

Effect of Khat consumption on blood biochemical parameters: Evidences from the Ethiopian Non communicable diseases STEPS Survey, 2015

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Abstract

Background: Khat, *Catha edulis* leaves is grown in Ethiopia and consumed as a natural stimulant by chewing the young buds and tender leaves that contain the stimulant “Cathinone”. In Ethiopia, this habit has a deep-rooted socio-cultural tradition in which consumers spend part of their time chewing khat. The effect of this habit on blood constituent has not been adequately studied in humans.

Objective: To analyze the effect of khat chewing on the level of clinical biomarkers in blood.

Methods: This analysis used data from the Ethiopian 2015 Non communicable diseases STEPS Survey. A total of 9,800 households were selected from the 513 enumeration areas. All men and women aged 15-69 years who had been living at their place of residence for at least six months prior to the survey were included in the study. Data were collected using WHO STEPS questionnaire and current khat chewing and associated factors. The descriptive statistics as well as the association tests were carried out using SPSS Version 20.

Results: The khat chewers showed significantly higher median fasting blood glucose and weight ($p<0.0001$), lower median total cholesterol ($p<0.05$), HDL and LDL than the non-khat chewers ($p<0.0001$). The sub analysis showed that, male khat chewer showed significantly higher median fasting blood glucose ($p<0.0001$) and median total cholesterol ($p=0.009$) and significantly lower median HDL than the non-khat chewer ($p<0.05$). Among female khat chewers showed significantly higher fasting blood glucose ($p<0.0001$), total cholesterol, Body mass index and weight than the females non- khat chewers ($p<0.05$). In urban dwellers, khat chewers showed significantly higher weight, BMI, and fasting blood glucose ($p<0.0001$), TG ($p<0.05$) and lower HDL ($p<0.0001$) than non- khat chewers ($p<0.05$). Moreover, in rural dwellers, khat chewers showed significantly higher weight, fasting blood glucose ($p<0.0001$), lower HDL and LDL ($p<0.0001$) and lower total cholesterol ($p=0.028$) than non- khat chewers.

Conclusion: Findings from this study demonstrate that khat chewer have altered blood biochemical parameters. Health promotion should be aimed to encourage quitting khat chewing considered to the general community and the public health authorities.

Keywords: khat, biochemical parameter, khat chewer, Ethiopia

Introduction

Khat, *Catha edulis*, belongs to the family, Celastraceae, it is an evergreen shrub that is planted and chewed in eastern through southern parts of Africa and the Arabian Peninsula. The cultivation originated in Ethiopia, and exported to Djibouti, Somalia, Kenya, Uganda, Tanzania, Zimbabwe, Zambia, South Africa and Yemen (Berhanu et al. 2014). It is commonly chewed to enhance concentration, self-confidence, creativity and imagination as well as communication abilities to associate ideas by virtue of its euphoric and stimulant effects (al'Absi et al. 2013; Damena et al. 2011). Globally, it is estimated that 5 to 10 million people consume khat each day, although its use is largely confined to East African countries and south western Arabia (Aseffa 1983; Erica et al. 2009). In Ethiopia, according to the 2011 Ethiopian Demographic Health Survey, the trends in women and

men who ever chewed 11% in 2011 and 12% in 2016 among women and 28% in 2011 and 27% in 2016 among men (CSA and ICF 2011; CSA and ICF 2017). Sometime later, the Ethiopian STEPs wise survey report on risk Factors for non-communicable disease and prevalence of selected NCDs showed that, the percentage of khat chewer (daily and non-daily chewer) were 15.8% (Teklie et al. 2017). This report has also showed the existence of more men khat chewer (21.1%) than women (9.4%) did, higher rural (16.8 %) khat consumers than urban dwellers (11.5%) (Teklie et al. 2017). The consumption of khat was found to be a common practice among university students, as they think that, it helps increase their academic performance, especially during exams and for recreational purposes (Hussain 2013; Deressa and Azazh 2011). Various studies have showed that the prevalence of khat chewing in Ethiopian university

students ranged from lowest 6.7% to highest 56.8% (Berhanu et al. 2014; Aseffa 1983; Deressa and Azazh 2011). In Ethiopia, there are various factors that are associated with chewing khat; such as, regions (Afar, Dire Dawa, Harari, and Somali), urban areas and tobacco users (Teklie et al. 2017).

Its chronic and excessive chewing practice has been related to serious social, psychological, sexual, economic, and health problems. High level and long-term consumption of khat have resulted in cognitive impairment, learning problems and behavioral abnormalities, dental, cardiovascular, gastrointestinal and genitourinary problems, and increment in adrenocorticotrophic hormone levels (al'Absi et al. 2013; Al-Habori 2005; Colzato et al. 2011). Hence, WHO classified khat as a possible drug of abuse, though with less addictive potential than alcohol or tobacco (Nutt et al. 2007). It also causes urine retention and gall bladder motility, gastro-intestinal tract constipation and hemorrhage (Berhanu et al. 2014; Hassan et al. 2000; Dhaifalaha and Santavy 2004; Selassie and Gebre 1996). Despite its publicized health consequences, the practice of khat use is increasing globally and becoming an everyday chewing culture for many people of East Africa, including Ethiopia (Selassie and Gebre 1996).

The effect of khat on blood parameters are not well established. Study conducted in Yemen indicates that the clinical parameters in blood showed a significant increment of urea, bilirubin and creatinine in khat chewer group compared with control (non-chewer) group, while glucose, albumin and total protein were significantly decreased in khat chewer group (Naji et al. 2012). Other study also showed there is a decrease in plasma triglycerides, total cholesterol, and LDL-cholesterol in khat chewing (Al-Zubairi et al. 2003). The study conducted in Yemen also shows the khat chewers have a better mean HbA1c and lower mean body mass index than the non- khat chewers (Al-Sharafi and Gunaid 2015). Furthermore, significant increase in lipid peroxidation biomarkers thiobarbituric acid reactive substances (TBARS), decrease in Levels of Catalase (CAT) and Glutathione (GSH) also observed in khat chewer than non- khat chewers (Al-Ashwal et al. 2013). However, there was no nationally representative study conducted on the consequences of khat on blood parameters in Ethiopia. Therefore, this study aimed to analyze the consequences of khat chewing on blood parameters using the 2015 national Non-Communicable Disease STEPS survey data.

Materials and Methods

Study design and setting: This analysis used data from the Ethiopian 2015 NCDs STEPS Survey. Detailed methods were presented in the assessment report (EPHI/MoH/WHO, 2016). Briefly, it was a cross-sectional community-based study, data were collected from April to June, 2015 in 9 regions (Amhara, Oromia, Tigray, and Southern Nations, Nationalities, and Peoples, Gambella, Somali, Benshangul Gumz, Afar) and two city administrations (Addis Ababa and Dire Dawa) of Ethiopia. The survey included all men and women age 15 – 69 years old who had lived at their place of residence for at least six months before the study. Individuals who were not a permanent resident of Ethiopia, who were institutionalized—including people residing in hospitals, prisons, nursing homes, and other similar institutions or residents whose primary residences are military camps or dormitories, critically ill, mentally disabled and those with some type of physical disability that is not suitable for physical measurement were excluded from this study.

Sampling and size determination: A single population-proportion formula ($X = z_{\alpha/2}^2 p(1-p)/d^2$) was used to determine the sample size. The assumptions used to estimate the sample size were, design effect = 1.5, Z-score = 1.96; proportion = 35.2%; marginal error = 0.04, design effect = 1.5; age-sex estimate and place of residence—sex estimate = 10 groups, and non-response rate = 20%. A total of 513 Enumeration Areas (404 rural EAs and 109 urban) were identified to have representation at national level. Taking into account the cost of the study and the level of precision—20 Households (HHs) per EA were selected using systematic random sampling and one eligible individual from each HH was selected using the Kish method (a random selection of eligible individuals at HH level). The final sample size was calculated to be 10,260 study participants.

Data collection tools: The survey was conducted using the WHO NCD STEPS instrument version 3.1. 2008 (WHO STEPS 2009) Step 1, Questionnaires based on interview on socio demographic data and behavioral status. Step 2, Physical measurement (such as height, weight, and hip circumference) Step 3: Biochemical measurement (fasting blood glucose, triglycerides, cholesterol, LDL and HDL). The sample determination and sampling procedure described in the report published in 2015 (EPHI/MoH/WHO, 2016).

Data collection and management: The data were collected by trained nurses and lab professionals with face to face interview. Data were collected using Personal Digital Assistants (PDA). The files were then transferred to a central server located at Ethiopian Public Health Institute (EPHI), Addis Ababa via Internet File Streaming System (IFSS). Data were managed using SPSS Version 20.

Physical measurement and biochemical analysis: Physical measurements: Body weight and height was measured with the electronic Growth Management Scale. It measures body weight and height, and calculates body mass index (BMI) (Body weight (kg)/ Body height/ (m²)). Boso Uno, fully automatic upper arm Blood pressure monitor with universal cuff from Bosch was used to take blood pressure. Laboratory tests were performed for blood glucose, total cholesterol and HDL cholesterol using CardioCheck PA analyzer (Polymer Technology System Inc., Indianapolis, IN) and for triglycerides using Cobas Integra 400 Plus (Roche Diagnostics GmbH, Mannheim, Germany) clinical chemistry analyzer. Concentrations of glucose (raised blood glucose level and percentage of respondents currently on medication for raised blood glucose), and lipid profile (total cholesterol, HDL (high-density lipoprotein), LDL (low -density lipoprotein), BMI (body mass index), TG (triglycerides) were measured the next day after STEPS 1 and 2 data collection. Eight hours fasting blood tests for glucose was performed for all survey respondents using a CardioChek PA Analyzer.

Data analysis: Descriptive analysis was used to describe the Socio-demographic characteristics of the respondents. The normal distribution of the biochemical parameters among the khat chewers and non-chewers were tested, Kolmogorov-Smirnov and Shapiro-Wilk result showed that $p < 0.05$, indicated that

the distribution were not normal. Thus, the independent samples Mann-Whitney U-test was used to show the significant differences between the biochemical tests with the khat chewers and non- khat chewers. The analysis was further stratified by gender and residence of the respondents. The data analysis was done using SPSS, Version 20 (SPSS Inc.). The significance level was set at a P-value of less than 5%.

Ethics approval: The primary study was reviewed and approved by Institution Review Board of Ethiopian Public Health Institute (EPHI) and National Ethics Review Committee of Ministry of Science and Technology. This further analysis was exempted from review.

Results

Out of, 9,800 respondents, more than half (59.4%) were females, 40.4% were aged between (15-29 years), 49% of them were without formal education and about 73% of the respondents were from the rural parts of the country. One-fifth (19%) of the respondents reported chewing khat at least once in their life time, and of these, 82% of them were current khat chewers (Table 1). The median fasting blood glucose value, total cholesterol, HDL, LDL and TG of khat chewers were 81.0, 130.0, 37.0, 91.3 and 103.3 mg/dl, respectively; while for the non- khat chewer it was 78.0, 132.0, 40.0, 96.1 and 103.0 mg/dl were fasting blood glucose, total cholesterol, HDL, LDL and TG, respectively. The median fasting blood glucose of the khat chewers and weight were found to be significantly higher than the non- khat chewers ($p < 0.0001$). The khat chewers had significantly lower median total cholesterol ($p < 0.05$), HDL and LDL than the non- khat chewer ($p < 0.0001$). However, the difference in body mass index and TG between the two groups were not significant (Table 2).

Table 1: Socio-demographic characteristics of the khat Chewer and non- khat chewer participants from 2015 Ethiopian STEPS survey

Characteristics	Categories	N	%
Gender	Male	3977	40.6
	Female	5823	59.4
Age (years)	15 - 29	3959	40.4
	30 - 44	3499	35.7
	45 - 59	1690	17.2
	60+	652	6.7
Education Level	No Schooling	4843	49.4
	Less than primary school	2818	28.8
	Primary school completed	975	9.9
	secondary school completed	653	6.7
	College/University completed	511	5.2
Residence	Urban	2742	27.3
	Rural	7287	72.7
Ever chewed khat?	Yes	1881	19.2
	No	7909	80.8
Currently chew khat?	Yes	1546	82.2
	No	334	17.8

Table 2: The Biochemical parameters of khat Chewer and non- khat chewer, from 2015 Ethiopian STEPS survey

	khat chewers		Non chat chewers		Sig (2sided test)
	n	Median (IQR)	n	Median (IQR)	
Weight (kg)	1818	55.5(12.2)	7463	53.0 (12.2)	<0.0001
BMI(kg/m ²)	1818	20.3(3.8)	7462	20.3(3.7)	0.377
Fasting blood glucose (mg/ml)	1678	81.0 (23.0)	7103	78.0 (19.0)	<0.0001
Total cholesterol (mg/dl)	1710	130.0 (45.0)	7221	132.0 (48)	0.016
HDL Cholesterol (mg/dl)	1697	37.0 (17.0)	7196	40.0(17.0)	<0.0001
LDL (mg/ml)	1574	91.3(43.9)	6621	96.1(47.5)	<0.0001
TG (mg/ml)	1574	103.3 (68.0)	6621	103.0 (63.6)	0.521

HDL= high-density lipoprotein-cholesterol, LDL = low -density lipoprotein-cholesterol, BMI=body mass index, TG= triglycerides, IQR = Inter quartile Range

Table 3 shows the sub analysis of the biochemical parameter differences of the khat chewer and non- khat chewer of respondents by gender. A Female khat chewer, had higher median fasting blood glucose ($p<0.0001$), total cholesterol, body mass index and weight than the non- khat chewers females ($p<0.05$). The study had found there is no significant difference in HDL, LDL and TG between the khat chewer and non- khat chewers. Male khat chewers had

significantly higher median fasting blood glucose ($p<0.0001$) and total cholesterol ($p<0.05$) than the non- khat chewers. Significantly lower median HDL level was observed in the khat chewers than the non- khat chewer ($p<0.05$). Furthermore, there were no significant difference in body mass index, LDL and TG between the males khat chewers and non- khat chewers (Table 3).

Table 3: The Biochemical parameters of khat Chewer and non- khat chewers, subcategorized by Gender, from 2015 Ethiopian STEPS survey

	khat chewers		Non chat chewers		Sig (2sided test)
	n	Median (IQR)	n	Median (IQR)	
Female Respondents					
Weight (kg)	630	52.0(12.5)	4741	51.0(11.8)	0.041
BMI(kg/m ²)	630	20.6(3.9)	4740	20.4(3.9)	0.031
Fasting blood glucose (mg/ml)	611	84.0 (21.0)	4617	78.0 (19.0)	<0.0001
Total cholesterol (mg/dl)	620	141.0 (48.0)	4686	139.0 (48.0)	0.048
HDL Cholesterol (mg/dl)	616	41.0 (16.0)	4675	42.0 (17.0)	0.882
LDL (mg/ml)	571	102.2 (44.5)	4311	101.0 (47.6)	0.860
TG (mg/ml)	571	100.0 (64.2)	4311	102.0 (63.4)	0.303
Male Respondents					
Weight (kg)	1188	56.8 (11.3)	2722	56.5 (11.0)	0.059
BMI(kg/m2)	1188	20.0 (3.6)	2722	19.9 (3.3)	0.777
Fasting blood glucose (mg/ml)	1067	79.0 (23.0)	2488	77.0 (19.0)	<0.0001
Total cholesterol (mg/dl)	1090	123.0 (42.0)	2535	120.0 (45.0)	0.009
HDL Cholesterol (mg/dl)	1081	35.0 (16.0)	2521	37.0 (16.0)	0.003
LDL (mg/ml)	1003	86.0 (40.4)	2310	87.0 (45.9)	0.797
TG (mg/ml)	1003	105.2 (69.2)	2310	105.0 (64.6)	0.233

HDL= high-density lipoprotein-cholesterol, LDL = low -density lipoprotein-cholesterol, BMI=body mass index, TG= triglycerides, IQR = Inter quartile Range

Table 4 shows the biochemical parameter difference among the khat chewer and non- khat chewer stratified by residences. Urban resident khat chewers had a median value of 83.0, 141.0, 38.0, 108.0 and 114.2 mg/dl Fasting blood glucose, Total cholesterol, HDL, LDL and TG of female khat chewers were, respectively. The urban dwellers khat chewers had a significantly higher median weight, fasting blood glucose ($p<0.0001$) and TG (0.017), and significantly lower median HDL than the non- khat chewers ($p<0.0001$). However, there was no significant

difference in Total cholesterol and LDL between the khat chewer and non- khat chewers urban dwellers. The khat chewers of rural dwellers showed a low blood biochemical parameter than the urban khat chewers. The khat chewers of rural dwellers showed significantly higher weight, fasting blood glucose ($p<0.0001$), lower HDL and LDL ($p<0.0001$ and lower total cholesterol ($p<0.05$) than the non- khat chewers of rural dwellers. However, there was no significant difference in BMI and TG between the khat chewer and non- khat chewers urban dwellers.

Table 4: The Biochemical parameters of khat chewer and non- khat chewers, subcategorized by residence (Urban and Rural), from 2015 Ethiopian STEPS survey

	Khat chewers		Non chat chewers		Sig (2sided test)
	n	Median (IQR)	n	Median (IQR)	
Urban respondents					
Weight (kg)	441	60.0 (17.0)	2106	56.0 (15.5)	<0.0001
BMI(kg/m ²)	441	21.8 (6.1)	2106	21.6 (5.1)	0.031
Fasting blood glucose (mg/ml)	396	83.0 (23.0)	1924	79.0 (19.0)	<0.0001
Total cholesterol (mg/dl)	406	141.0 (51.0)	1969	144.0 (51.0)	0.778
HDL Cholesterol (mg/dl)	404	38.0 (17.0)	1964	42.0 (17.0)	<0.0001
LDL (mg/ml)	370	108.0 (49.6)	1812	110.5 (51.0)	0.631
TG (mg/ml)	370	114.2 (79.1)	1812	111.0 (69.9)	0.017
Rural respondents					
Weight (kg)	1377	54.3 (11.0)	5357	52.2 (11.4)	<0.0001
BMI(kg/m ²)	1377	19.8 (3.3)	5356	19.9 (3.3)	0.312
Fasting blood glucose (mg/ml)	1282	80.0 (22.0)	5178	77.0 (19.0)	<0.0001
Total cholesterol (mg/dl)	1304	125.0 (42.0)	5252	127.0 (46.0)	0.028
HDL Cholesterol (mg/dl)	1293	37.0 (16.0)	5232	39.0 (18.0)	<0.0001
LDL (mg/ml)	1204	86.4 (40.2)	4809	91.1(44.8)	<0.0001
TG (mg/ml)	1204	101.0 (65.1)	4809	100.6 (61.0)	0.769

HDL = high-density lipoprotein-cholesterol, LDL = low -density lipoprotein-cholesterol, BMI=body mass index, TG= triglycerides, IQR = Inter quartile Range

Discussion

In this study, significantly higher fasting blood glucose and weights were observed in khat chewer as compared to the non- khat chewer. The khat chewers showed significantly lower total cholesterol, HDL and LDL than the non- khat chewer. The findings disclosed the effect of khat chewing on the level of clinical biochemical blood parameters. Several steps were taken to ensure the quality of the data collected. All data collectors received five days training. Regular supervision of questionnaire completion, along with using electronic data collection approaches contributed to high quality. In addition, the electronic transfer system was utilized regularly reviewed the quality of the data and provided feedback while the data collectors were still in the field.

The khat chewers showed significantly lower total cholesterol, HDL and LDL than the non- khat chewer. This result is supported by the study conducted in Yemen (Naji et al. 2012) showed that total cholesterol is lower in khat chewer than the non- khat chewers. The current findings were also supported by study of (Al-Habori and Al-Mamary 2004) who demonstrated the same findings on the levels of plasma lipids on experimental animals who were fed khat. Other evidences negate these findings that the level of total cholesterol in khat chewers were greater than the non-khat chewers and the level of glucose in khat chewers were less than the non- khat chewers (Naji et al. 2012; Al-Ashwal et al.2013). Moreover, study conducted in Yemen, showed that there was no significant difference in the levels of total cholesterol and triglyceride, non-significant decrease in the level of low-density lipoprotein-cholesterol and non-

significant increase in the level of high-density lipoprotein-cholesterol among the khat chewers in comparison with the non-chewer (Atef et al. 2017). This indicates that despite variations in study area, the case control study and difference in source population as using diabetic patients as a source population may use treatment for their diseases conditions of the previous study.

Our study showed the difference in the level of blood biochemical levels in male khat chewers and non-chewers. Male khat chewer significantly higher fasting blood glucose, weight gain, total cholesterol, lower HDL, and no significance difference in LDL and TG than the non- khat chewers. Supporting to our study, studies showed that the level of total cholesterol in khat chewers were greater than the non- khat chewers (Naji et al 2012; Al-Ashwal et al. 2013), however, the level of glucose in khat chewers were less than the non- khat chewers from the case control study conducted on male khat chewers. Other study (Al-Dubai et al. 2006) on human also showed that no effect of fresh khat on the plasma cholesterol and triglycerides in male khat chewers for after 4-hour khat administration, while the analysis of the present study is a cross sectional-based study on currently chewing of khat.

The khat chewers of urban dwellers showed significantly higher weight and fasting blood glucose, lower HDL than the non- khat chewers of urban dwellers, while the khat chewers of rural dwellers showed significantly higher weight, fasting blood glucose, lower HDL and LDL than the non- khat chewers of rural dwellers. In this study, significantly higher median body weight was observed in khat

chewer respondents as compared to the non- khat chewer respondents. This finding is in line with the study conducted in type-2 diabetic mellitus groups that showed khat chewers higher mean body weight compared to non-chewer diabetic patients (Al-Sharafi and Gunaid 2015). However, other cross-sectional studies in urban healthy humans showed that khat chewers were associated with less mean body weight compared to non-chewers (Girma et al 2015). This variation may due to the study area, almost half of the study participants (48%) had a history of ever chewing Khat and one third of participants were current chat chewer (36%) which higher than this national study.

In this analysis, the khat chewers did not show significant difference in BMI than the non- khat chewers except in the case of male khat chewer and urban residents that showed a significant larger median body weight than their counterparts. However, a cohort study (Al-Dubai et al. 2014) showed a reduction of BMI among 19 to 23 years khat chewer respondents compared to non- khat chewers. Further study is required to substantiate this finding in higher age groups.

In this study, significantly higher fasting blood glucose was observed in khat chewer respondents as compared to the non- khat chewer respondents. This finding is also in line with the study conducted in Yemen, there was a non-significant increase in the level of blood glucose among khat chewers with type 2 diabetes patients (Atef et al. 2017). These findings may be explained by the fact that the sympathetic action of khat may increase glucose production through activation of glycogenolysis especially that of muscles, which leads to increase in the level of blood glucose by an indirect mechanism through increased glycolysis and subsequently release of lactate, which is transported to the liver where it serves as a gluconeogenic substrate (Shafirir and Bergman, 1987). The study is not without limitations. First, it is not possible to establish causal relationship between the independent and outcome variables such as khat chewing and the level of biochemical blood parameters because of the nature of the study.

This study has a number of policy implications. Since One-fifth of the respondents reported chewing khat at least once in their life time and chewing khat caused altered blood biochemical parameters public health intervention including health education and promotion aimed to encourage to quit chewing khat should be implemented.

Conclusion

Chewing khat could result for increased level of blood glucose and body weight and lower total cholesterol, HDL and LDL. The effect of chewing khat among female was increased blood glucose and total cholesterol. Exceptional to females, there was significantly lower HDL level among khat chewers. The findings from this study demonstrate that khat chewer have altered blood biochemical parameters, these may contribute in the failure of the body organs. This analysis adds evidence to the limited evidence on the effects of khat chewing on the level of blood parameters in Ethiopia. However, further detailed studies are recommended and health promotion should be considered to the general community and the public health authorities. Further study needs to be substantiated with prospective longitudinal study to ascertain the effects of the frequent use khat.

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