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RESEARCH ARTICLE

KHAT CHEWING AND LONG SLEEP DURATION ARE ASSOCIATED WITH ALTERED COAGULATION AND PLATELET PROFILES IN YOUNG YEMENI ADULTS: A MULTI-CENTER CROSS-SECTIONAL STUDY

Radfan Saleh Abdullah[1,2,3,*], Naif Taleb Ali[1,2,3], and Mansour Abdelnabi H. Mehdi[1]

[1] *Dept. of Laboratory Sciences, Radfan College University, University of Lahej, Al-Houta, Yemen*
[2] *Dept. of Health Sciences, Faculty of Medicine and Health Sciences, University of Science and Technology, Aden, Yemen*
[3] *Dept. of Laboratory Sciences, Aden Gulf International University, Al-Dhale, Yemen*

***Corresponding author: Radfan Saleh Abdullah; E-mail: r.saleh@ust.edu**

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Abstract

The hematological effects of khat chewing, a widespread habit in East Africa and Yemen, remain inadequately characterized, particularly regarding coagulation. Similarly, evidence linking sleep duration to hematological markers in young, healthy populations is limited. In a cross-sectional study of 600 Yemeni university students, we assessed khat chewing frequency, sleep duration. Prothrombin time (PT), activated partial thromboplastin time (APTT), and complete blood count were measured. Multivariate logistic regression models adjusted for age, gender, and BMI. Weekly khat chewers had significantly higher odds of abnormal PT (aOR = 2.31, 95% CI: 1.05–5.08, p=0.037) and abnormal APTT (aOR = 3.78, 95% CI: 1.55–9.22, p=0.003) compared to never-users. A non-linear dose-response was observed, with weekly users showing the most pronounced coagulation abnormalities. Participants reporting long sleep duration (>8 hours) had over four times the odds of abnormal platelet counts (aOR = 4.12, 95% CI: 1.62--10.49, p=0.003) compared to the reference group (7-8 hours). Khat chewing is independently associated with significant coagulation abnormalities, suggesting potential interference with both intrinsic and extrinsic pathways. Furthermore, long sleep duration is a novel predictor of platelet count disturbances in this young cohort. These findings highlight potential public health risks, calling for greater clinical awareness of the hematological sequelae of khat use and suboptimal sleep patterns in this population.

Keywords: Khat; Catha edulis; Coagulation; Prothrombin Time; Partial Thromboplastin Time; Sleep; Platelets; Hematology; Yemen.

Introduction

Khat (Catha edulis Forsk), a psychoactive plant traditionally cultivated and consumed in the Arabian Peninsula and the Horn of Africa, represents a deeply embedded sociocultural practice with significant public health implications [1]. The leaves of the khat plant are chewed to release cathinone, an amphetamine-like stimulant that induces euphoria, alertness, and suppression of appetite [2]. While the acute psychoactive effects are well-documented, the chronic systemic consequences of this habit, particularly its impact on hematological and hemostatic systems, remain a critical area of investigation. Emerging evidence suggests that khat chewing may be an independent risk factor for cardiovascular diseases, including acute myocardial infarction and stroke, potentially through mechanisms involving coronary vasospasm and thrombus formation [3, 4]. However, the precise pathophysiological pathways linking khat to a prothrombotic state are not fully elucidated. Specifically, there is a paucity of robust clinical data examining its direct effects on the coagulation cascade, as measured by standard parameters such as Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT).

Concurrently, the influence of sleep patterns on hematological health is gaining recognition. Sleep is a fundamental physiological process that regulates numerous biological functions, including immune response, inflammation, and metabolism [5]. Deviations from optimal sleep duration, both short and long, have

been associated with adverse health outcomes, including an increased risk of cardiovascular morbidity and mortality [6]. While the link between sleep deprivation and platelet activation has been explored, the hematological effects of long sleep duration are less understood [7]. Platelets, key mediators of hemostasis and thrombosis, are known to exhibit diurnal variations in their activity, suggesting a potential regulatory role for the sleep-wake cycle [8]. However, large-scale epidemiological studies investigating the association between prolonged sleep and platelet homeostasis, particularly in young and otherwise healthy populations, are scarce. This knowledge gap is significant, as alterations in platelet count or function could represent a subclinical risk factor for future thrombotic or hemorrhagic events.

This study is situated at the intersection of these two public health concerns in the context of Yemen, a country where khat use is endemic and sleep disturbances are prevalent. By investigating the independent and combined effects of khat chewing and sleep duration on coagulation and platelet profiles in a cohort of young Yemeni adults, this research aims to address a significant gap in the current literature. The primary objectives are twofold: first, to determine the association between khat chewing and abnormalities in PT and APTT, and second, to assess the relationship between long sleep duration and alterations in platelet counts. The findings of this study are expected to provide novel insights into the hematological sequelae of these common lifestyle behaviors, thereby informing clinical practice and public health strategies in the region and beyond.

Methods

Study Design and Participants

This descriptive,multi-center, cross-sectional investigation was conducted between January and May 2025, recruiting 600 undergraduate students aged 18-25 years from three universities in Southern Yemen. A stratified random sampling technique ensured proportional representation from key faculties (Medical Sciences, Engineering, and Humanities). The sample size provided >80% power to detect moderate effect sizes in multivariate analyses.

Data Collection and Exposure Assessment

Behavioral Exposures:A standardized, pre-tested questionnaire was administered by trained staff. Khat chewing habit was self-reported and categorized into four groups: 'Never,' 'Occasionally,' 'Weekly,' and 'Daily.' Based on preliminary analysis indicating a potential threshold effect on coagulation, the 'Weekly' group was selected as the primary exposure for formal testing. Sleep duration was self-reported as average total hours per 24-hour period and categorized as 'Short (< 7 hours),' 'Reference (7-8 hours),' and 'Long (>8 hours).

Laboratory Measurements

Venous blood samples(4 mL) were collected under aseptic conditions. For hematological analysis, 2 mL was placed in a K3 EDTA tube and analyzed within 2 hours using an automated hematology analyzer (Mindray BC-3000 Plus) to determine CBC parameters (WBC, RBC, HGB, PLT, MCV, MCH, MCHC). For hemostatic analysis, 2 mL was collected into a 3.2% sodium citrate tube, centrifuged to obtain platelet-poor plasma, and analyzed for Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) on a semi-automated coagulation analyzer (BA-88A). International Sensitivity Index (ISI)-adjusted INR was calculated automatically. Both analyzers were subject to rigorous daily calibration and internal quality control protocols. Abnormal values were defined using ICSH-standardized reference ranges as follows: Prothrombin Time (PT) > 14.5 seconds, Activated Partial Thromboplastin Time (APTT) > 35.0 seconds, and thrombocytopenia as a platelet count < 150,000/µL.

Statistical Analysis

Analyses were performed using IBM SPSS Statistics Version 28. Descriptive statistics characterized the study population. Prevalence of abnormal hematological and coagulation parameters was calculated. Multivariable binary logistic regression models were constructed to assess the independent associations of (1) weekly khat use (vs. never) with abnormal PT and APTT, and (2) long sleep duration (vs. reference) with abnormal platelet count. All models were adjusted for age, gender, BMI, and university site, with results reported as Adjusted Odds Ratios (aOR) and 95% Confidence Intervals (CI). A p-value < 0.05 was deemed statistically significant. The initial associations were also assessed using Chi-square tests for trends.

Ethical Approval

The study received full ethical approval from the institutional review boards of all participating universities.The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. All participants provided written informed consent.

Results

Participant Characteristics and Behavioral Prevalence

The final analytical sample included 600 students with a mean age of 21.8 years(± 2.3 SD). The distribution of key behavioral exposures was as follows: the majority of participants (69%) reported never using khat, while 13%

were weekly users and 10% were daily users. Regarding sleep patterns, the majority (67%) reported short sleep duration (< 7 hours), 18% were within the reference range (7-8 hours), and 15% reported long sleep duration (> 8 hours).

Association between Khat Chewing and Coagulation Parameters

Khat chewing demonstrated a significant dose-response relationship with coagulation abnormalities.Weekly khat users exhibited the most pronounced abnormalities, with 66.7% showing abnormal PT values and 83.3% showing abnormal PTT values. This pattern suggested a potential threshold effect for hemostatic impact, as both occasional and daily users showed lower prevalence rates. In multivariable logistic regression models adjusted for age, gender, BMI, and university site, weekly khat use was independently associated with significantly higher odds of abnormal PT (aOR = 2.31, 95% CI: 1.05--5.08, p = 0.037) and abnormal APTT (aOR = 3.78, 95% CI: 1.55--9.22, p = 0.003) compared to never-users (Table 1). Comprehensive analysis of complete blood count parameters (WBC, RBC, Hb, MCV, MCH, MCHC, PLT) revealed no significant differences across khat chewing categories.

Table 1: Multivariate Analysis of Khat Chewing and Coagulation Abnormalities

Behavioral Factor	Outcome Variable	n / N (%)	Adjusted Odds Ratio (aOR)	95% CI for aOR	p-value
Khat Chewing (Weekly vs. Never)	Abnormal PT	52 / 78 (66.7%)	2.31	1.05 – 5.08	0.037
	Abnormal APTT	65 / 78 (83.3%)	3.78	1.55 – 9.22	0.003

Models adjusted for age, gender, BMI, and university site. PT: Prothrombin Time; APTT: Activated Partial Thromboplastin Time. The 'n/N' column represents the number of participants with the abnormality (n) over the total number in the exposure group (N).

Association between Sleep Duration and Hematological Parameters

Sleep duration emerged as a significant predictor of platelet count abnormalities(p = 0.012). Participants reporting long sleep duration (8-11 hours) demonstrated the highest prevalence of abnormal platelet counts (17.6%), compared to 1.5% in the 4-7 hour (reference) group and 6.7% in the less than 3-hour group. After adjusting for covariates, long sleep duration was associated with over a four-fold increase in the odds of thrombocytopenia (low platelet count) (aOR = 4.12, 95% CI: 1.62--10.49, p = 0.003) (Table 2).

Analysis of other hematological and coagulation parameters (WBC, RBC, Hb, MCV, MCH, MCHC, PT, PTT, INR) revealed no significant associations with sleep duration categories.

Table 2: Multivariate Analysis of Sleep Duration and Platelet Abnormalities

Behavioral Factor	Outcome Variable	n / N (%)	Adjusted Odds Ratio (aOR)	95% CI for aOR	p-value
Sleep Duration (> 8h vs. 7-8h)	Abnormal Platelet Count (Thrombocytopenia)	19 / 108 (17.6%)	4.12	1.62 – 10.49	0.003

Model adjusted for age, gender, BMI, and university site. Reference category for sleep duration is 7–8 hours. The 'n/N' column represents the number of participants with the abnormality (n) over the total number in the exposure group (N). The abnormality for platelet count is specified as thrombocytopenia (low platelet count).

Summary of Key Findings

The comprehensive analysis revealed distinct association patterns:khat chewing was primarily associated with disturbances in the coagulation cascade, while long sleep duration was specifically linked to aberrations in platelet counts.

Discussion

This study provides novel evidence on the distinct hematological alterations associated with khat chewing and long sleep duration in a young, healthy Yemeni population. Our findings reveal two key independent associations: a significant disturbance in the coagulation cascade linked to weekly khat use, and a four-fold increased odds of abnormal platelet counts among individuals reporting long sleep duration. These results underscore the potential for common lifestyle factors to sub-clinically impact hemostatic and hematological systems, even in the absence of overt disease.

The association between khat chewing and coagulation abnormalities, specifically the prolongation of PT and APTT, suggests that the active compounds in khat may interfere with both the extrinsic and intrinsic pathways of the coagulation cascade. This finding aligns with previous research indicating that khat chewing can induce a prothrombotic state, potentially contributing to the increased risk of cardiovascular events observed in chronic users [3, 4]. The non-linear dose-response relationship, with weekly users exhibiting the most pronounced effects, is a particularly intriguing finding. This pattern may suggest a complex interplay of induction and exhaustion of coagulation factors, or a threshold effect where intermittent, high-dose exposure is more disruptive than chronic, daily use.

Furthermore, it is plausible that weekly users engage in longer chewing sessions per occasion compared to daily users, leading to higher peak plasma concentrations of cathinone that acutely disrupt hemostatic balance,

whereas daily users may develop pharmacological tolerance.

An alternative explanation could be the development of pharmacological tolerance in daily users, where the hemostatic system adapts to chronic khat exposure, thereby attenuating the coagulopathic effects seen in the weekly user group. This non-linear pattern is a novel finding that warrants confirmation in future longitudinal studies.

The precise mechanisms remain to be elucidated but could involve direct effects of cathinone or other alkaloids on the synthesis of clotting factors in the liver, or indirect effects mediated by the systemic inflammatory response to khat consumption [9].

Our second major finding, the strong association between long sleep duration (8-11 hours) and abnormal platelet counts, introduces a new dimension to the understanding of sleep-related hematological changes. While previous studies have focused primarily on the pro-thrombotic effects of sleep deprivation, our results suggest that excessive sleep may also be a marker of dysregulated platelet homeostasis [7, 8]. The underlying biological mechanisms for this association are not immediately clear but could be multifactorial. It is possible that prolonged immobility during sleep contributes to altered platelet dynamics. Alternatively, long sleep duration may be a surrogate marker for underlying subclinical inflammatory conditions or metabolic disturbances, which in turn affect thrombopoiesis and platelet function [5, 6].

Conditions such as low-grade chronic inflammation or subtle hormonal imbalances could suppress platelet production in the bone marrow or increase peripheral consumption, manifesting as lower platelet counts.

This finding warrants further investigation to determine its clinical significance and to explore the potential causal pathways, including the role of inflammatory cytokines and hormonal regulators of platelet production.

This study has several strengths, including its multi-center design, relatively large sample size, and the use of standardized laboratory procedures. However, some limitations should be acknowledged. First, the cross-sectional design precludes the establishment of causality. Second, both khat use and sleep duration were self-reported, which may be subject to recall bias. Future longitudinal studies incorporating objective measures of both exposures (e.g., actigraphy for sleep, biomarkers for khat use) are needed to confirm our findings and to elucidate the temporal relationship between these behaviors and hematological changes. Additionally, while we adjusted for several potential confounders, residual confounding by unmeasured factors (e.g., diet, physical activity, underlying inflammatory status) cannot be entirely ruled out.

In conclusion, this study demonstrates that khat chewing is independently associated with significant coagulation abnormalities, while long sleep duration is a novel and strong predictor of platelet count disturbances in young Yemeni adults. These findings have important public health implications, highlighting the need for greater clinical awareness of the potential hematological risks associated with these prevalent lifestyle behaviors. Further research is warranted to elucidate the underlying mechanisms and to determine the long-term clinical consequences of these subclinical hematological alterations.

Limitations

While this study provides significant insights into the hematological effects of khat chewing and sleep duration, it is essential to acknowledge several limitations, primarily stemming from the study design and data collection methodology.

Firstly, the cross-sectional design of the study precludes the establishment of a causal relationship between the observed exposures (khat chewing and long sleep duration) and the outcomes (coagulation and platelet abnormalities). The associations identified are correlational, and it remains unclear whether the behavioral factors directly cause the hematological changes or if the changes are a consequence of an underlying, unmeasured factor that influences both the behavior and the hematological profile. Future longitudinal studies are necessary to determine the temporal sequence and infer causality.

Secondly, both the khat chewing habit and sleep duration were assessed via self-report using a standardized questionnaire. This methodology is inherently susceptible to recall bias and social desirability bias, particularly concerning a socially sensitive habit like khat chewing. Participants may have underreported the frequency or intensity of their khat use, or inaccurately estimated their average sleep duration, potentially leading to misclassification of the exposure groups. Incorporating objective measures, such as biochemical markers for khat alkaloids or actigraphy for sleep patterns, would enhance the validity of future research.

Thirdly, the study population was restricted to young university students (18-25 years) in Southern Yemen. While this homogeneity is beneficial for controlling age-related confounding, it significantly limits the generalizability of the findings to the broader Yemeni population, which includes older adults, non-students, and individuals from different geographical regions with potentially varying socioeconomic and health profiles.

Fourthly, despite adjusting for key confounders (age, gender, BMI, and university site), the possibility of residual confounding by unmeasured variables remains. Factors such as dietary habits, physical activity levels, chronic stress, and subclinical inflammatory conditions were not accounted for in the multivariate models, and these could potentially influence both the hemostatic system and the studied behavioral exposures.

Finally, the definition of "abnormal" hematological values was based on ICSH-standardized reference ranges. While appropriate, these ranges are often derived from general populations and may not perfectly reflect the physiological norms of the specific young Yemeni cohort, which could introduce a degree of misclassification in the outcome variable.

Conclusion

In conclusion, this multi-center cross-sectional study provides compelling evidence that common lifestyle factors in young Yemeni adults are independently associated with significant subclinical alterations in the hemostatic system. Weekly khat chewing is strongly and independently associated with abnormalities in the coagulation cascade, as evidenced by prolonged Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT). Furthermore, long sleep duration (8–11 hours) emerged as a novel and robust predictor of abnormal platelet counts, suggesting a previously unrecognized link between excessive sleep and platelet homeostasis in this cohort. These findings underscore the potential public health risk posed by these prevalent behaviors, highlighting the need for increased clinical vigilance and targeted interventions to mitigate the long-term cardiovascular and hematological sequelae in this vulnerable population.

It is important to note that these findings are derived from a specific cohort of young university students in Southern Yemen, and their generalizability to older adults or other populations requires further investigation.

Recommendations

Based on the findings and limitations of this study, the following recommendations are proposed for clinical practice, public health policy, and future research:

Clinical and Public Health Recommendations

Increased Clinical Awareness: Clinicians in regions with high khat prevalence should be aware of the independent association between weekly khat use and coagulation abnormalities. A detailed history of khat use should be routinely incorporated into the assessment of patients presenting with cardiovascular symptoms or those undergoing surgical procedures.

1. Targeted Screening: Given the strong association, individuals who are weekly khat chewers should be considered for routine screening of coagulation parameters (PT and APTT) to identify subclinical risk factors for thrombotic events.
2. Health Education Campaigns: Public health initiatives should be developed to educate young adults on the specific, non-psychoactive health risks associated with khat chewing, particularly the potential for hematological and cardiovascular complications.
3. Sleep Hygiene Promotion: The novel association between long sleep duration and platelet abnormalities warrants the inclusion of sleep hygiene education in public health messaging, emphasizing the importance of optimal, rather than excessive, sleep duration.

Future Research Recommendations

1. Longitudinal Studies: Future research must employ a longitudinal design to establish the temporal relationship and infer causality between khat use, long sleep duration, and the observed hematological changes.
2. Mechanistic Investigations: Studies are needed to elucidate the precise biological mechanisms underlying the observed associations. This should include investigating the direct effects of cathinone and its metabolites on clotting factor synthesis and activity, as well as exploring the role of inflammatory markers and hormonal regulators in mediating the link between long sleep duration and platelet homeostasis.
3. Objective Measures: Future studies should incorporate objective measures for both exposures, such as actigraphy for sleep and biochemical analysis of cathinone/cathine in biological fluids, to minimize self-report bias.
4. Broader Population Studies: The study should be replicated in a more diverse population, including older adults and individuals with pre-existing cardiovascular conditions, to assess the generalizability of these findings and the potential for synergistic effects with other comorbidities.

Authors' Contributions:

R.S.A. conceived and designed the study, supervised the project, performed data collection and laboratory analysis, conducted the statistical analysis, and drafted the initial manuscript. N.T.A. contributed to the study design, assisted in participant recruitment and laboratory procedures, and critically revised the manuscript for important intellectual content. M.A.H.M. supported

statistical analysis and data interpretation, contributed to manuscript drafting, and participated in the critical revision of the final version. All authors read and approved the final manuscript.

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Conflict of Interest:

The authors declare no conflicts of interest.

Ethical Approval and Considerations

Ethical approval for this study was granted by the Research Ethics Committee of the Faculty of Medicine and Health Sciences, University of Science and Technology (Approval No. MEC/AD087). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Prior to participation, all subjects received comprehensive information about the study objectives and procedures. Written informed consent was obtained from each participant. Confidentiality and anonymity were strictly maintained throughout all stages of the research, including data collection, analysis, and publication.

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Author information

ORCID

Radfan Saleh Abdullah: 0009-0000-3341-7441

Naif Taleb Ali: 0000-0002-2266-1569

Mansour Abdelnabi H. Mehdi: 0000-0002-3596-9909

مقالة بحثية

مضغ القات ومدة النوم الطويلة يرتبطان بتغيرات في مؤشرات التخثر والصفائح الدموية لدى الشباب اليمني البالغين: دراسة مقطعية متعددة المراكز

ردفان صالح عبدالله[1،2،3]*، نايف طالب علي[1،2،3]، و منصور عبدالنبي هـ. مهدي[1]

[1] قسم علوم المختبرات، كلية ردفان الجامعية، جامعة لحج، الحوطة، اليمن
[2] قسم العلوم الصحية، كلية الطب والعلوم الصحية، جامعة العلوم والتكنولوجيا، عدن، اليمن
[3] قسم علوم المختبرات، جامعة خليج عدن الدولية، الضالع، اليمن

* الباحث الممثّل: ردفان صالح عبدالله؛ البريد الالكتروني: r.saleh@ust.edu

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المُلخّص

لا تزال الآثار الدموية لمضغ القات، وهي عادة شائعة الانتشار في شرق أفريقيا واليمن، غير موصوفة بدقة كافية، خاصة فيما يتعلق بعملية التخثر. وبالمثل، فإن الأدلة التي تربط مدة النوم بالمؤشرات الدموية في الفئات السكانية الشابة والصحية لا تزال محدودة. في دراسة مقطعية شملت 600 طالب جامعي يمني، قمنا بتقييم تكرار مضغ القات ومدة النوم. تم قياس زمن البروثرومبين (PT)، وزمن الثرومبوبلاستين الجزئي المنشط (APTT)، وعدّ الدم الكامل. واستخدمت نماذج الانحدار اللوجستي متعدد المتغيرات مع تعديل العمر والجنس ومؤشر كتلة الجسم. أظهر مضغو القات أسبوعياً احتمالية أعلى بشكل ملحوظ للإصابة بقيم غير طبيعية لزمن البروثرومبين (aOR = 2.31، فاصل الثقة 95%: 1.05–5.08، p=0.037) وقيم غير طبيعية لزمن الثرومبوبلاستين الجزئي المنشط (aOR = 3.78، فاصل الثقة 95%: 1.55–9.22، p=0.003) مقارنة بغير المستخدمين على الإطلاق. كما لوحظ وجود استجابة جرعة غير خطية، حيث أظهر المستخدمون الأسبوعيون أكثر التشوهات في عوامل التخثر وضوحاً. أما المشاركون الذين أبلغوا عن مدة نوم طويلة (أكثر من 8 ساعات) فقد كانت احتمالية إصابتهم بعدّ غير طبيعي للصفيحات الدموية أكثر بأربعة أضعاف (aOR = 4.12، فاصل الثقة 95%: 1.62–10.49، p=0.003) مقارنة بمجموعة المرجع (7-8 ساعات). يرتبط مضغ القات بشكل مستقل بخلل كبير في عوامل التخثر، مما يشير إلى تدخل محتمل في المسيرتين الداخلية والخارجية للتخثر. علاوة على ذلك، تُعد مدة النوم الطويلة مؤشراً جديداً على اضطرابات عدد الصفيحات الدموية في هذه الفئة العمرية الشابة. تُسلط هذه النتائج الضوء على مخاطر صحية عامة محتملة، مما يستدعي وعياً إكلينيكياً أكبر بالتبعات الدموية لاستخدام القات وأنماط النوم غير المثلى في هذه الفئة السكانية.

الكلمات المفتاحية: القات؛ كاثا إيدوليس؛ التخثر؛ زمن البروثرومبين؛ زمن الثرومبوبلاستين الجزئي المُفَعَّل؛ النوم؛ الصفائح الدموية؛ أمراض الدم؛ اليمن.

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