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KHAT (*CATHA EDULIS*) USE IS ASSOCIATED WITH THE DEVELOPMENT OF GASTRITIS AMONG ADULTS IN NAIROBI COUNTY, KENYA
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KHAT (*CATHA EDULIS*) USE IS ASSOCIATED WITH THE DEVELOPMENT OF GASTRITIS AMONG ADULTS IN NAIROBI COUNTY, KENYA

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ABSTRACT

***Background*: Khat (Catha edulis) chewing leads to a number of health related problems in the gastro-intestinal tract (GIT). Few studies have examined the effects of regular Khat chewing in relation to gastritis. Experimental studies with animals have shown that an association exists between Khat chewing and the incidence of gastritis.**
***Objective*: To compare the prevalence of Khat chewing among cases with gastritis cases and cases without gastritis.**
***Design*: Individual matched case control study.**
***Setting*: Kenya Medical Research Institute's Centre for Clinical Research (CCR) and St. Michael's Digestive Disease and Medical Care.**
***Subjects*: Ninety three cases were selected using Rome III criteria for functional dyspepsia, and the controls (n=93) were matched on age and gender.**
***Results*: Among the 93 dyspepsia cases, 64.5% were Khat chewers and 35.5% were non-chewers. Khat chewing was associated with the presence of functional dyspepsia (OR 3.8, 95% CI 1.6- 9.4). Of the 60 Khat chewers, 60% (36/60) had erosions in the upper GIT. Chewing Khat was associated with upper GIT erosions (OR 4.095% CI: 1.6, 10.1) It was determined that Khat chewers are four times more likely to have upper GIT erosions than non-chewers.. Khat chewers are 5.5 times (OR 5.5 95% CI: 1.9, 22.0)) more likely to have OGD (Oesophagitis, Gastritis and Duodenitis) compared to non-chewers. Among cases and controls, smoker (p-value<0.001) and non-smoker (p-value<0.001) Khat chewers were significantly different. The prevalence of H. pylori among Khat chewers was significantly found to be higher (62.9%, p = 0.042); the two groups (Khat chewers and non-chewers) showed significant difference**
***Conclusion*: These results reveal that regular Khat chewing is positively associated with gastritis, which is consistent with previous experimental studies on animals.**

INTRODUCTION

Khat is the name generally used for *C.edulis*, a dicotyledonous evergreen shrub of the family *Celastraceae*. It is also known as 'Miraa' or 'Qat' in Kenya, while in Ethiopia the Amharas calls it 'tchat' and the Gallas 'Jimma'. Khat trees grow wild in the forests and are cultivated widely in various locations in Kenya, especially in the Nyambene Hills, a mountain range lying northeast of Mount Kenya. Khat leaves are crimson-brown and glossy but become yellow-green and leathery as they age. The leaves are up to 5 cm wide and up to 10 cm long. The leaves emit a strong aromatic smell and have an astringent and slightly sweet taste. Khat is a cash crop profitable for a large number of people involved in its production and marketing including farmers, distributors and retail merchants. Taxes levied on the production and sale of Khat are an important source of revenue to the government (1, 5). This shrub is regularly cultivated in certain areas of East Africa and in the Arabian Peninsula (1-3). The habit of chewing Khat leaves continues to be practiced for its stimulant effects on the central nervous system (4). In Kenya the practice is widespread among Somali and Meru ethnic groups. The National Agency for the Campaign Against Drug Abuse (NACADA) estimates that 25% of the Kenyan population chews Khat.

The chemical profile of Khat leaves varies depending on environmental and climate conditions (6). Fresh leaves of Khat may contain 60 different cathedulins(7). Compounds found in Khat include

alkaloids, terpenoids, flavonoids, sterols, glycosides, tannins, amino acids, vitamins and minerals (8). The pharmacologically active constituent of Khat is cathinone, which has amphetamine- like properties that affects the central nervous system (8, 9).

Khat use has a number of health-related complications that includes increased blood pressure, tachycardia, insomnia, anorexia, gastritis, stomatatis, oesophagitis, gastric ulcers, hemorrhoids, constipation, general malaise, irritability, migraine headaches, cardiovascular complications, loss of appetite, and impaired sexual potency in men (4,6,10,11).

Though gastritis has many possible causes, clinical observations have shown that habitual Khat chewers often complain of symptoms suggestive of stomatitis, oesophagitis, gastritis and constipation. In experiments on animals, Khat extract has been shown to cause gastritis and duodenitis (11). In addition, dose-related association between Khat chewing and gastrointestinal symptoms was confirmed (12, 13). These effects were believed to be caused mainly by the strongly astringent tannins and the alkaloids that affect motility (intestinal contractions) and secretions (13-15).

Studies on the effect of Khat on the gastrointestinal tracts of humans are scarce despite the increase in the knowledge of Khat pharmacology and chemistry, thus the need for this study to show whether an association exists between Khat chewing and gastritis.

MATERIALS AND METHODS

Study site and design: The study was conducted in the county of Nairobi. The city of Nairobi lies 1° South of the equator and its longitude is 36° East. It has area of 684 squares kilometers and a population of 3.1 million (16). Khat is chewed widely across Nairobi mostly by the Somali, Borana and Meru communities (1).

A one-to-one age (±5 years) and gender matched Case Control study was undertaken to assess the medical risks of Khat chewing with respect to gastritis. The matching of the control group with cases was done to improve efficiency in the estimation of the effect of exposure by protecting against the situation in which the distributions of the confounder are substantially different between the two groups, for completeness of control for confounding variables, for control of unmeasured confounders, and for time comparability especially related to age (35).

Inclusion criteria: Cases were defined as those aged between 18 and 60 years, and diagnosed as having functional dyspepsia using the Rome III questionnaires for functional dyspepsia adopted from the Journal of Gastroenterology (http://www.rome criteria.org) (17). In addition they should have provided voluntarily consented to participate.

Controls were defined as persons aged between 18 and 60 who have not been diagnosed as having functional dyspepsia and who consented to participate. Selection of controls involved individual matching on age and gender variables because they represent strong confounders epidemiologically (34).

Exclusion criteria: Patients in the following categories were excluded,

- Persons younger than 18 or older than 60 and who live in the study area
- Persons between the ages of 18 and 60 who do not consent, and
- Persons who use NSAIDs (non-steroidal antiinflammatory drugs).

Sampling and sample size: The sample was determined using the formula for comparison of two proportions developed by Casagrande *et al*; 1978 (18).

$$\frac{\{Z_{1-\alpha/2}\sqrt{[2P(1-P)]} + Z_{1-\beta}\sqrt{[P(1-P_1) + P_2(1-P_2)]}\}^2}{(P_1 - P_2)^2}$$

Where,

n= Minimum sample size required.

α = Type I error / level of statistical significance (0.05).

β= Type II error (0.20).

$Z_{1-\alpha/2}$ = Standard normal deviation for α (1.96).

$Z_{1-\beta}$ = Standard normal deviation for β (0.84).

P_1= Estimated prevalence of Khat chewers with gastritis

P_2= Prevalence of abuse of Khat as defined by NACADA (19).

$$\frac{(P_1 + P_2)^2}{2}$$

In this study P1 was assumed to be 50% while P2 is 25%; using the Casagrande for comparison of two proportions, this gave a sample size of 84. To account for non-responders we added 10%; 84 plus 8.4 will be approximately 93. Hence, the sample size was 93 case-control pairs.

Data collection and patient selection: Nurses and pharmacy assistants participated in the recruiting of study participants as well as in the collection of data after going through training in this process. The World Health Organization (WHO), (20) tool for data collection was modified and used for the data collection process. Field teams were based at respective pharmacies and chemist shops within the study area, that is, Nairobi County and in particular Eastleigh, Majengo and South C.

Patients buying drugs such as antacids, or H2 receptor antagonists also called H2 blockers or those buying proton pump inhibitors (PPI) were approached by the data collectors who requested them to take part in the study having observed all the ethical requirements of the study. In order to up hold privacy and confidentiality, pharmacies and chemists with separate counseling spaces were used. After explaining the reasons and the objectives of the study to the participant, the investigator or data collector requested the participant to choose between two folded pieces of paper in a box that had yes or no, respectively, written on them. Those who qualified as having dyspepsia as per Rome III criteria were recruited as case studies and subjected to the study questionnaire. The investigators collected relevant demographic data for purposes of completing the recruitment process for the study (21). Study controls were matched by age and gender of the recruited cases. None of the control group had any GIT complaints or functional dyspepsia as per Rome III criteria.

Study participants who were recruited and who signed a written consent form were referred to a gastroenterologist at KEMRI's Centre for Clinical Research (CCR) and to St. Michael's Digestive Disease and Medical Care for an endoscopic examination and taking of biopsies.

Endoscopy procedure: Two biopsy specimens were taken during an upper gastrointestinal endoscopy, one from the corpus and one from the gastric antrum; this was done for a histological assessment of gastritis and *H. pylori* infection. For *H.pylori* diagnosis, biopsy specimens were fixed in 10% formalin and stained with haematoxylin-eosin and Giemmsa stain (22). The version of the visual analogue scale in the updated Sydney system was used to grade the density of *H.pylori* (23). A histological examination of gastric mucosal biopsies was necessary in order to establish a diagnosis of gastritis.

Data management: The quantitative data collected from the field was coded and double entered into a computer database designed using EpiData Version 3.1. Files were backed-up regularly to avoid loss or data tampering. All questionnaires were stored in a locked drawer for confidentiality purposes.

Data analysis: The analysis was conducted using IBM SPSS Statistics Version 20 statistical software. Exploratory data techniques were used at the initial stage of analysis to uncover the structure of data and identify outliers or unusual entered values.

Univariate analysis: Descriptive statistics such as proportions were used to summarise categorical variables with measures of central tendency such as mean, SD, median and ranges used for continuous variables.

Bivariate analysis: Conditional Logistic Regression using age as the strata was used to test for the strength of association between categorical variables. When data was small (cell values less than 5) or the data was sparse, Fishers Exact Test was used to test the association. All Independent variables (including chewing of Khat) was associated with the presence or absence of functional dyspepsia to determine which ones would have significant association. Odds Ratio (OR) and 95% Confidence Interval (CI) were used to estimate the strength of association between independent variables and the presence or absence of functional dyspepsia.

Event rate (ER) was used to determine the risk to case subjects in comparison with control subjects. Control event rate (CER) and case event rate (EER) were used to refer to those in control and case groups of subjects, respectively. The absolute arithmetic difference in risk of harmful outcomes between cases (EER) and controls (CER).was calculated as the risk of harmful outcome in the case group minus the rate of harmful outcome in the control group (EER – CER). Relative risk increase (RRI) was calculated for a harmful exposure that is, EER -CER / CER . Number needed to harm (NNH) was also calculated. All statistical tests were conducted at α=0.05 level of significance.

Multivariate Logistic Regression Analysis: McNemar's test for association was used in this individual matched case-control study. All independent variables identified to significantly associate with the presence or absence of functional dyspepsia at conditional bivariate logistic regression analysis were considered together in a multiple logistic regression for pair-matched case-control analysis (36). This was performed using conditional logistic regression where the backward conditional method was specified in order to identify confounders and / or effect modifiers. Adjusted odds ratio (AOR) at corresponding 95% confidence intervals (CI) was used to estimate the strength of association between the presence of functional dyspepsia and the retained independent predictors. Model diagnosis statistics for the pair-matched study was obtained using conditional logistic regression (36).

Ethical considerations: Ethical clearance and permission to carry out the study was obtained from the Ethical Review Board of Jomo Kenyatta University of Agriculture and Technology (JKUAT) and from the Kenya Medical Research Institute (KEMRI) Scientific Committee and Ethics Review Committee. Participants were enrolled into the study only after written voluntary informed consents were given. All patient data were handled with confidentiality and were used only for intended purposes. The participants were given the results of the tests they undertook.

RESULTS

Ninety three case-control pairs who voluntarily agreed to participate, and met the eligibility criteria were recruited into the one-to-one matched casecontrol study. Demographic data, information regarding Khat usage, Upper GIT endoscopy and Histology were collected.

Demographics: The proportion of Christians and Muslims was significantly different among Khat chewers (p-value<0.001) and non-chewers (p-value=0.113). Among the 93 cases, 64.5% were Khat chewers and 35.5% were non-chewers while among the 93 controls, 46.2% were Khat chewers and 53.8% were non-chewers.

The individual matching criteria employed for this case-control study was based on overall age (± 5years and gender distribution. (Table 3) shows the mean age in years (±SD) of cases was 31.9(±9.7); there was no significant mean age difference (p-value=0.082) between chewers (33.2(±9.0)) and non-chewers (29.5(±10.7)). Mean age among chewers and non-chewers was not significantly different among cases and controls Table 2. Majority of the chewer cases 81.7% (49/60) and controls79.1% (34/43) were aged 40 years and below. There was no discernible association between age groups and functional dyspepsia within either cases or controls (Table 3).

Majority of Khat chewer cases were single 45.0% (27/60) or divorced 31.7% (19/60) while for controls, the majority were single 46.5% (20/43) followed by married 37.2% (16/43). However, among cases, divorcees were more than six times more likely to be Khat chewers than non-chewers (OR 6.2, 95% CI 1.7, 26.8). Majority of Khat chewer cases were Khat traders 41.7% (25/60), Matatu drivers and touts 30.0% (18/60) while for controls it was casual laborers 56.0% (28/43) or house-wife/house-husband 20.0% (10/43). However, among cases, Matatu drivers and touts were 4.5 times more likely to be chewers than non-chewers (OR 4.5, 95% CI 1.1, 21.3) (Table 3).

Case-control analysis: Odds ratio (OR) measures the level of association in matched case-control analysis. Thus, in this matched cases-control study, an OR of 3.8(23/6) (95% CI 1.6, 9.4) Table 1 (which is a strong positive association) (X1 2 =9.966),p-value=0.002, highly statistically significant) is an indication that functional dyspepsia is highly associated with Khat chewing. This implies that regular and sustained exposures to Khat chewing increases one's risk of having functional dyspepsia.

Odds of exposure (chewing Khat) among cases was 1.8 (60/33) and the odds of exposure (chewing Khat) among controls was 0.9(43/50), (Table 2). Event rate for cases and controls explains the event ratio as a measure of how often a particular statistical exposure results in the occurrence of gastritis within the cases. Thus, an event rate of 64.5% explains the extent of risk to chewers as compared with non-chewers within the cases.

In this case-control study, absolute risk increase was18.3% of chewing Khat among cases. The study also reports a relative risk increase of 39.5% among chewers compared to non-chewers. In this matched case-control study, the number needed to harm is five (Table 2). Relative risk (risk ratio) of gastritis associated with Khat chewing was 1.4. Thus, chewers are 1.4 times as likely as non-chewers to develop gastritis

Behavioral characteristics of Khat chewers: The reported frequency of Khat chewing among chewer cases was daily 40.0% (24/60), more than three times a week 51.7% (31/60) and once or twice a week 8.3% (5/60). Of the chewer cases, majority chew Khat quantities of Marduuf (100 to 120 sticks) 51.7% and 2 Marduuf 40.0%.Of the Khat chewer cases, 51.7% have used for more than 5 years while 48.3% have used Khat for 2 to 5 years (Table 4). The main reported reasons for chewing Khat among cases were: to works more efficiently 58.3%, kills time 46.7%, to keep company 26.7% and peer pressure 21.7%. Among the cases, there were several symptoms of GIT complaints: there was sufficient evidence that chewer cases differ with respect to their GIT symptom complaints, from non-chewer cases: blood in the stool (chewers 84.6% and non-chewers 15.4%) (p-value<0.001), vomiting blood(chewers 85.7% and non-chewers 14.3% (p-value=0.008), constipation (chewers 79.7% and nonchewers 20.3%)(p-value<0.001), bloating (chewers 88.0% and non-chewers 12.0%) (p-value<0.001) and abdominal pain (chewers 64.8% and non-chewers 35.2%)(p-value=0.005). The proportion of Khat chewer cases who take food while chewing were 26.7% while those who do not take food while chewing was73.3%; the two were significantly different (p-value<0.001). Of the chewer cases, smokers were significantly different (p-value<0.001) from non-smokers and similarly for the chewer controls. In the matched case-control analysis, smoking (p-value=0.442) and alcohol use (p-value=0.960) were not associated with the presence or absence of functional dyspepsia among chewers in either cases or controls.

Upper GIT endoscopy and histology results: All 93 casecontrol pairs had results for both upper GIT endoscopy and histology. Of the 93 cases, 57.0% had oesophagitis with a majority being Khat chewers 66.0% (35/53) with the two groups being significantly different (p-value=0.020) (Table 5). Among the gastritis cases 95.7% (89/93), Khat chewers (67.2%) and non-chewers (34.8%) were significantly different (p-value=0.004). In addition, of the 30.1% (28/93) gastritis ulcer cases, Khat chewers (75.0%) and non-chewers (25.0%)

were significantly different (p-value=0.008). Of the 93 cases, 34.4% had duodenitis with the majority being Khat chewers 71.9% (23/32); Khat chewers and non chewers were significantly different (p-value=0.013). A combination of oesophagitis, gastritis and duodenitis positive cases, 96.8% (90/93) had one, two or all three positive, Khat chewers (64.4%) and non-chewers (35.6%) were significantly different (p-value=0.005). Of the 93 controls, only three had confirmed esophagitis with no statistical difference between chewers and non-chewers (p-value=0.180) (Table 5). This combination of esophagitis, gastritis and duodenitis was highly associated (OR 5.5, 95% CI: 1.9, 22.0) with Khat chewing in the pair-matched case-control study.

Of the 60 chewer cases, 60% had erosions in the upper GIT. Khat chewing was associated with upper GIT erosivity (OR 4.0, 95% CI: 1.6, 10.1). Therefore, Khat chewers were four times more likely to have upper GIT erosions than non-chewers (Table 5).

Histology results concurred with the upper GIT endoscopy results, where 56.7% had erosions. Khat chewers were 5.9 times (OR 5.9, 95% CI 2.1 16.3) more likely to have erosions than non-chewers. None of the 93 controls had GIT or histology positive test results for erosivity (Table 5).

Of all the cases, 67.7% were diagnosed as having *H. pylori* with the majority being Khat chewers 62.9%; and the two groups (Khat chewers (62.9%) and non-chewers (37.1%) were significantly different (p-value=0.042). H. pylori results were classified into negative (chewers 35.0% and non-chewers 30.3%) and positive (chewers 62.9% and non-chewers 37.1%) with four categories: mild (P+), moderate (P++), numerous (P+++ and P++++) . Only moderate *H. pylori* was seen to be significantly different (p-value=0.041) between Khat chewers (69.0%) and non-chewers (31.0%).There was no increasing or decreasing trend for all the categories of *H. pylori* and Khat chewing (p-value=0.440). For cases, gastritis was classified into four categories: negative (Khat chewers 1.7% and non-chewers 9.1%), mild (21.7% chewers and non-chewers 30.3%), moderate (60.0% chewers and non-chewers 45.5%) and severe (16.7% chewers and non-chewers 15.2%). Only moderate gastritis was significantly different between Khat chewers and non-chewers (p-value=0.003) (Table 5).

Statistical Modelling: Multiple logistic regression analysis was used to identify risk factors associated with Khat chewing among cases. The predictor variables obtained using p-value<0.25 were used as main effects. However, due to the small sample size and sparseness, no interactions were considered during the model building process (24). The predictor variable with the highest insignificant p-value was dropped from the model. The parameter values of the remaining main effects were assessed for any changes due to possible confounding. Multiple logistic regression analysis showed that gender, age and marital status of participants were statistically associated with Khat chewing among cases. The final model was

*logit[Pr{Y= 1][X = x]] = 3.603-1.993 *Sex + 0.100 *Age + 2.497 *Single + 3.240 *Divorced + 0.945 *Widowed + 3.576 *Separated -0.525 *Religion*

Khat chewing among females is protective (OR 0.1, 95% CI: 0.0; 0.5) compared to males keeping all other predictors constant, (Table 6). In model diagnostics, Hosmer-Lemeshow goodness-of-fit test was not statistically significant (p-value=0.142) an indication that the model fits the data well. The final model inference did not change when the cases of categories causing sparseness were deleted from the data set.

Table 1

Matched case-control study distribution among chewers and non chewers in Nairobi, Kenya

		Control		
		Chewer	Non-Chewer	Total
Case	Chewer	37	23	60
	Non-chewer	6	27	33
	Total	43	50	93

Table 2
Case-control study ratios distribution among chewers and non chewers in Nairobi, Kenya

Cases (E)	Controls (C)	Total	
Chewers	EE =60	CE =43	103
Non-Chewers	EN =33	CN =50	83
Total	ES =EE+EN=93	CS =CE+CN =93	186
ER%	EER =EE/ES=64.51%	CER =CE/CS=46.24%	
Other Ratios			
Ratio	Variable	Equation	Risk Increase
ARI	Absolute risk increase	EER -CER	18.28%
RRI	Relative risk increase	(EER-CER)/CER	39.53%
NNH	Number needed to harm	1/(EER-CER)	5
RR	Relative risk	EER /CER	1.40

EE=Exposed Cases,EN=Non-exposed Control, ES=Total case subjects, ER=Event Rate, EER=Cases event rate, CE=Exposed Controls, CN=Non-exposed Controls, CS=Total control subjects, CER= Control event rate

Table 3
Socio-Demographic distribution of cases and controls for chewers and non-chewers of Khat in Nairobi, Kenya

Controls					Cases			
	Chewers	Non-chewers	OR (95%)	P-Value	Chewers	Non-chewers	OR (95%)	P-Value
Religion	n(%)	n(%)			n(%)	n(%)		
Islam	35(70.0)	32(74.4)	1	0.6363	45(75.0)	21(63.6)	1	0.2483
Christian	15(30.0)	11(25.6)	0.8(0.3,2.0)	15(25.0)	12(36.4)	0.6(0.2,1.5)		
Sex								
Male	30(69.8)	31(62.0)	1	0.4323	47(78.3)	14(42.4)	1	0.0013
Female	13(30.2)	19(38.0)	0.7(0.3,1.7)	13(21.7)	19(57.6)	0.2(0.1,0.5)		
Age(years)								
Age in years	31.9(9.9)	30.0(8.9)	0.3151	33.2(9.0)	29.5(10.7)	0.0821		
Age groups								
<=30 years	20(46.5)	29(58.0)	1	0.7442	23(38.3)	17(51.5)	1	0.6792
31-40 Years	14(32.6)	3(26.0)	1.6(0.5,4.5)	26(43.3)	11(33.3)	1.7(0.7,4.6)		
41-50 Years	8(18.6)	7(14.0)	1.6(0.4,6.3)	2(3.3)	1(3.0)	1.7(0.5,7.0		
>50 Years 1(2.3)	1(2.0)	1.4(0.0, 117.7)	9(15.0)	4(12.1)	1.5(0.1,33.3)			
Marital status								
Married	16(37.2)	18(36.0)	1	0.6382	10(16.7)	13(39.4)	1	0.0772
Single	20(46.5)	27(54.0)	0.8(0.3,2.0)	27(45.0)	14(42.4)	2.5(0.9,7.3)		
Divorced	6(14.0)	4(8.0)	1.7(0.4,7.6)	19(31.7)	4(12.1)	6.2(1.7,26.8)		
Widowed	0(0.0)	1(2.0)	-	1(1.7)	1(3.0)	1.3(0.0,35.7)		
Separated	1(1.3)	0(0.0)	-	5(5.0)	1(3.0)	3.9(0.4,85.6)		
Main occupation								

Housewife / House husband	1(14.0)	10(20.0)	1 0.0022	4(6.7)	8(24.2)	1	0.0652
Khat Trader	12(27.9)	0(0.0)	-	25(41.7)	0(0.0)	-	
Casual	17(39.5)	28(56.0)	1.0(0.3,3.4)	12(20.0)	9(27.3)	2.7(0.6,12.8)	
Labourer drivers and touts							
Matatu	5(11.6)	7(14.0)	1.2(0.3,5.6)	18(30.0)	8(24.2)	4.5(1.1,21.3)	
Employed	3(7.0)	5(10.0)	1.0(0.1,5.7)	1(1.7)	8(24.2)	0.3(0.0,2.2)	

[1]T-test, [2]Fishers Exact Test, [3]Chi-Square Test

Table 4
Behavioral characteristics of Khat chewers among cases and controls

	Controls		Cases			
	Chewers(43)	P-value	Chewers(60)	P-value	OR(95% CI)	P-value
Frequency of chewing Khat						
Daily	11(25.6)		24(40.0)		1	
More than 3 times a week	12(27.9)		31(51.7)		0.5(0.1;2.0)	0.428
Once or twice a week	10(23.3)		5(8.3)		0.3(0.0;2.0)	0.291
Not frequently	10(23.3)		0(0.0)		2.0(-0.4;Infinity)*	0.171
Quantity of Khat chewed						
Mijin (12 to 20 sticks)	9(9.3)		1(1.7)		0.4(0.0;5.5)	0.837
Marduuf (100 to 120 sticks)	33(76.7)		31(51.7)		1	
2 marduuf	6(14.0)		24(40.0)		7.3(1.7;66.2)	0.003
More than 2 marduuf	0(0.0)		4(6.7)		6.6(0.7;Infinity)*	0.170
Duration of Khat chewing						
Less than two years	1(2.3)		0(0.0)		2.30.0;42.8)	1.000
2 to 5 years	25(58.1)		29(48.3)	0.7964	1	
More than 5 years	17(39.5)		31(51.7)		2.0(0.5;9.1)*	0.388
Why chew Khat?						
Addicted	13(30.2)		13(21.7)			
Kill time	20(46.5)		28(46.7)			
To keep company	13(30.2)		16(26.7)			
and peer pressure						
To work more efficient	26(60.5)		35(58.3)			
Symptoms of GIT complained of						
Heart burn			18(64.3)	0.131		
Blood in the stool			22(84.6)	<0.001		
Vomiting blood			12(85.7)	0.008		
Constipation			47(79.7)	<0.0014		

Bloating			22(88.0)	<0.001		
Abdominal pain			59(64.8)	0.005		
Have food while chewing Khat						
Yes	36(83.7)	<0.0014	16(26.7)	<0.001	1	
No	7(16.3)		44(73.3)		0.4(0.1;1.6)	0.267
Use of other drugs/ stimulants/chemicals						
Yes	41(95.4)	<0.0014	48(80.0)	<0.0014	0.1(0.0;0.9)	0.039
No	2(4.7)		12(20.0)		1	
Smoking						
Smoker	35(81.4)	<0.0014	45(75.0)	<0.0014	1	
Non-smoker	8(18.6)		15(25.0)		2.0(0.5;9.1)	0.388
Alcohol use						
Alcohol	22(51.2)	0.8794	31(51.7)	0.796	1	
No Alcohol	21(48.8)		29(48.3)		1.2(0.3;5.0)	1.000
Duration of using these other drugs/stimulants/ chemicals						
Less than a year	4(9.8)	<0.0014	10(20.8)	<0.0014	1	
More than a year	37(90.2)		38(79.2)		0.5(0.2;1.7)	0.390
Frequency of using these other drugs/stimulants/ chemicals						
Daily	28(68.4)	21(43.8)	0.3874	1		0.180
When chewing Khat	10(24.4)		27(56.3)		4.5(1.0;20.8)	
Once a month	3(7.3)					

[4]2-proportion Z-test; * indicates a median unbiased estimate

Table 5

Comparison of upper GIT Endoscopy, Erosivity and Histology results of chewers and non chewers among cases and controls

	Cases	Controls						
	Chewers	Non-chewer	OR (95%CI)	P-value	Chewers	Non-chewers	O R (95%CI)	P-value
Upper GIT								
Oesophagitis	35(66.0)	18(34.0)		0.0124	4(80.0)	1(20.0)		0.1804
Gastritis	58(65.2)	31(34.8)		0.0044	12(92.3)	1(7.7)		0.0024
	Gastritis	grading						
Mild	9(39.1)	14(60.9)		0.2974	12(92.3)	1(7.7)		0.0024
Moderate	25(71.4)	10(28.6)		0.0114	0(0.0)	0(0.0)		
Severe	24(77.4)	7(22.6)		0.002[4]	0(0.0)	0(0.0)		
Gastric Ulcers	21(75.0)	7(25.0)		0.0084	0(0.0)	0(0.0)		
Duodenitis	23(71.9)	9(28.1)		0.0134	0(0.0)	0(0.0)		
OGD	58(64.44)	32(35.56)		0.0054	13(86.7)	2(13.3)		0.0054

(Oesophagitis+Gastritis+Duodenitis)							
Erosivity - Upper GIT endoscopy							
Erosive	36(60.0)	9(27.3)	4.0(1.6,10.1)	0.0033	3(7.0)		
Non-Erosive	24(40.0)	24(72.7)	1		40(93.0)	50(100.0)	
Erosivity – Histology							
Erosive	34(56.7)	6(18.2)	5.9(2.1,16.3)	<0.0013	5(11.6)		
Non-Erosive	26(43.3)	27(81.8)	1		38(88.4)	50(100.0)	
Histology results							
H. pylori	39(62.9)	23(37.10)		0.0424	30(65.2)	16(34.8)	0.0394
(positive)							
H. pylori Categories							
P+	5(45.5)	6(54.6)		0.7634	27(64.3)	15(35.7)	0.0644
P++	20(69.0)	9(31.0)		0.0414	3(75.0)	1(25.0)	0.3174
P+++	14(63.6)	8(36.4)		0.2014	0(0.0)	0(0.0)	
Gastritis 59(66.3)	30(33.7)			0.0024	19(73.1)	7(26.9)	0.0194
Gastritis							
Mild	13(56.5)	10(43.5)		0.5324	18(72.0)	7(28.0)	0.0284
Moderate	36(70.6)	15(29.4)		0.0034	1(100.0)	0(0.0)	-
Severe	10(66.7)	5(33.3)		0.1974	0(0.0)	0(0.0)	

42-proportion Z-test, 3Chi-Square Test

Table 6
Parameters estimates of Adjusted Odds Ratios and 95% CI

		Cases		
Predictora	Category	Estimate (se)	OR (95% CI)	P -Value
Intercept	Constant	-3.60 (2.081)		0.083
Gender	Male		1	0.004
	Female	-1.99 (0.70)	0.1 (0.0, 0.5)	
Age	Age	0.10 (0.05)	1.1 (1.01, 1.2)	0.042
Marital Status	Married		1	0.022
	Single	2.50(1.08)	12.1(1.7, 121.1)	
	Divorced	3.24(1.01)	25.522(4.1, 230.7)	
	Widowed	0.95(1.64)	2.6(0.1, 105.6)	
	Separated	3.58 (1.71)	35.7(1.8, undefined)	
Religion	Christian	-0.55(0.65)	0.6(0.2, 2.2)	0.421

Note: n=93; OR: Odds Ratio; CI: Confidence Interval; se: Standard error; a: reference categories for categorical predictors

DISCUSSION

The findings of this study reveal that there is a significant risk of gastritis among adult Khat chewers in Nairobi County which is also positively associated with functional dyspepsia (OR 3.8, 95% CI: 1.6, 9.4). The upper GIT endoscopy results clearly indicated that cases with oesophagitis, gastritis and duodenitis that were Khat chewers had a prevalence of 66.0%, 65.2% and 71.9%, respectively. This outcome concurs with previous studies that have shown Khat use elicits GIT-related disorders such as gastritis, oesophagitis, and duodenitis (1, 11). The results equally reveal that of ulcer cases, 75.0% (21/28) were Khat chewers. This is supported by an observational study that documented a significant association of stomach and duodenal ulcers with Khat chewing (25).

Significantly, more Khat chewers were found to have erosions in their stomach and duodenum. Both the upper GIT endoscopy and the histological examinations of the biopsies showed that Khat chewing was associated with upper GIT erosivity (OR 4.0, 95% CI: 1.6, 10.1), with a four times more likelihood of upper GIT erosions than non-chewers. Previous studies reported that high amounts of tannin present in plants were suspected of having an ulcerogenic effect in the mouth, oesophagus and GIT in test animals (26, 27, and 28). At the same time, it was found that farmers use a number of pesticides in Khat cultivation, which causes considerable acute and chronic adverse effects on the digestive system (29).

Similarly the current study shows that Khat chewing is associated with *H. pylori* infection. Khat chewers and non-chewers were statistically different (p-value=0.042) among the two groups. The increasing prevalence and colonization of *H. pylori* may be a major role in pathogenesis of ulcers or the cause of the erosions.

Delayed gastric emptying was found to be more among Khat chewers, hence food intake while chewing was minimal. Complaints such as constipation, heartburn, bloating and abdominal pain were reported more among Khat chewers as illustrated in the results section of Table 4. These findings are similar to other studies that previously reported a significant decrease in gastric emptying time after Khat chewing (30). This contributes to an increased rate of gastro-oesophageal reflux manifested as heartburn and acid regurgitation, (30). Constipation was also found to be a common complaint among Khat chewers. Equally, Khat chewing is associated with significant delays of both the orocaecal transit time and the whole gut transit time, hence the delay in gastric emptying (31).Lack of appetite when chewing Khat as seen in this study may lead to other health complications. As Table 4 shows, only 26.7% (16/60) of cases were found to be taking food while chewing Khat, while in the control group it was 83.7% (36/43). These findings points to the formation of a coating in the stomach lining that may absorb the responsible chemicals for gastritis and increase gut transit. Others have found that there is an association between Khat use and anorexia, hence malnutrition (32).

The study has also quantified Khat use to see if there was relationship between the quantity consumed, the duration of use and resulting health complaints. More than half (51.7%) of Khat chewers consumed a Marduuf or a bundle of 100 to 120 sticks while the reported frequency of Khat chewing among chewer cases was daily at 40.0%. These finding are similar to what has been reported by Getahun et al (33)

In conclusion, this study has shown that a positive association exists between Khat chewing and functional dyspepsia and gastritis. However, these findings call for further research especially in a longitudinal study which is more costly and time-consuming to strengthen our current case-control study findings. The association of regular Khat chewing and gastritis in the human population has direct relevance for public health studies. Regulatory bodies may need to devise strategies to counter the expansion of Khat chewing and other substance uses which pose continuing public health risks.

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