C-reactive protein.

The study has several limitations that must be acknowledged. First, the cross-sectional design precludes causal inference, and the directionality of any association cannot be established. Second, the precise duration, frequency, and quantity of SLT use were not available in the dataset, preventing dose-response analysis that would considerably strengthen interpretation. Third, while the sample size was adequate for a preliminary characterisation, a larger study with greater statistical power might detect modest effect sizes that the current study was underpowered to identify. Fourth, the lack of data on dietary iron intake, nutritional status, or comorbid conditions represents a potential source of confounding. Finally, the single-centre and geographically defined nature of the sample limits generalisability to other SLT-using populations with different product preferences.

Notwithstanding these limitations, the study contributes valuable baseline data from one of the most underrepresented regions in haematological research in Pakistan. The null finding should not be interpreted as evidence that SLT is haematologically benign in the long term; rather, it underscores the need for longitudinal studies incorporating detailed exposure quantification, a broader biomarker panel, and sufficient follow-up duration to capture the trajectory of haematological change.

Conclusion

Smokeless tobacco users demonstrated lower hemoglobin-related indices, including hemoglobin concentration, RBC count, hematocrit, and MCH, compared with non-users. Although these differences were not statistically significant, they suggest a possible tendency toward anemia-related hematological alterations among users. Further large-scale prospective studies are required to determine whether chronic smokeless tobacco use contributes to the development of anemia and other hematological abnormalities.

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