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ORIGINAL PAPER

Khat chewing, poly-substance use, and lower urinary tract symptoms: A cross-sectional analysis among Yemeni Medical University students

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Summary

***Background:** Khat (Catha edulis) chewing is highly prevalent in Yemen, but its potential urological effects are poorly characterized. The pharmacological action of its alkaloids on alpha-adrenergic receptors suggests a plausible link to voiding dysfunction. This study explored the association between khat chewing patterns, concurrent stimulant use, and lower urinary tract symptom (LUTS) severity.*
***Methods:** In this cross-sectional study, 112 medical and paramedical university students from seven Yemeni governorates completed a structured digital questionnaire being recruited via convenience sampling. LUTS severity was assessed using the International Prostate Symptom Score (IPSS). Exposure variables included khat chewing (status, duration, daily hours), coffee, soda, and tobacco use. Participants were categorized into poly-substance use clusters. Multivariable linear and logistic regression models identified predictors of LUTS, adjusting for confounders including age and sex.*
***Results:** Among participants (mean age 24.3 ± 5.7 years), 86 (76.8%) were current khat chewers. A significant dose-response relationship was observed. Each additional hour of daily chewing was associated with a 1.85-point increase in IPSS score (95% CI: 1.32-2.38; $p < 0.001$). The concurrent use of khat, coffee, and soda was associated with the highest mean symptom score (21.4) and a significantly elevated adjusted odds ratio for severe LUTS (IPSS ≥ 20) of 17.15 (95% CI: 6.28-47.10; $p < 0.001$) compared to non-users. Daily coffee consumption and tobacco smoking were also independent predictors of higher IPSS scores.*
***Conclusion:** Among this sample of Yemeni university students, khat chewing demonstrated a strong, dose-dependent association with more severe LUTS. This association was markedly amplified by the co-use of caffeine-containing beverages. While the cross-sectional design precludes causal inference, these findings highlight a potential public health concern and underscore the need for longitudinal studies and clinical awareness of urological symptoms in khat-chewing populations.*

KEY WORDS: *Catha edulis; Khat; Lower urinary tract symptoms; LUTS; Poly-substance use; Stimulants; Yemen.*

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INTRODUCTION

Catha edulis (Khat) chewing is a deeply rooted cultural practice in regions of East Africa and the Arabian Peninsula, with lifetime prevalence rates exceeding 80% in endemic countries like Yemen (1, 2). While its psychostimulant effects are well characterized, comprehensive research into its systemic health consequences remains an evolving field. The cardiovascular and neuropsychiatric effects of khat have been documented, but its potential impact on urological health, particularly concerning *lower urinary tract symptoms* (LUTS), constitutes a significant and under-investigated area of clinical concern (3-5).
The pharmacological basis for a urological effect is plausible. The primary psychoactive alkaloids, cathinone and cathine, are potent sympathomimetic agents (6). Their activity on α1-adrenergic receptors is of particular urological relevance, as such stimulation can increase smooth muscle tone at the bladder neck and prostate, potentially leading to voiding dysfunction – a mechanism implicated in conditions like benign prostatic hyperplasia (7, 8). Preliminary clinical evidence supports this; a randomized trial demonstrated that acute khat chewing reduces urinary flow rate, an effect reversible by α1-adrenergic blockade (9). Epidemiological surveys further indicate that habitual khat users report higher rates of LUTS (10). However, robust evidence characterizing the dose-response relationship and the long-term urological sequelae of chronic use is notably scarce.
The public health context in Yemen amplifies the urgency of this research. Khat consumption is ubiquitous, often beginning in adolescence and involving prolonged daily sessions (2, 11). Concurrently, LUTS represent a common and burdensome condition, even among younger men, significantly impairing quality of life and productivity (10). This confluence of high exposure and significant unmet urological need highlights a critical gap in patient care and health literacy.
Several key questions persist. First, the relationship

between chewing intensity – such as session duration and cumulative years of use – and LUTS severity requires precise quantification. Second, the real-world context of khat use is rarely isolated; it is frequently accompanied by the consumption of caffeinated beverages like coffee and soda. The potential additive or synergistic effects of this common poly-substance use on the lower urinary tract have not been systematically examined (12, 13). Third, understanding the socio-cultural drivers that perpetuate use despite potential health risks is essential for designing effective interventions.

This study therefore aimed to investigate the associations between khat chewing behaviors, poly-substance use, and LUTS severity among a cohort of Yemeni university students. We employed a cross-sectional design to quantify dose-dependent relationships and explore the role of common stimulant combinations. While acknowledging the inherent limitations of this design for causal inference, this research seeks to provide foundational epidemiological data to inform clinical suspicion, patient counseling, and the direction of future longitudinal and mechanistic studies in khat-endemic populations.

MATERIALS AND METHODS

Study design and ethical considerations

A cross-sectional study was conducted between June 2023 and January 2024. The study protocol was reviewed and approved by the *Institutional Review Board of Ibb University, Ibb, Yemen* (Protocol No: IBBUNI.AC.YEM.2025.23).

All participants provided informed digital consent prior to enrollment.

Study setting and participant selection

The study was conducted across seven governorates in Yemen (including *Ibb, Taiz, Sana'a, Al Dhalea, Al Hudaydah, Aden,* and *Al Mahwit*) to capture geographic and socio-cultural diversity. Participants were recruited from medical and paramedical university faculties using a convenience sampling method. Eligible individuals were students aged 18 years or older. To minimize confounding from known urological pathologies, exclusion criteria comprised a self-reported history of: neurological disorders affecting bladder function (e.g., spinal cord injury, multiple sclerosis), prior prostate or bladder surgery, or active urological conditions such as benign prostatic hyperplasia, urinary tract infection, or bladder cancer. The final analytical sample included 112 participants. We explicitly acknowledge that the non-random sampling method and modest sample size limit the statistical power for subgroup analyses and the generalizability of findings.

Data collection instrument and procedures

Data were collected via a structured, self-administered electronic questionnaire hosted on a secure, anonymous Google Sheets platform (*Google LLC, Mountain View, CA, USA*). The instrument was developed in Arabic and comprised the following domains:

1. *Sociodemographic Characteristics*: Age, sex, marital status, geographic region of residence, and self-reported socioeconomic status (categorized as low, medium, or high based on a composite of reported household income, assets, and educational level).
2. *Substance Use Profile*: Detailed questions on khat chewing (current status, total duration in years, average hours chewed per session, and frequency). Additional items assessed habitual consumption of coffee, carbonated soda, and tobacco, including frequency and typical quantities.
3. *LUTS*: Assessed using the validated Arabic version of the *International Prostate Symptom Score* (IPSS). This 7-item tool evaluates voiding and storage symptoms over the preceding month, with total scores categorized as mild (0-7), moderate (8-19), or severe (20-35).

The questionnaire was pilot-tested with 15 students from the target population to ensure clarity, cultural appropriateness, and face validity. Digital safeguards prevented duplicate submissions.

Variable definitions and operationalization

- *Primary Outcome*: LUTS severity, analyzed as a continuous variable (total IPSS score) and an ordinal categorical variable (IPSS severity category).
- *Primary Exposures*: Khat chewing behaviors: status (current vs. never/former), cumulative duration (years), and intensity (average daily chewing hours).
- *Covariates*: Included frequency of coffee, soda, and tobacco use; age; sex; socioeconomic status; marital status; and self-reported physical activity level.
- *Poly-Substance Use Clusters*: For exploratory analysis, participants were categorized post-hoc into five mutually exclusive groups based on their reported habitual use: (1) Non-users of khat, coffee, and soda; (2) Khat-only users; (3) Khat + coffee users; (4) Khat + soda users; (5) Users of khat, coffee, and soda. This clustering is based on the presence of habitual use and serves as a simplified model of real-world co-consumption patterns.

Statistical analysis

Data were analyzed using Python, version 3.11, with the Statsmodels library (v. 0.14.4). Descriptive statistics are presented as mean (± standard deviation), median (interquartile range), or frequency (percentage).

Normality of continuous variables was assessed using the Shapiro-Wilk test.

Bivariate analyses employed Pearson's correlation (continuous-continuous), Chi-square or Fisher's exact tests (categorical-categorical), and the Cochran-Armitage test for trends across ordinal categories.

The primary inferential analysis used multivariable linear regression to identify independent predictors of the total IPSS score. All primary exposures and pre-specified covariates were entered into a single model. Model assumptions (linearity, homoscedasticity, normality of residuals) were checked graphically. Multicollinearity was assessed using variance inflation factors (VIF < 5 considered acceptable).

A secondary multivariable logistic regression model was used to calculate *adjusted odds ratios* (aORs) for the odds of experiencing severe LUTS (IPSS ≥ 20) across the poly-substance use clusters, adjusting for age and sex. The small cell sizes within some clusters necessitate caution in interpreting these estimates.

All tests were two-sided, with a p-value < 0.05 considered statistically significant. Missing data were minimal (< 2% for any variable) and handled by listwise deletion in the regression models.

RESULTS

Participant characteristics

The final analytical sample comprised 112 university students. Baseline characteristics, stratified by khat chewing status, are presented in Table 1.

The majority of participants (76.8%, n = 86) were current khat chewers. The overall mean age was 24.3 (+-5.7) years. Compared to non-chewers, khat chewers were significantly older (25.1 +- 5.2 *vs.* 22.4 +- 4.9 years; p = 0.021) and more likely to be male (77.9% *vs.* 46.2%; p < 0.001). The cohorts did not differ significantly in geographic distribution, socioeconomic status, or marital status (all p > 0.05). Substance use profiles differed markedly: daily coffee consumption was far more prevalent among chewers (86.0% *vs.* 38.5%; p < 0.001), and current tobacco smoking was reported exclusively within the khat-chewing group (9.3%).

Among chewers, the median duration of use was 6.0 years (IQR: 3.0-12.0), with 44.2% reporting daily chewing sessions exceeding six hours.

Primary associations: Khat chewing and LUTS severity

While the binary comparison of chewers vs. non-chewers showed no significant difference in IPSS severity categories (p = 0.855), analyses of chewing intensity revealed clear gradients. A significant positive trend was observed between increasing daily chewing duration and LUTS severity (Cochran-Armitage test for trend, p < 0.001). For instance, the prevalence of severe LUTS (IPSS ≥ 20) was 21.1% among those chewing > 6 hours/day, compared to 3.8% in those chewing ≤ 2 hours/day. Similarly, longer cumulative duration of use (years) was associated with higher symptom burden (p < 0.001).

Poly-substance use clusters and LUTS

The habitual co-use of khat with caffeine-containing beverages was associated with incrementally higher urinary symptom scores.

As illustrated in Figure 1A, mean IPSS scores demonstrated a graded increase across substance-use clusters: non-users (9.8, 95% CI 7.2-12.4), khat-only users (14.2), khat+coffee users (16.8), khat+soda users (18.1), and users of all three substances (khat+coffee+soda: 21.4). A one-way ANOVA confirmed significant differences between these groups [$F(4, 107) = 15.2$, $p < 0.001$]. Post-hoc Tukey tests indicated that the khat+coffee+soda group had significantly higher scores than all other clusters (p < 0.001 for each comparison). Correspondingly, the proportion of participants with severe LUTS rose with each additional substance (Table 2).

Multivariable analysis of predictors

In a multivariable linear regression model adjusted for demographic and lifestyle factors, both measures of khat exposure remained independently associated with higher

Table 1.
Baseline Characteristics of Study Participants, Stratified by Khat Chewing Status (n = 112).

Characteristic	Total Sample (n = 112)	Khat Chewers (n = 86)	Non-Chewers (n = 26)	p-value
Age (years), Mean ± SD	24.3 ± 5.7	25.1 ± 5.2	22.4 ± 4.9	**0.021**
Sex, n (%)				**< 0.001**
Male	75 (67.0)	67 (77.9)	12 (46.2)	
Female	37 (33.0)	19 (22.1)	14 (53.8)	
Marital Status, n (%)				0.452
Single	89 (79.5)	67 (77.9)	22 (84.6)	
Married	23 (20.5)	19 (22.1)	4 (15.4)	
Socioeconomic Status, n (%)				0.689
Low	31 (27.7)	25 (29.1)	6 (23.1)	
Medium	62 (55.4)	47 (54.6)	15 (57.7)	
High	19 (17.0)	14 (16.3)	5 (19.2)	
Primary Governorate, n (%)				0.155
Ibb	86 (76.8)	69 (80.2)	17 (65.4)	
Taiz	15 (13.4)	9 (10.5)	6 (23.1)	
Sana'a	11 (9.8)	8 (9.3)	3 (11.5)	
Substance Use, n (%)				
Daily Coffee Consumption	84 (75.0)	74 (86.0)	10 (38.5)	**< 0.001**
Daily Soda Consumption	106 (94.6)	82 (95.3)	24 (92.3)	0.623
Current Tobacco Smoking	8 (7.1)	8 (9.3)	0 (0.0)	0.195
Khat Use Profile				
Duration, years, Median (IQR)	-	6.0 (3.0 - 12.0)	-	-
Daily Hours, Median (IQR)	-	4.0 (2.0 - 6.0)	-	-
Family History of Use, n (%)	-	70 (81.4)	-	-

SD: Standard Deviation; IQR: Interquartile Range.
p-values derived from independent t-test (Age), Chi-square test (categorical variables), or Fisher's exact test as appropriate.

Table 2.
Prevalence of Lower Urinary Tract Symptoms (LUTS) by Khat Chewing Patterns and Poly-Substance Use Clusters.

Exposure Category	N	Mild LUTS (IPSS 0-7) n (%)	Moderate LUTS (IPSS 8-19) n (%)	Severe LUTS (IPSS ≥ 20) n (%)	p for trend *
Age (years), Mean ± SD	24.3 ± 5.7	25.1 ± 5.2	22.4 ± 4.9	0.021	
Daily Chewing Duration					**< 0.001**
Non-Chewer	26	8 (30.8)	14 (53.8)	4 (15.4)	
≤ 2 hours	18	6 (33.3)	12 (66.7)	0 (0.0)	
3 - 6 hours	30	7 (23.3)	19 (63.3)	4 (13.3)	
> 6 hours	38	4 (10.5)	26 (68.4)	8 (21.1)	
Cumulative Chewing Duration					**< 0.001**
Non-Chewer	26	8 (30.8)	14 (53.8)	4 (15.4)	
1 - 5 years	30	9 (30.0)	17 (56.7)	4 (13.3)	
6 - 10 years	28	5 (17.9)	18 (64.3)	5 (17.9)	
> 10 years	28	3 (10.7)	15 (53.6)	10 (35.7)	
Poly-Substance Use Cluster					**< 0.001**
Non-User	23	10 (43.5)	11 (47.8)	2 (8.7)	
Khat Only	31	9 (29.0)	18 (58.1)	4 (12.9)	
Khat + Coffee	36	6 (16.7)	23 (63.9)	7 (19.4)	
Khat + Soda	33	5 (15.2)	21 (63.6)	7 (21.2)	
Khat + Coffee + Soda	35	2 (5.7)	21 (60.0)	12 (34.3)	

Cochran-Armitage test for trend.

Table 3.
Multivariable Linear Regression Analysis of Predictors for Total IPSS Score (Continuous Outcome).

Predictor	Unstandardized Beta Coefficient (β)	95% Confidence Interval	Standard Error	p-value
Khat Use Intensity				
Daily Chewing Hours (per hour)	1.85	1.32 to 2.38	0.27	**< 0.001**
Chewing Duration (per year)	0.62	0.21 to 1.03	0.21	**0.003**
Other Substance Use				
Daily Coffee Consumption (Yes *vs.* No)	1.32	0.29 to 2.35	0.52	**0.012**
Daily Soda Consumption (Yes *vs.* No)	1.07	0.06 to 2.08	0.51	**0.038**
Current Tobacco Smoking (Yes *vs.* No)	2.41	1.01 to 3.81	0.71	**0.001**
Demographic & Socio-Cultural Factors				
Age (per year)	0.15	0.01 to 0.29	0.07	**0.042**
Sex (Male vs. Female)	0.87	-0.24 to 1.98	0.56	0.122
Traditional Justification for Use (Yes *vs.* No)	1.26	0.18 to 2.34	0.55	**0.022**
Number of Chewing Family Members (per member)	0.38	0.05 to 0.71	0.17	**0.025**
(Constant)	5.12	2.01 to 8.23	1.57	**0.001**

** Model Adjusted R^2 = 0.59. All variance inflation factors (VIF) < 3.0.**

IPSS scores (Table 3). Each additional hour of daily chewing was associated with a 1.85-point increase in IPSS (95% CI 1.32-2.38; p < 0.001), and each additional year of chewing history was associated with a 0.62-point increase (95% CI 0.21-1.03; p = 0.003).

Daily coffee consumption (b = 1.32; 95% CI 0.29-2.35; p = 0.012) and current tobacco smoking (b = 2.41; 95% CI 1.01-3.81; p = 0.001) also emerged as significant independent predictors. Notably, daily soda intake showed a positive association (b = 1.07; p = 0.038), but this result should be interpreted with caution given the very high baseline prevalence (94.6%) limiting variability. Several socio-cultural factors, including citing tradition as a justification for khat use and the number of chewing family members, were also associated with higher symptom scores.

Logistic regression, adjusting for age and sex, indicated that the odds of severe LUTS were markedly elevated in the poly-substance use clusters (Table 4). Compared to non-users, the aOR for severe LUTS was 17.15 (95% CI 6.28-47.10; p < 0.001) for the khat+coffee+soda cluster. Given the modest overall sample size and the subsequent small cell sizes within clusters, this point estimate, while statistically significant, should be considered preliminary (Figure 1B).

Dose-response and exploratory geospatial analyses

A simple linear regression confirmed a significant dose-response relationship between daily chewing hours and IPSS score (IPSS = 8.3 + 1.85 x hours; R^2 = 0.41; p < 0.001) (Figure 1C). Exploratory analysis of symptom burden by governorate showed variation in mean IPSS scores [one-way ANOVA, F(3, 108) = 3.8; p = 0.012], with the highest scores observed in *Ibb* (18.5) and *Dhale* (17.8) (Figure 1D).

Poly-Substance Use Cluster	N	Cases of Severe LUTS (n)	Adjusted Odds Ratio Ratio (aOR)*	95% Confidence Interval	p-value
ANon-User	23	2	1.00	(Reference)	-
Khat Only	31	4	1.85	0.41 to 8.35	0.424
Khat + Coffee	36	7	3.22	0.78 to 13.31	0.107
Khat + Soda	33	7	3.95	0.94 to 16.55	0.061
Khat + Coffee + Soda	35	12	**17.15**	**6.28 to 47.10**	**< 0.001**

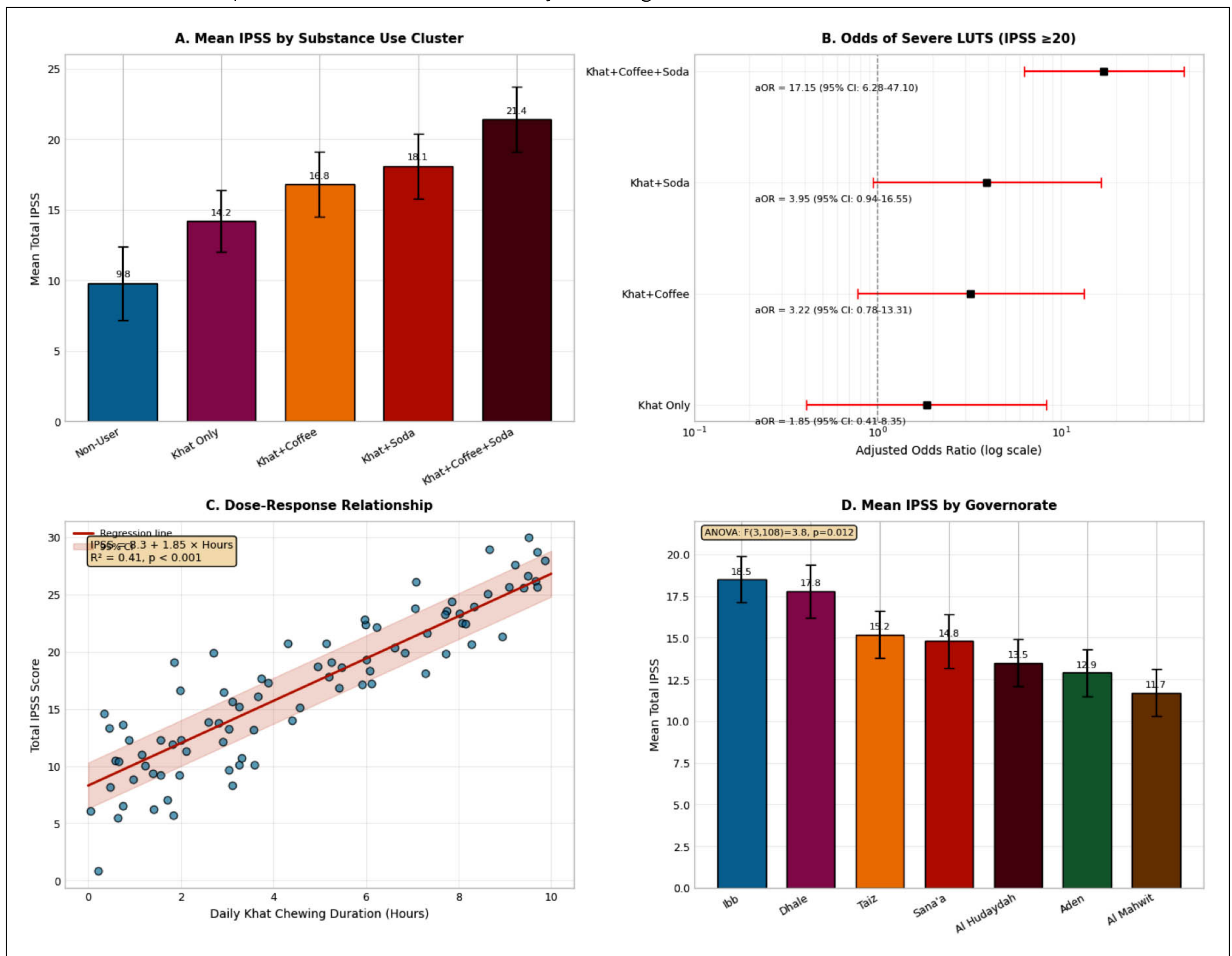
Adjusted for age and sex in a multivariable logistic regression model.

Table 4.
Adjusted Odds Ratios for Severe LUTS (IPSS ≥ 20) by Poly-Substance Use Cluster.

Figure 1.
Association between khat use patterns, poly-substance use, and lower urinary tract symptom severity among Yemeni university students.

***(A)** Mean IPSS by substance use cluster. Bar heights represent mean total IPSS, with error bars indicating 95% confidence intervals. Substance use clusters are defined based on habitual use of khat, coffee, and/or soda.*

***(B)** Forest plot of adjusted odds ratios for severe LUTS (IPSS ≥ 20). The plot shows adjusted aORs with 95% confidence intervals for different substance use clusters compared to non-users. The model was adjusted for age and sex. The dotted reference line indicates an odds ratio of 1.0.*



***(C)** Dose-response relationship between daily khat chewing duration and total IPSS score. Scatter plot shows individual data points for khat chewers (n = 86). The solid regression line (IPSS = 8.3 + 1.85 × Hours; $R^2 = 0.41$, $p < 0.001$) illustrates the linear association, with the shaded band representing the 95% confidence interval.*

***(D)** Mean IPSS by governorate. Bar plot shows geographical variation in symptom burden across seven Yemeni governorates. Error bars represent 95% confidence intervals. One-way ANOVA indicated significant differences between regions [$F(3,108) = 3.8$, $p = 0.012$].*

Given the small sample size distributed across multiple regions, this geospatial analysis is considered hypothesis-generating rather than definitive.

Discussion

In this cross-sectional study of Yemeni medical and paramedical students, more intensive and prolonged khat chewing was associated with higher LUTS burden as measured by the IPSS. When khat use was treated simply as a binary exposure, IPSS severity categories did not differ significantly between chewers and non-chewers. However, quantitative measures of exposure – particularly daily chewing hours and cumulative years of use – showed graded, positive associations with symptom severity in multivariable models. Concurrent use of other stimulants, including coffee, carbonated soft drinks, and tobacco, was also associated with higher IPSS scores and a greater prevalence of severe LUTS. In exploratory analyses, students from governorates with more intensive khat cultivation tended to report higher mean IPSS, although these comparisons were based on small and uneven group sizes and should be interpreted cautiously.

The observed dose-response pattern between khat chewing intensity and LUTS is broadly consistent with previous epidemiological and experimental findings. In our adjusted linear models, each additional hour of daily chewing was associated with an approximately 1.85-point increase in IPSS, and each additional year of use with a smaller but statistically significant increment. These associations remained after adjustment for age, sex, socioeconomic indicators, marital status, and physical activity. Likewise, *Babakri et al.* reported higher mean IPSS scores among khat chewers compared with non-chewers in a young male population (10), and experimental work by *Nasher et al.* demonstrated that acute khat chewing can reduce urinary flow rates, an effect reversed by α1-adrenoceptor blockade (9). Taken together, these data support the hypothesis that both the intensity and chronicity of khat exposure may be relevant to LUTS, although our cross-sectional design does not allow inference about temporal direction or causality.

Pharmacological studies provide a plausible mechanistic framework for these associations. Cathinone and related khat alkaloids have sympathomimetic properties and can stimulate α-adrenergic receptors (6, 14). Increased α1-adrenergic tone at the bladder neck and proximal urethra is thought to contribute to voiding dysfunction in other conditions, including benign prostatic hyperplasia (15-17). It is therefore biologically credible that chronic or intensive exposure to khat could promote or exacerbate obstructive and irritative urinary symptoms. However, the present study relied on symptom-based self-report (IPSS) without urodynamic measurements, and we did not directly assess outlet resistance or bladder contractility. As such, our findings should be viewed as consistent with, but not definitive for, an α-adrenergic-mediated pathway.

Poly-substance use emerged as another important correlate of LUTS in this student population. Participants who reported consuming khat in combination with both coffee and soda had higher mean IPSS scores and greater odds of severe LUTS compared with non-users, and there was a graded increase in symptom burden across substance use clusters. These patterns suggest that co-use of stimulants may contribute additively or even synergistically to LUTS. This interpretation aligns with pharmacological and ethnopharmacological literature indicating that methylxanthines in coffee and cola can potentiate central and peripheral sympathetic effects and may prolong the physiological impact of cathinone (9, 18-20). Caffeine is also known to increase urinary frequency and urgency in some individuals through direct effects on the bladder (21). Nonetheless, the very large adjusted odds ratio observed for the khat-coffee-soda group was estimated from a modest sample with limited numbers of severe cases, and the wide confidence intervals indicate substantial statistical uncertainty. These logistic regression findings should therefore be considered exploratory and hypothesis-generating rather than definitive.

Beyond pharmacology, our results are compatible with a role for socio-cultural and familial influences in shaping khat use patterns and, indirectly, LUTS risk. In multivariable models, traditional justifications for khat chewing and the number of family members who chew were associated with higher IPSS scores, alongside measures of khat exposure. This is consistent with prior work emphasizing the importance of social norms, family practices, and regional culture in sustaining khat use (22-25). However, our assessment of these constructs was limited to a small number of questionnaire items, and we did not undertake in-depth qualitative or ethnographic data collection. As such, the socio-cultural interpretations presented here should be regarded as tentative and in need of confirmation through dedicated mixed-methods research.

The exploratory geospatial analysis suggested that governorates with intensive khat cultivation, such as Ibb and Al Dhalea, may have higher average IPSS scores compared with regions where khat cultivation and use are perceived to be less intensive. While this pattern conceptually aligns with ecological models in which environmental availability and community norms reinforce individual behavior (26, 27), our data are not sufficient to support strong conclusions at the community level. Most participants were from a single governorate, and cell sizes for some regions were small. The geospatial findings should therefore be interpreted with caution and primarily as a prompt for more rigorous, population-based studies with adequate geographic representation.

Clinical and public health implications

Several clinical and public health implications can be cautiously inferred. First, our findings suggest that simple binary categorization of khat use may obscure important risk gradients; clinicians and researchers in khat-endemic settings may benefit from routinely assessing intensity and chronicity of use when evaluating LUTS. Second, the associations observed with poly-substance use highlight the potential value of addressing broader stimulant co-use, particularly combinations of khat with caffeine-containing beverages and tobacco, in any counseling or harm-reduction strategies. Third, given that our sample consisted of young adults, these data raise the possibility

that LUTS associated with stimulant use may emerge earlier in life than is often assumed. However, because of the cross-sectional design, convenience sampling, and reliance on self-report, these implications should be considered preliminary.

Study limitations

This study has several limitations that influence interpretation. The cross-sectional nature of the data precludes determination of temporal or causal relationships between khat exposure, poly-substance use, and LUTS. Reverse causation and unmeasured confounding cannot be excluded. The use of a convenience sample of medical and paramedical students limits generalizability, particularly to older adults, women, non-students, and residents of underrepresented regions. Substance use and LUTS were self-reported, which may introduce recall and social desirability bias, despite the use of a validated Arabic IPSS. Although we adjusted for several potential confounders, residual confounding by factors such as dietary habits, fluid intake, psychological stress, or subclinical urological conditions remains possible. Sample size, especially for some substance use clusters and governorates, constrained statistical power and may have contributed to imprecise effect estimates and potential overestimation of odds ratios in logistic models. Finally, while IPSS is widely used to capture LUTS, it was originally developed in the context of benign prostatic hyperplasia, and its application in younger, largely non-BPH populations warrants careful interpretation.

Despite these limitations, the internal consistency of the dose–response findings, their agreement with prior experimental and epidemiological data, and the biological plausibility of the proposed mechanisms provide supportive, though not conclusive, evidence that intensive khat use and concomitant stimulant consumption may be relevant contributors to LUTS in young adults in khat-endemic settings. Future research should build on these observations using longitudinal designs, larger and more representative samples, and objective measures of both exposure and urinary tract function, including urodynamics. Such studies would help clarify temporal relationships, quantify absolute and relative risks, and evaluate potential preventive and therapeutic interventions, including behavioral modifications and, where appropriate, pharmacological approaches such as α1-adrenergic blockade.

Conclusions

Although limited, this study offers solid initial findings of a positive, dose related relationship between khat chewing and LUTS severity in a young, educated Yemeni cohort, and the effects are increased by the co-use of caffeine. Clinically, these results indicate that the investigation into the use of khat and stimulants need to be considered as a part of the evaluation of young patients with the unexplained voiding symptoms in the endemic areas. The data support harm-reduction measures to deal with common poly-substance use patterns, but not khat itself, to the benefit of the public health.

The causal question needs to be filled in future research by longitudinal cohort studies. Investigators are advised to focus on the use of more diverse and representative samples, use objective measures of exposure (e.g., levels of cathinone in the urine), and use urodynamic studies to identify the exact pathophysiological processes. Moreover, the qualitative study is necessary to comprehend the socio-cultural forces of the continued use despite possible health outcomes. Finally, the combined, culturally competent approach to clinical education, community mobilization and future-oriented policy will be necessary to reduce the possible burden of khat-related LUTS.

Declarations

Ethical approval and consent for participate: *This cross-sectional study was conducted in accordance with the ethical principles of the Declaration of Helsinki. The study protocol was reviewed and approved by the Institutional Review Board of Ibb University, Yemen (Approval Code: IBBUNI.AC.YEM.2025.23; Date: February 2, 2025). The IRB granted a waiver of written informed consent as the research presented no more than minimal risk to participants, and the anonymous nature of the survey made obtaining written consent impractical without compromising data integrity. Informed consent was implied upon voluntary completion and submission of the online questionnaire.*

Consent for publication: *Not applicable. This study does not contain any individual person's data in any form.*

Availability of data and material: *The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.*

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