

Habitual *Khat* Chewing is linked with Neurotic Depression and Anxiety among Medical Students in Hodeida University, Yemen (during December 2023 - June 2024)

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ABSTRACT

Background: *Khat* is a flowering plant of *Catha edulis* which belongs to Celastraceae family having pharmacological amphetamine-like effects; it is widely consumed in some parts of Africa as well as Yemen, as *khat* fresh leaves chewing. Prevalence of *khat* ever chewing in Yemen reaches around 68% and of daily chewing reaches 24%. Habitual *khat* chewing has been reported to have adverse health effects including mental health disorders, elevated blood pressure, increased incidence of acute myocardial infarction, GIT problems. In addition, *khat* has socio-economic deteriorating effect. The study aimed to explore risk relation between habitual *khat* chewing and neurotic depression and anxiety.

Methods: Analytical retrospective cohort study has been conducted during December 2023 - June 2024, on two identified cohorts of medical students at Hodeida University, Yemen. The first cohort have composed of 68 known habitual *khat* chewing medical student and the second have composed of 68 non-*khat* chewing medical students. Exposure variable (*Khat* chewing) and some related factors (*khat* chewing duration, daily chewing hours, concomitant tea or coffee drinking and type of *khat* chewing sitting, shared or individual) all have followed retrospectively through structured, pre tested, validated questionnaire, while the outcome variables (anxiety and depression) have assessed using structured, pre tested, validated, previous mental health studies used, self-reported questionnaires including Patient health-9 scaled questionnaire (PHQ-9) for assessment of depression and Generalized anxiety disorders 7 scaled questionnaire (GAD-7) for assessment of anxiety.

Data analysis: Data have statistically analyzed using SPSS program, version 27 including descriptive statistics, the χ^2 test or Fisher's exact test was used to test for comparison between categorical variables, mean, standard deviation an independent t test used for comparison between two groups of normally distributed data and Mann-Whitney U test for two groups of not normally distributed data. A two-tailed p-value less than or equal to 0.05 was considered statistically significant.

Results: Proportions of study members having depression and anxiety were found as higher in *khat* chewing cohort members compared to non-*khat* chewing cohort members, both have been found at statistically significant differences ($X^2=13.425$, $P<0.009$ for depression and $X^2=11.181$, $P<0.011$ for anxiety)

Conclusion: Habitual khat chewing is a risk factor for neurotic depression and anxiety and chewing khat in individual sitting has been found to be a further risk; for anxiety among khat chewing medical students of medical college at Hodeidah University in Hodeidah city, Yemen.

INTRODUCTION

Khat is a flowering plant of *Catha edulis* which belongs to Celastraceae family having pharmacological amphetamine-like effects; it is widely consumed as khat fresh leaves chewing in some parts of Africa as well as Yemen⁽¹⁾. Approximately 20 million people worldwide are putting their health at considerable health risk through daily khat-chewing habit⁽²⁾.

In last decade, the traditional habit of khat leaves chewing has undergone profound changes in Africa and Yemen, from a socially regulated use pattern to uncontrolled consumption⁽¹⁾. In Yemen, khat chewing is a deep-rooted sociocultural habit; one of every 4 peoples is daily khat chewer, while khat leaves ever chewing prevalence reaches 68%⁽³⁻⁴⁾.

In Yemen as other countries having khat consuming peoples, the trend of khat chewing among higher educational institutions students have been increased during last decade. Although khat chewing is believed to play a role in making students alerted and focused during long study hours, many studies have reported negative impact of khat use on student's health, socio economic, and psychological aspects, in addition to an overall negative impact on students' educational performance⁽⁵⁾.

Khat leaves contain multiple chemical components which interfere with almost all human body organs functions. The essential active ingredients of khat leaves are cathinone (nor pseudo ephedrine) and cathines, in addition to phenyl alkyl amines and other alkaloids. Most effects of chewing khat are thought to be coming from cathinone and cathines. Cathinone is the upper and the most active component; which it has estimated to be 7–10 folds more potent than cathines⁽⁶⁾. The chemical structure and biological activity of cathinone is similar to that of Amphetamine

and it accounts for both sympathomimetic and pharmacological amphetamine-like effects of khat matter⁽⁶⁻⁷⁾.

As physical health adverse effects of khat chewing, some published studies reported cardiac arrhythmias, hypertension, ischemic heart diseases, cardiomyopathy, periodontal disease, stomatitis, gingivitis, esophagitis, gastritis, constipation, prostatic congestion, dysuria and mild to moderate urine retention⁽⁷⁾.

The effects which are noticed on the khat chewing people, while chewing include euphoria, enhanced alertness and other cognitive functions, high sociability, followed (after khat discharging) by depressed mode, irritability and sleep disorders⁽⁸⁻⁹⁾.

Regarding mental side, there is evidence from published studies that, khat chewing; especially in high doses can induce manic illness, grandiose and persecutory delusions and schizophrenic psychosis. In majority of cases, the symptoms have relieved when khat had withdrawn and antipsychotic medications had used, but there was a predisposition for the recurrence of these mental disorders on khat chewing resumption⁽⁸⁻⁹⁾.

Socioeconomically, there is evidence that, habitual khat chewing leads to, decreased working hours, diminution of economic production and neglecting family needs⁽¹⁰⁾.

Due to khat chewing aspect is still neglected in Yemeni national health promotion programs, and in vision of fewer studies which have been conducted on investigation of khat chewing relation with depression and anxiety, and noticed high khat chewing among university students, this study had been decided to be conducted.

METHODS

Analytical retrospective cohort study has been conducted during December 2023 -

June 2024, on 2 cohorts, first cohort have composed of 68 known habitual khat chewing medical student and the second have composed of 68 non-khat chewing medical students in Hodeida university, at Hodeida city, Yemen

Sampling

Study sample size has been calculated using online research sample size calculator ⁽¹¹⁾, yielding 136 study members (68 as khat chewing student's cohort and 68 as Non khat chewing cohort). Parameters used for sample size estimation were P = 50%, 95% CI, and errors below 5%. The sampling frame has composed of official register lists of different medical college grades. Firstly, all registered medical students have been sorted to khat chewing and non-khat chewing lists through asking each student himself is he/she habitually chewing khat or not. Then systematic random sampling has done for selecting both cohorts' members, from sorted khat chewing and non-khat chewing student's lists

Data collection

Data have been collected using three types of structured, pre tested questionnaires including:

1. Study member data questionnaire which is a structured, pre tested, validated

questionnaire which has been dedicated to get study member identifying data (name, age, gender, residence (with or out family) and inquiries to investigate exposure variable (Khat chewing) and its related factors including; khat chewing duration, daily chewing hours as a clue for the dose of khat, associated tea or coffee drink and type of chewing sitting (shared or individual)

2. Patient health scale-9 (PHQ-9) questionnaire for assessment of depression which is a structured, pre tested validated, previous mental health studies used, self-reported questionnaire (which is allowed to be used by researchers without permission) for assessment of depressive disorders ⁽¹²⁾, it has been used for assessment of neurotic depression in study members of both study cohorts. The assessment technique of depression using (PHQ-9) is illustrated down in table No 1.

3. General anxiety disorders scale-7 (GAD-7) questionnaire for assessment of anxiety which is a structured, pre tested validated, previous mental health studies used, self-reported questionnaire (which is allowed to be used by researchers without permission) for assessment of anxiety ⁽¹³⁾, it has been used for assessment of neurotic anxiety in study members of both study cohorts. The assessment technique of anxiety using (GAD-7) is illustrated down in table No 2

Table 1: Patient Health Questionnaire (PHQ-9) for depression assessment

Over the last 2 weeks, how often have you been bothered by any of the following problems? use to indicate your answer	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could be noticed.	0	1	2	3
9. Thoughts that it would be better if dead, or of hurting yourself.	0	1	2	3
Add totals of columns	++
Total score			=	

Conversion of total score to depression severity (This will be hold with researcher, not given to patient)

1-4	Minimal depression	5-9	Mild depression
10-14	Moderate depression	15-19	Moderately severe depression
20-27	Severe depression		

Table 2: GAD-7 Questionnaire for Anxiety assessment

Over the last 2 weeks, how often have you been bothered by any of the following problems?				
use to indicate your answer	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious, or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid, as if something awful might happen	0	1	2	3
Add totals of columns	++
Total score				=

Conversion of total score to Anxiety grade (This will be hold with researcher, not given to patient)

1-4	Minimal Anxiety	5-9	Mild Anxiety
10-14	Moderate Anxiety	15-21	Moderately severe Anxiety

Although, PHQ-9 and GAD-7 scales are validated, we tested them with study member data questionnaire using Cronbach test yielding high consistency and reliability for the three tools as shown in the table 3.

Table 3: Cronbach Alpha values of data collection tools

No.	Scale	Cronbach Alpha value
1	study unit data questionnaire	0.79
2	PHQ-9 questionnaire	0.91
3	GAD-7 questionnaire	0.87

Piloting test: Piloting of data collecting tools have done on 10 cases (5 khat chewing and 5 non-khat chewing students. Piloting revealed satisfying outcomes

Data entry and analysis

SPSS version 27 used for data entry and statistical analysis, χ^2 test or Fisher's exact test was used to test for comparison between categorical variables, as appropriate. Quantitative data were described as mean and standard deviation (mean \pm SD) and after testing for normality by Kolmogorov-

Smirnov, an independent t test used for comparison between two groups of normally distributed data. And a nonparametric Mann-Whitney U test for two groups of not normally distributed data. A two-tailed p-value less than or equal to 0.05 was considered statistically significant

Study sample characters

Study sample characters per each study cohort are shown down in table 4, revealing nearly similar mean age in both cohorts, while it reveals male high predominance

(95.6%) in khat chewing cohort members opposite of relative female predominance (66.2%) in non khat chewing cohort members, and this is accepted in view of khat chewing habit is considerably more prevalent in males than females.

Regarding monthly income; there is relatively higher proportion of good income members (36.8%) among khat chewing cohort apposite (16.2%) among non khat chewing cohort, and this locks logic in view of khat chewing is more prevalent in more

rich peoples who can buy the daily cost of khat.

Regarding residence (with or out the family), the table 4 shows 85.3% of non khat chewing cohort members are residing with their families (as two thirds of this cohort are females who are residing with their families in same Hodeida city, opposite 70.6% of khat chewing cohort members (as most of them are males coming from other cities who are residing during study period as groups in rented houses in Hodeida city)

Table 4: Distribution of study sample per age, gender, income and residence with or out family

Variable		Khat chewing cohort n= 68		Non Khat chewing cohort n= 68	
		n	%	N	%
Age	mean ± SD	23.69±2.87		22.78±3.04	
	<25	45	66.2	52	76.5
	≥25	23	33.8	16	23.5
Gender	Male	65	95.6	23	33.8
	Female	03	4.4	45	66.2
Income	Good	25	36.8	11	16.2
	Average	12	17.6	12	17.6
	Poor	31	45.6	45	66.2
Residence	with family	20	29.4	58	85.3
	Out family	48	70.6	10	14.7

RESULTS

A-The study reached statistically significant link of habitual khat chewing with incidence of depressive disorders, as table No.5 reveals higher proportions among khat chewing cohort members having various severity grades of depression (14.7% as sever, 33.8% as moderate and 42.6% as mild) compared to (7.4% as sever, 26.5% as moderate and 39.7% as mild) among non khat chewing cohort members. In addition, 16.2% of non khat chewing cohort members have found as non-having depression opposite no body in khat chewing cohort members. Mentioned outcomes have been reached at statistically significant difference ($\chi^2=13.425$, $p=0.009$). Also, depression mean symptom score for khat chewing cohort members has found as significantly higher (12.60 ± 6.14) than for non-khat chewing cohort (9.88 ± 5.72), with a significant Z value (-2.697 , $p=0.007$).

B-The study reached statistically significant link of habitual khat chewing with incidence

of anxious disorders, as table 6 reveals higher proportions among khat chewing cohort members have sever and moderate anxiety (17.6% as sever and 29.4% as moderate) compared to (11.8% as sever, 20.6% as moderate) among non khat chewing cohort members. In addition 17.6% of non khat chewing cohort members have found as not having anxiety opposite 1.5% in khat chewing cohort study members. Mentioned outcomes have been reached at statistically significant difference ($\chi^2=11.181$, $p=0.011$). Also Anxiety mean symptom score for khat chewing cohort members has found significantly higher (10.53 ± 4.66) than for non-khat chewing cohort (8.66 ± 4.60), with a significant Z value (-2.321 , $p=0.020$).

C- The study reached statistically significant link for chewing khat individually with anxiety severity grades ($\chi^2=5.107$, $p=0.024$) as have shown in table 7, while no significant link found for chewing khat individually with depression. Also no

significant link found for any of other with anxiety or depression. investigated khat chewing related factors

Table 5: Incidence of depression among khat chewing cohort compared to non khat chewing cohort

Depression grades	Khat chewing Cohort N=68		Non Khat chewing Cohort N=68		Chi value	P-value
	No	%	No	%		
Non	0	0.0	11	16.2	13.425	0.009
Mild	29	42.6	27	39.7		
Moderate	23	33.8	18	26.5		
Moderate to sever	6	8.9	7	10.3		
Sever	10	14.7	5	7.3		
Mean ± SD	12.60±6.14		9.88±5.72			
Median (Mini – Maxi)	10(5 – 27)		9(0 – 27)		Z value -2.697	P-value 0.007

Table 6: Incidence of anxiety among khat chewing cohort compared to non khat chewing cohort

Anxiety grades	Khat chewing Cohort N=68		Non Khat chewing Cohort N=68		Chi value	P-value
	No	%	No	%		
Non	1	1.5	12	17.6	11.181	0.011
Mild	35	51.5	34	50.0		
Moderate	20	29.4	14	20.6		
Sever	12	17.6	8	11.8		
Mean ± SD	10.53±4.66		8.66±4.60			
Median (Mini – Maxi)	9(4 – 21)		8(0 – 21)		Z value --2.321	P-value 0.020

Table 7: Khat chewing associating variables link with depression and anxiety

Independent Variable	Depression		Anxiety	
	Chi value	P value	Chi value	P value
Khat chewing duration	1.441	0.486	2.242	0.326
Khat chewing daily hours	4.431	0.109	3.895	0.143
Coffee and tea drinks with khat chewing	0.655	0.418	0.101	0.751
Khat chewing Individually or e friends	0.034	0.855	5.107	0.024*

DISCUSSION

Natural psychoactive substances abuse seems to be globally high community concern. Of approximately 4,000 plant-derived psychoactive substances, about 60 have been in constant use in different forms, somewhere in the world, (e.g. khat, coca, tea, coffee, tobacco, cannabis, opium). In Yemen, Khat is a major cultural concern⁽¹⁴⁾. Many published studies reported various health adverse effects for habitual khat chewing including psychiatric disorders; one of these studies is a recent meta-analysis study that have reached 122% increased prevalence of psychiatric symptoms in khat chewing peoples⁽¹⁵⁾, and more ancient study that have reached significant association of different mental distress with khat use⁽¹⁶⁾.

As going with above mentioned studies outcomes, the current study reached positive link of khat chewing with both depression and anxiety, as also going with previous Yemeni prospective study conducted during 2000 in Sana'a, using Hospital Anxiety and Depression scale, reached significant increased median score on the scale indicating mood disturbance among khat chewing group compared with the control group⁽¹⁷⁾, and Ethiopian cross-sectional study conducted during 2020 reached 27.4% prevalence of depression and 40.6% of Anxiety among studied khat chewing peoples⁽⁸⁾. Also, a further cross-sectional study conducted during 2018 in Saudia Arabia on 642 students from Jazan University, reached 53.6% prevalence of depression and 65.7% of anxiety among khat chewing students⁽¹⁸⁾.

The current study has investigated effects of khat chewing duration, daily chewing hours, tea or coffee concomitant drinking and if chewing is practiced in social or individual sittings), reaching statistically significant link for individual khat chewing with anxiety severity, which could be attributed to absence of socialism calming effect in khat chewing common sittings. In this regard, it locks that, the current study is among the first Yemeni studies as reported in one of the last conducted Yemeni studies⁽¹⁹⁾.

There is scarcity of the type of the current study even in other countries having khat chewing peoples, so it was high difficult to reach previous studies to compare the current study outcomes in this part, except some study reported high schizophrenic illness, mania, and less depression are more occurring in khat long chewers, while the daily dose have not found as significantly affecting the mental disorders severity in khat chewing peoples due to khat dose effect is self-limited as reported⁽²⁰⁾.

Regarding effect of concomitant tea or coffee drinking, some tutorials found as concluding that, caffeine have health diverse effects near from khat effects, so synergetic action of caffeine (in coffee and tea) and cathinone in khat leaves is highly supposed⁽²¹⁻²²⁾.

Lastly, the current study members could be not having significant differences in khat chewing durations, daily hours of khat chewing and amounts of coffee and tea drinks with khat chewing, so the effects of these factors have not addressed in current study outcomes.

CONCLUSION

The aim of this study was to explore risk relation between habitual khat chewing and neurotic depression and anxiety. Habitual khat chewing has concluded as having significant risk relation with neurotic anxiety and depression. In addition, individual khat chewing sitting has found to be a further risk for anxiety severity.

Declaration by Authors

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Ethical Approval: The proposal for this research had approved by Research Ethics Committee in Faculty of medicine at Hodeida University, Yemen.

Conflict of Interest: The authors report no conflict of interest regarding this report.

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