

Impact of chronic khat (*Catha edulis* Forsk) chewing on pulmonary function test and oxygen saturation in humans: A comparative study

SAGE Open Medicine

Volume 7: 1–7

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DOI: 10.1177/2050312118824616

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Abstract

Background: Chronic consumption of khat affects many organ systems and leads to various health disturbances in the chewers. Few studies examined the acute effects of khat ingestion on lung function parameters. However, studies which assessed the long-term effects of khat chewing on pulmonary function parameters and oxygen saturation are lacking.

Objective: The aim of this study was to assess the impact of chronic Khat chewing on pulmonary function parameters and oxygen saturation among chronic Khat chewers in Wolkite, Ethiopia.

Methods: A community-based comparative cross-sectional study was conducted in Wolkite, Ethiopia from 1 June 2018 to 15 August 2018. A total of 324 participants, 162 khat chewers and 162 non-chewers were included in the study. The data were collected through face-to-face interview by trained data collectors. British Medical Research Council respiratory questionnaire was used to assess respiratory symptoms. A spirometer was used to assess various lung function parameters. Moreover, oxygen saturation of hemoglobin was measured using pulse oximeter. Data were entered into CSPro version 6.2 and analyzed using SPSS version 23.

Results: This study showed statistically significant ($p < 0.05$) reduction in the mean values of forced vital capacity, forced expiratory volume in first second and maximum ventilation volume among khat chewers as compared to non-chewers. There was no significant difference in the mean values of other lung function parameters between the two groups. Similarly, there was no significant difference ($p = 0.642$) in mean oxygen saturation of hemoglobin (SaO_2) across the two groups.

Conclusion: It is evident from this study that long-term khat consumption is associated with decreased mean forced vital capacity, forced expiratory volume in first second and maximum ventilation volume. Hence, there is a need for further study to strengthen the current findings and to explore the mechanisms of khat chewing effect on lung function parameters.

Keywords

Khat, pulmonary function tests, oxygen saturation

Date received: 19 October 2018; accepted: 20 December 2018

Introduction

Khat refers to the leaves and the young shoots of the plant *Catha edulis* Forsk, which belonging to the plant family Celastraceae.^{1–3} Khat is an evergreen tree grown mainly in the Middle East and East Africa including Ethiopia.¹ There have been concerns raised about the physiological disturbances associated with or caused by the use of khat.⁴

Khat contains many different compounds including alkaloids, terpenoids, flavonoids, sterols, glycosides, tannins, amino acids, vitamins and minerals.^{2,5} Of these, emphasis has been given mainly to cathinone. It is the constituent mainly responsible for the effects of khat and has amphetamine-like

effects in humans.⁶ When cathinone is broken down in the body, it produces chemicals including cathine and norephedrine, which have a similar structure to amphetamine and adrenaline.⁷

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The chewing of khat leaves is common in certain countries of East Africa and Arabian Peninsula mainly Yemen but is much less prevalent in other areas of the world.^{8,9} Chewing khat may have many adverse effects.² The main effects are on the nervous system and gastro-intestinal system.⁵ Moreover, it affects cardiovascular, respiratory, endocrine^{2,5} reproductive systems¹ and has psychiatric effects.⁵

Chronic consumption of khat can cause various health disturbances in the chewer⁹ including esophagitis, gastritis, duodenal ulcer, liver damage, depression, autoimmune hepatitis, migraine, cerebral hemorrhage, constipation, malnutrition, myocardial infarction, pulmonary oedema,^{7,8,10} tachypnea and bronchitis.^{4,11} Khat usage is also associated with memory impairment, psychoses and psychological dependence.^{7,12} Moreover, it leads to socioeconomic damage to the individual or the community.⁹

The active ingredients of khat have sympathetic-like effects on lung volumes and ventilatory capacity.¹³ Study conducted in humans showed that acute ingestion of khat leaves leads to an overall increase in the total lung volume and functional capacities. Pulmonary indices which showed significant increment after khat chewing includes vital capacity (VC), forced vital capacity (FVC), forced expiratory volume in first second (FEV₁), peak expiratory flow rate (PEFR) and forced expiratory flow 25–75% (FEF_{25–75%}).¹³

Another study conducted by Freund-Michel et al.¹⁴ reported that cathinone presynaptically inhibits acetylcholine release from airway parasympathetic nerves through activation of both $\alpha 2$ and 5-hydroxytryptamine 7 presynaptic receptors that may contribute to the beneficial effects of khat in airway diseases.

The effects of long-term khat chewing on pulmonary function are not clearly defined. There is lack of previous published study on the assessment of lung function indices among chronic khat chewers. While knowledge and understanding of the problems associated with khat use has been increasing, there is a need to further understand the effect of khat chewing on pulmonary functions. Hence, the present study was undertaken to assess the effect of khat chewing on pulmonary function test and oxygen saturation of hemoglobin among chronic Khat chewers in Wolkite, Ethiopia.

Methods

Study setting and design

This study was conducted in Wolkite town of Gurage Zone, Southern Ethiopia. Wolkite town is the capital city of Gurage zone and located 158 km away from Addis Ababa, the capital city of Ethiopia. The total population of Wolkite town is estimated to be 28,866.¹⁵ A community-based comparative cross-sectional study was conducted to assess the effect of khat chewing on pulmonary function test and oxygen saturation of hemoglobin. The study was conducted from 1 June 2018 to 15 August 2018.

Study population and sampling techniques

The participants of this study were adults who never chewed khat and those who chewed khat during the past 5 years. The inclusion criteria for this study were adults between the ages of 18–65 years and those who were volunteered to participate in the study. Smokers, athletes, pregnant women, those on chronic therapy for any diseases, those who had previous history of cardio-respiratory disease, other chronic diseases (diabetes, hypertension, renal diseases, etc) and any contraindication for lung function tests were excluded from the current study.

The required sample size for this study was calculated using the general formula for comparison of two means.¹⁶ The sample size was estimated by considering the mean PEFR and standard deviation measured in a previous study,¹³ 95% confidence interval (CI), 80% power, khat chewer to non-chewer ratio of 1:1 and 10% non-response rate. Hence, a total of 324 participants (162 khat chewers and 162 non-chewers) who fulfill the eligibility criteria were recruited in the study. Using the sampling frame of the town household lists, sample households were selected randomly. Individuals residing in the household that fulfilled the inclusion criteria were selected until the required sample size was attained. Khat chewers and non-chewers were selected using the same procedures.

Data collection procedures

A modified version of British Medical Research Council (BMRC) respiratory questionnaire¹⁷ was used to record personal information and respiratory symptoms. Moreover, khat chewing status of the participants was collected using pre-tested structured questionnaires (see supplemental material). The data were collected on a face-to-face interview by trained data collectors. After interview, anthropometric measurements were done. Height was measured and recorded to the nearest 0.1 cm using an erect height measuring device. Weight was measured and recorded to the nearest 0.1 kg using a standard balance. Body mass index (BMI) of the study participants was then calculated from the body weight and height (weight in kilograms divided by square of height in meters).¹⁸

Lung function was measured using a digital portable Spirometer (Spirolab MIR, Italy) based on the American Thoracic Society (ATS) guidelines¹⁹ and all khat chewers consumed khat before 12 h from the time of lung function measurements. Before performing pulmonary function test, the test procedure was clearly explained to all subjects. Each subject was advised to sit and take rest for at least 5 min. Then after, the relaxed subject wore a nose clip and prepared to grip the sterile mouth piece. When the subject was ready, he or she was asked first to perform maximal inspiration after a deep expiration. The subject was then instructed to breathe out quickly with maximum effort through the mouth piece. The mouth piece was then removed and the actual, predicted and percentage values of lung function parameters were printed for analysis. Each test was repeated for a minimum of three times with adequate rest in between, and the

best of the three reading was recorded for analysis. The parameters taken during lung function test includes FVC, FEV₁, FEV₁%, FEF_{25%}, FEF_{50%}, FEF_{75%}, FEF_{25–75%}, forced expiratory time (FET), PEFR and maximum ventilation volume (MVV). Besides lung function test, arterial oxygen saturation of hemoglobin (SaO₂) was measured using pocket size digital pulse oximeter (Shenzhen Creative Industry Co. Ltd, Germany).²⁰

Data quality control

To ensure good quality of data, training was given for all data collectors. The collected data were checked for completeness and consistency at the end of each day. The questionnaires were pre-tested and some corrections were undertaken accordingly. The spirometer was regularly checked prior to every measurement. All test procedures were carried out at a fixed time of the day and performed by the same instructions to ensure its validity.

Data analysis

Data were coded and entered into CSPro version 6.2 and then exported to Statistical Package for Social Science (SPSS) version 23 for analysis. Descriptive statistics was used to summarize socio-demographic and Khat chewing status of the participants. While chi-square (χ^2) tests were used to compare categorical variables, continuous variables were compared using independent sample t-test. A p-value of <0.05 was considered as statistically significant.

Operational definitions

Based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, we classified subjects into the following categories using the FEV₁, FVC and FEV₁/FVC ratio as severe obstructive lung diseases (FEV₁/FVC <0.70 and FEV₁ $<30\%$ predicted), moderate obstructive lung diseases (FEV₁/FVC <0.70 and FEV₁ $\geq 30\%$ to $<80\%$ predicted), mild obstructive lung diseases (FEV₁/FVC <0.70 and FEV₁ $\geq 80\%$), restrictive lung diseases (FEV₁/FVC ≥ 0.70 and FVC $<80\%$ predicted), symptoms only (if they had symptoms of cough, phlegm, wheeze or shortness of breath) and no lung diseases.^{21,22}

Results

Socio-demographic characteristics

A total of 324 (162 chewers and 162 non-chewers) participants were involved in the study. Out of the total study participants, 176 (54.3%) were males and the overall mean age was 36.48 (± 10.66) years, within the range of 18–65 years. Majority of khat chewers and non-chewers were in age group of 28–37 years. The mean age of khat chewers and non-chewers was 37.11 (± 11.96) years and 35.85 (± 9.18) years,

respectively. Among the khat chewers, 93 (57.4%) were males, 101 (62.3%) were Muslim by religion, 100 (61.7%) were married, 79 (48.8%) had more than high school education and about 75 (46.3%) were government employed. Except the marital status, there was no significant difference in socio-demographic characteristics of chewers and non-chewers ($p > 0.05$) (Table 1).

Anthropometric measurements

The mean ($\pm$ SD (standard deviation)) height and weight of the participants were slightly higher among Khat chewers than non-chewers. But, mean BMI was found to be higher among non-chewers as compared to chewers. However, there was no significant difference between khat chewers and non-chewers with regard to the mean height, weight and BMI ($p > 0.05$) (Table 2).

Khat chewing status of the chewers

This study showed that out of the total participants who currently chew khat, 88 (54.3%) were start chewing within the age group of 15–24 years. The mean (SD) duration of khat chewing was 11.2 (± 7.70) years and majority, 119 (73.5%) of the Khat chewers chewed Khat for 5–14 years. Similarly, this study also found that among current chewers about 63 (38.9%) chew daily, 100 (61.7%) spent 2–3 h for single consumption and 68 (42%) were drink alcohol. The reported reasons for chewing Khat in this study include peer pressure, to stay awake, addiction, religious prayer and to increase social interaction. Majority of the chewers were chewing khat due to peer pressure (Table 3).

Pulmonary function tests

Independent sample t-test was conducted to compare lung function indices of khat chewers and non-chewers. The result showed that the mean values of FVC, FEV₁% and MVV were significantly ($p < 0.05$) lower among khat chewers as compared to non-chewers. However, most of the lung function values did not show significant difference ($p > 0.05$) between the two groups. Similarly, there was no significant difference ($p = 0.642$) in mean oxygen saturation of hemoglobin (SaO₂) across the two groups (Table 4).

Respiratory symptoms

The respiratory symptoms observed in khat chewers and non-chewers are shown in Figure 1. The percentage prevalence of cough was 26.5% for khat chewers and 14.8% for non-chewers. Of the participants with cough, 25 (37.3%) chewers and 12 (17.9%) non-chewers experienced cough for 3–4 days per week. Similarly, 7 (10.4%) chewers and 10 (14.9%) non-chewers had cough for 1–2 days per week. The rest of the participants (10 (14.9%) chewers and 3 (4.5%) non-chewers) experienced cough for 5–7 days per week. Moreover, the

Table 1. Socio-demographic characteristics of Khat chewers and non-chewers in Wolkite, Ethiopia, 2018.

Characteristics	Chewer (N = 162), n (%)	Non-chewer (N = 162), n (%)	Total, n (%)	p-value
Sex				
Male	93 (57.4)	83 (51.2)	176 (54.3)	0.265
Female	69 (42.6)	79 (48.8)	148 (45.7)	
Age (years)				
18–27	43 (26.5)	32 (19.8)	75 (23.1)	0.075
28–37	48 (29.6)	60 (37)	108 (33.3)	
38–47	45 (27.8)	55 (34)	100 (30.9)	
≥48	26 (16)	15 (9.3)	41 (12.7)	
Religion				
Muslim	101 (62.3)	31 (19.1)	132 (40.7)	<0.001
Orthodox	45 (27.8)	89 (54.9)	134 (41.4)	
Protestant	12 (7.4)	30 (18.5)	42 (13)	
Catholic	4 (2.5)	12 (7.4)	16 (4.9)	
Marital status				
Single	57 (35.2)	76 (46.9)	133 (41)	0.095
Married	100 (61.7)	81 (50)	181 (55.9)	
Widowed or divorced	5 (3.1)	5 (3.1)	10 (3.1)	
Educational status				
Illiterate	17 (10.5)	18 (11.1)	35 (10.8)	0.075
Primary school	41 (25.3)	28 (17.3)	69 (21.3)	
High school	25 (15.4)	16 (9.9)	41 (12.7)	
Certificate and above	79 (48.8)	100 (61.7)	179 (55.2)	
Occupational status				
Government employed	75 (46.3)	91 (56.2)	166 (51.2)	0.188
Self-employed	58 (35.8)	45 (27.8)	103 (31.8)	
Unemployed	29 (17.9)	26 (16)	55 (17)	

Table 2. Anthropometric measurements of khat chewers and non-chewers in Wolkite, Ethiopia, 2018.

Anthropometric Characteristics	Chewers (n = 162), Mean ± SD	Non-chewers (n = 162), Mean ± SD	Mean difference	p-value
Height (cm)	167.38 ± 7.45	166.37 ± 10.76	1.01	0.325
Weight (kg)	63.17 ± 8.59	61.19 ± 13.17	1.98	0.112
BMI (kg/m ²)	22.61 ± 3.23	23.18 ± 18.42	−0.57	0.697

presence of wheezing, phlegm, breathlessness and chest pain were observed in 6 (3.7%), 14 (8.6%), 14 (8.6%) and 2 (1.2%) of the chewers, respectively (Figure 1).

Proportions of respiratory diseases among the study participants

In the present study, obstructive pattern of lung function impairment was found in 70 (21.6%) participants; of these, 34 (10.5%) were khat chewers and 36 (11.1%) were non-chewers. Among the khat chewers, 6 (3.7%), 26 (16.1%) and 2 (1.2%) had mild, moderate and severe obstructive lung diseases, respectively. Similarly, 13 (8%), 21 (13%) and 2 (1.2%) of non-chewers had mild, moderate and severe obstructive lung diseases, respectively. This study also revealed that majority of khat chewers, 65 (40.1%), had restrictive patterns of lung diseases (Figure 2).

Discussion

A range of respiratory diseases can be caused by various factors. Hence, this study was done to investigate the effects of chronic khat chewing on pulmonary function parameters and oxygen saturation of hemoglobin. Our study compared mean pulmonary function parameters between chronic khat chewers and non-chewers in Wolkite, Ethiopia.

This study showed statistically insignificant difference in the mean values of most pulmonary function parameters between khat chewers and non-chewers. However, the mean FVC, FEV₁ and MVV were significantly lower among khat chewers as compared to non-chewers. Study conducted in humans after 2 h of khat chewing reported that ingestion of khat leaves leads to significant increment in the measurement of FVC, FEV₁, PEF, and FEF_{25–75%}. The explanation given for the increment of those parameters in the previous

Table 3. Khat chewing status of khat chewers in Wolkite, Ethiopia, 2018 (n = 162).

Characteristics	n (%)
Age at start of khat chewing (years)	
15–24	88 (54.3)
25–34	46 (28.4)
35–44	22 (13.6)
≥45	6 (3.7)
Chewing duration (years)	
5–14	119 (73.5)
15–24	30 (18.5)
≥25	13 (8)
Chewing frequency	
Daily	63 (38.9)
≥Three times per week	42 (25.9)
Two times per week	32 (19.8)
Once a week	25 (15.4)
Time spent on single chewing	
<1 h	42 (25.9)
2–3 h	100 (61.7)
>3 h	20 (12.4)
Amount of khat chewed per single consumption	
<1 bundle	49 (30.2)
1 bundle	104 (64.2)
2 bundle	9 (5.6)
Reason for chat chewing	
Peer pressure	90 (55.6)
To stay awake	30 (18.5)
Addiction	16 (9.9)
Religious prayer	12 (7.4)
To increase social interaction	14 (8.6)
Current alcohol drinkers	
Yes	68 (42)
No	94 (58)

study was due to reduction in airway resistance or an increased expiratory pressure after khat ingestion.¹³ The main active constituent of khat leaves, cathinone inhibits acetylcholine-induced contractions of the airway smooth muscle.¹⁴ Another study conducted by Dhaifalah and Santavy⁹ reported that cathinone can stimulate the respiratory center and increases in some lung function parameters after khat ingestion, which can explain the feeling of comfort for asthmatic khat chewers.

The acute and chronic effects of khat chewing may be different because of the effect of adaptation and down regulation of receptors and a resultant toxicity. Intoxication with khat is self-limiting, but chronic consumption can lead to different adverse effects.²³ However, the long-term effect of khat chewing on respiratory system has not been clearly elucidated. The reported adverse effect of khat chewing on the respiratory system includes bronchitis, tachypnea and dyspnea, but the mechanism is not clearly understood.²³ The present study can only suggest the possible effect of chronic khat chewing on lung function parameters, which should be substantiated by further investigations. In the

Table 4. Comparison of lung function parameters between Khat chewers and non-chewers in Wolkite, Ethiopia, 2018.

Measurements	Mean ± SD		p-value
	Chewer (n = 162)	Non-chewer (n = 162)	
FVC (L)	3.08 ± 1.28	3.38 ± 1.11	0.024
FEV ₁ (L/s)	2.39 ± 0.94	2.65 ± 0.94	0.015
FEV _{1%}	83.44 ± 17.75	82.19 ± 17.45	0.525
FEF _{25%}	3.33 ± 1.86	3.27 ± 1.72	0.779
FEF _{50%}	2.91 ± 1.63	2.88 ± 1.53	0.858
FEF _{75%}	2.12 ± 1.19	2.23 ± 1.12	0.379
FEF _{25–75%}	2.77 ± 1.45	2.78 ± 1.41	0.962
FET	2.16 ± 1.28	2.15 ± 0.96	0.925
PEFR	3.74 ± 1.93	3.85 ± 1.80	0.595
MVV (L/m)	81.69 ± 32.57	90.31 ± 32.19	0.017
SaO ₂	96.97 ± 1.65	97.06 ± 1.92	0.642

FVC: forced vital capacity; FEV₁: forced expiratory volume in first second; FEF: forced expiratory flow; FET: forced expiratory time; PEFR: peak expiratory flow rate; MVV: maximum ventilation volume; SaO₂: oxygen hemoglobin saturation.

Numerical data in italics indicate the level of significance ($p < 0.05$).

present study, the reduction in FVC, FEV₁ and MVV among khat chewers could possibly explain the decrease in the respiratory efforts or lung function after chronic consumption of khat. This is due to the fact that recording of FVC, FEV₁ and MVV needs respiratory efforts of the subjects. However, the reason or mechanisms for a negative effect of chronic khat chewing on FVC, FEV₁ and MVV in this study needs further investigation.

The present study also assessed respiratory symptoms (cough, phlegm, wheezing, breathlessness and chest illness) of the study participants. Accordingly, the percentage prevalence of cough was higher among khat chewers as compared to non-chewers (26.5% vs 14.8%) and the difference was statistically significant ($p < 0.05$). This might be due to the long-term effect of khat chewing on the respiratory system. Detailed studies on the effect of khat chewing on this organ system are lacking. However, the limited available data revealed that chronic khat chewing has a negative impact on respiratory system.^{8,10,24} But, evidence showing the clear casual link was not found. In this study, the percentage prevalence of remaining respiratory symptoms did not show significant difference across the two groups.

The present study investigated the prevalence and types of lung function impairments observed among the study participants. The result of this study showed that the prevalence of restrictive lung diseases was higher in khat chewers than in non-chewers. In restrictive lung disease, both FEV₁ and FVC are reduced. However, the decline in FVC is more than that of FEV₁, resulting in a higher FEV₁/FVC ratio. The predominant pathologic changes of restrictive lung diseases are found in the lung parenchyma or extrinsic to it.²⁵ Hence, chronic khat chewing may have a negative effect on the lung parenchyma or extraparenchymal structures. However, there

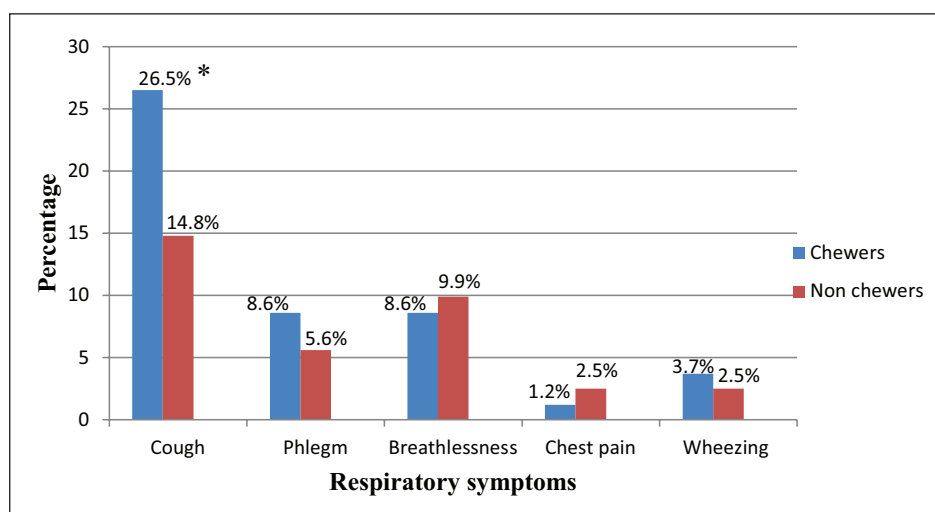


Figure 1. Respiratory symptoms of khat chewers (n = 162) and non-chewers (n = 162) in Wolkite, Ethiopia, 2018. The symbol “*” indicates $p < 0.05$ (statistically significant).

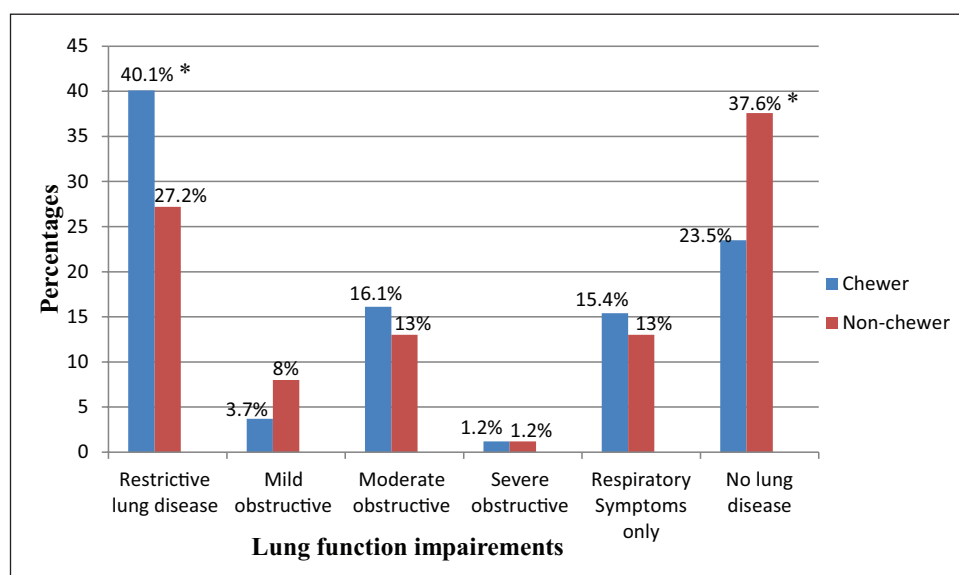


Figure 2. Percentages of khat chewers (n = 162) and non-chewers (n = 162) stratified by lung function category in Wolkite, Ethiopia, 2018. The symbol “*” indicates $p < 0.05$ (statistically significant).

is no any previous evidence relating to increased risk of restrictive lung diseases with chronic khat chewing. Thus, this finding should be confirmed by further studies.

This study had some limitations. Since many different compounds are found in khat, it is not known whether the effect of khat chewing on lung function tests in this study is caused by cathinone or by other khat constituents. The current study used duration of khat use as a reference for recruited khat chewers. However, the effect of khat chewing may vary depending on freshness, type, amount of khat chewed and the chewing pattern.^{5,26} Use of self-reported khat chewing duration may be subjected to recall bias. The reading of FVC could be influenced by the physiological variations between the two groups. However, efforts were

made to ensure that the two groups were comparable. Moreover, we could not identify subclinical cardiopulmonary and other systemic diseases that may affect the result of the study. Nevertheless, this study provides valuable information about the effect of long-term khat chewing on various pulmonary function parameters and oxygen saturation of hemoglobin.

In conclusion, this study has shown that long-term khat consumption is associated with decreased mean FVC, FEV₁ and MVV. However, further studies taking into consideration of the frequency of chewing, amount and type of khat to be chewed are needed to strengthen the current findings and to draw more systematic scientific conclusions about the long-term effects of khat on the lung function.

Acknowledgements

The authors would like to thank our data collectors for their kindly support in data collection and all study subjects who were volunteered to participate in the study. GGW: designed the study, collected data, analyzed it, interpret the result and prepare the manuscript for publication. TGG: participated in designing the study, data entry and interpretation of the results and reviewed the draft of the manuscript. Both authors read and approved the final draft of the manuscript.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Ethical approval was obtained from Institutional Review Board (IRB) of Wolkite University, Wolkite, Ethiopia with ethical approval reference number IRB/85/2010. In addition, letter of permission to conduct the study was obtained from Gurage Zone Health Bureau.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Informed consent

Data were collected after obtaining written informed consent from all study participants and confidentiality was maintained throughout the study. Written informed consent was obtained from all subjects before the study.

Supplemental material

Supplemental material for this article is available online.

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