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## KHAT USE AND KHAT INDUCED ORAL WHITE LESIONS AMONG KHAT AND TOBACCO USERS AT TWO SITES IN KENYA

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### Abstract

**Background:** Long term chewing of khat is associated with white lesions on the oral mucosa some of which depict histopathological changes. However, due to the limited number of studies in this area, the clinical nature of these white lesions has not been clearly defined, especially when khat is used alongside tobacco.

**Objective:** The purpose of this study was to describe user characteristics and clinical features of lesions induced by chronic chewing of khat on the oral mucosa.

**Material and Methods:** This was a descriptive cross sectional study carried out among 54 volunteers in Eldoret and Meru towns of Kenya. These consisted of 14 chronic khat chewers, 30 chronic khat chewers who also smoked tobacco and 10 nonchewers. Their oral mucosa was examined for clinical changes and comparisons were made between the three groups in terms of user characteristics and clinical appearance of the lesions.

**Results:** Fifty seven percent of all khat chewers preferred to chew on the left side compared to 9% who preferred the right side. Whereas all khat chewers presented with lesions on the buccal mucosa, nonchewers did not present with any pathological changes. The lesions extended to involve the tongue in 36% and the gingiva in 25% of the chewers. Most khat chewers (86%) presented with mixed white and brown discoloration with only a few presenting with purely white or brown lesions. Sixty three percent of the chewers presented with smooth and plaque-like lesions and the rest presented with mild wrinkling. Smoking tobacco had limited effect on khat induced oral mucosa lesions.

**Conclusions:** Results show that chronic khat use is associated with changes on the oral mucosa that manifest mainly as white, brown or mixed white and brown discoloration.

**Key Words;** - Khat, oral lesions, clinical, buccal mucosa

### Introduction

In Kenya, the habit is more common in animal studies has shown that khat decreases the systemic capacity of the body to handle reactive oxygen species (3). During chewing sessions, large amounts of khat leaves, shoots and barks are placed in the oral cavity and chewed while kept in the vestibule in close contact with the buccal mucosa (4). The khat bolus is then chewed gradually over 2-10 hours. On average, Fresh leaves and shoots of the khat North Eastern, coastal, Nairobi and Meru regions. plant contain a chemical known as cathinone which has a psychoactive effect comparable to amphetamine. According to previous research, khat chewing is associated with pathological conditions in various organ systems as well as in oral tissues (1). It has been reported that khat is genotoxic to human oral cells (2) and evidence from

100-500g of khat is chewed by chronic users per day. Over 90 percent of the alkaloid content of khat is extracted into saliva during chewing and most of it is absorbed through the oral mucosa (5). Therefore, oral tissues, especially the oral mucosa, are exposed to high doses of khat constituents during khat chewing rendering them susceptible to its potentially toxic effects.

Khat has been associated with oral keratotic white lesions which occur in the same region within the vestibule or buccal mucosa where the khat bolus is placed while chewing (6). Some of these oral lesions have been reported to show histopathological changes like acanthosis, hyperkeratosis and mild dysplasia (6). According to some previous research, the risk for developing these lesions is especially high among khat chewers who also use tobacco products (7). In another study, khat chewing was found to be a risk factor for developing cellular atypia, in addition to hyperkeratosis and infiltration by chronic inflammatory cells (8). Even though some studies have found a higher incidence of head and neck cancer in khat chewers compared to nonchewers (9, 10) lesions induced by khat have not been considered to be potentially malignant(11,12). Due to the relatively small number of studies on khat and the weaknesses of the studies already carried out, there is currently no consensus as to whether khat chewing is a risk factor for development of oral cancer. There is an increasing prevalence in khat use around the world, yet many oral health workers have limited knowledge on specific clinical features of khat induced oral conditions. The aim of the present

study was to determine user characteristics and the clinical changes induced by chronic khat use alone and when used together with tobacco on the oral mucosa among volunteers in Meru and Uasin Gishu counties of Kenya.

## **Methods**

### ***Study design and study subjects***

This study was a descriptive cross sectional study where participants were identified through purposive sampling. Based on previous studies (11, 12), a calculated minimum sample size of 14 participants was required for each study group. The study was approved by the regional Institutional Research and Ethics Committee (IREC) (approval number 000985). A public call by study assistants for volunteers to participate in the study was made in Eldoret and Meru towns of Kenya, and those willing to participate were requested to visit specified dental clinics for screening. A total of 54 participants who met the inclusion criteria upon screening were selected from among many volunteers who responded to the public call. All selected participants were male and 37 of them were from Meru while 17 participants were from Eldoret. All participants included in the study were informed of the purpose of the study and signed consent forms. The study subjects were divided into three groups; 1) a control group of 10 volunteers who were neither tobacco smokers nor khat chewers, 2) a study group of 14 volunteers who were chronic khat chewers but nonsmokers, and 3) a second study group 30 volunteers who were both chronic khat chewers and tobacco smokers. The first group was the control group, and consisted of clinically healthy adult

male volunteers who had come to the specific clinics for surgical removal of wisdom teeth.

### **Clinical procedures**

All those recruited into the two study groups were khat chewers who had used khat for more than 5 years (chronic khat chewers). Patients were first subjected to a short interviewer administered questionnaire designed to collect biographic data and information related to khat use, tobacco use and alcohol drinking. Patients were then subjected to a standard clinical examination of the oral mucosa on a dental chair in adequate lighting using dental mirrors and wooden spatulas. Clinical images (photographs) of the mucosa showing the oral lesions were taken for patients in each study group using a Kodak hand held camera (Kodak Easy-Share M575). The photographs were used in further analysis and digital comparison of mucosal changes on a computer. The color and textural changes on the mucosa were clinically graded in four levels namely normal, mild, moderate and severe.

### **Statistical analysis and generation of figures**

Comparison of group ages and generation of figures was done using Sigma Plot software version 12.5 (Systat Software, Inc., San Jose, CA, USA). Age sets from the three groups were first subjected to Shapiro-Wilk normality test and then compared using one way analysis of variance (ANOVA). This was followed by multiple comparisons using the Holm-Sidak method to determine the levels of significance between groups. A *p*-value of less than

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0.05 was considered significant.

## Results

### *Age characteristics of the study subjects*

The control group of 10 volunteers had a mean age of 25.4 years (range 20 to 37). The first study group of 14 volunteers had a mean age of 31.6 years (range 21 to 52) while the second study group of 30 volunteers had a mean age of 37.0 (range 23 to 55). Sixty percent of all khat chewers were aged above 35 years, 37% were aged between 25 and 35 years and the rest were below 25 years. Among khat chewers who also smoked tobacco, 7% were below 25 years of age, 37% were between 25 and 35 years and the remainder (54%) were above 35 years. Half of the khat chewers who were not smokers were aged between 25 and 35 years and the other half were above 35 years. In the analysis of age differ-

ences between the study groups, there was a statistically significant difference in the ages of the control group and the second study group composed of khat chewers who also smoked tobacco ( $p = 0.027$ ). Other than the two habits considered under the study and the said age difference, there were no other differences in health or behavioral characteristics between these groups.

### *Tobacco and alcohol use*

Regular alcohol dinking (of about five beer bottles per week) was noted in only one (2.3%) khat chewer, and the khat chewer was also a smoker. Four (29%) of the khat chewers, eight (27%) of the khat chewers who also smoked tobacco and two (20%) of the nonchewers reported to take alcohol occasionally, especially during special functions such as birthdays. The only method of tobacco use reported was smoking. Eleven (37%) of the smokers

had smoked tobacco for less than ten years and the remainder (63%) had smoked for less than 10 years. Seven (23%) of the smokers reported to use less than 1 cigarette per day, 11 (37%) of them used between 1 and 10 cigarettes per day, 6 (20%) of them used between 11 and 20 cigarettes per day and the rest (20%) of the smokers used over 20 cigarettes per day.

### *Duration of khat chewing*

All those recruited into the two study groups were khat chewers who had used khat for more than 5 years (chronic chewers), with 20 (45%) of them having used khat for between 10 and 15 years and 14 (32%) having used khat for more than 15 years (**Table 1**). Thirty six (82%) of the khat chewers used khat on a daily basis and 17 (39%) of them spent more than 10 hours chewing khat every day. The amount of khat chewed per day ranged from 0.5 kg to 2.5kg with 30 (68%) of

## Table

Table 1. Comparison of user characteristics between smokers and non smokers

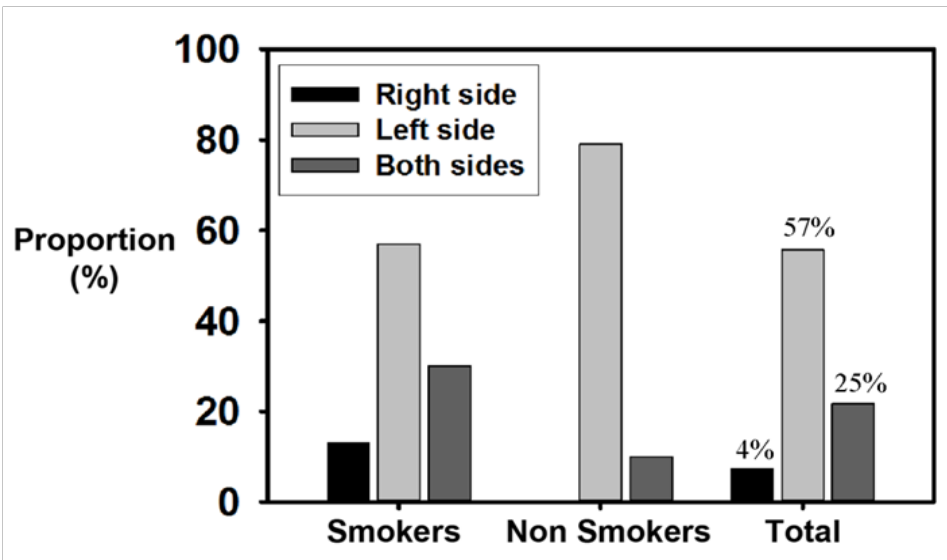
	Smokers N (%)	Non smokers N (%)	Total N (%)
Duration of khat use (yrs)			
5 - 9	6 (20)	4 (30)	10 (23)
10 - 15	13 (43)	7 (50)	20 (45)
>16	11 (37)	3 (20)	14 (32)
Duration of khat use per day (hrs)			
≤ 10	20 (67)	7 (50)	27 (61)
>10	10 (33)	7 (50)	17 (39)
Amount of khat use per day (kg)			
> 0.5	5 (17)	0 (0)	5 (11)
0.5 - 0.9	6 (20)	3 (21)	9 (21)
1 - 1.4	14 (46)	8 (58)	22 (50)
>1.5	5 (17)	3 (21)	8 (18)
Frequency of khat use in a week			
Daily	26 (87)	10 (70)	36 (82)
>5 days	4 (13)	4 (30)	8 (18)

the participants using over 1 kg of fresh leaves of khat every day.

### ***Khat chewing characteristics***

Participants recorded variations in their khat chewing characteristics, particularly their preference to chew khat using only one side of the mouth. Among all khat chewers, 25 (57%) of them preferred to chew on the left side compared to only 4 (9%) of them who preferred to chew on the right side, and 11 (25%) of them who used both sides of the mouth to chew khat. Of the non-smokers who also chewed khat, 8 (57%) of them preferred to chew on the left side while only 2 (14%) preferred to chew on the right side (Figure 1).

### **Figures and figure legend**



**Figure 1.** Distribution of khat chewers based on the chewing side.

### ***Site of the lesions***

Participants who did not chew khat did not show any pathological discolorations on their mucosa. On the contrary, khat chewers presented with various forms of oral mucosal color changes in various parts of the mouth. All khat chewers had pathological color changes affecting more than one part

of the oral mucosa particularly the buccal mucosa, the tongue, gingiva and the palatal mucosa. The pathological color changes were observed on the buccal mucosa adjacent to the posterior teeth in all (100%) of the khat chewers. These buccal lesions were particularly more pronounced on the side reported as the chewing side by the patient (Figure 2). The next most affected site was the lateral border of the tongue observed in 16 (36%) of the chewers, followed by the gingiva around the posterior teeth observed in 11 (25%) of the chewers and the palate seen in 10 (23%). On the tongue, the pathological color changes were localized on the side of the tongue that contacts the khat bolus while chewing khat (Figure 3) and this coincided with

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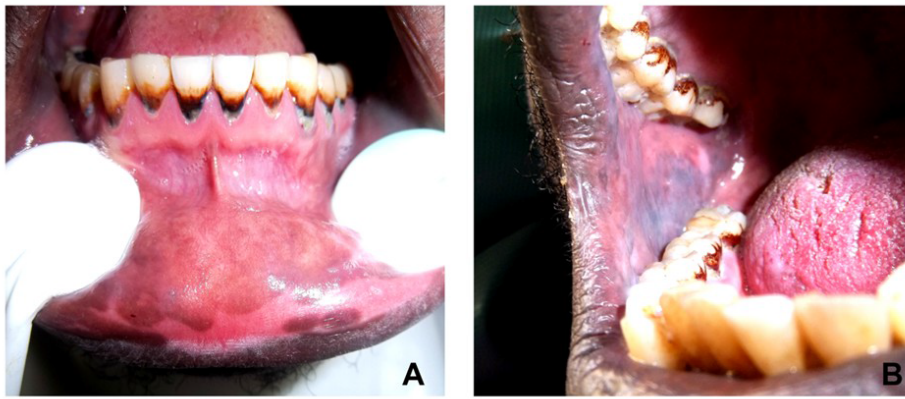
consistently more pronounced on the buccal mucosa and the adjacent lateral border of the tongue where the khat bolus was placed while chewing khat.

### ***Color of the lesions***

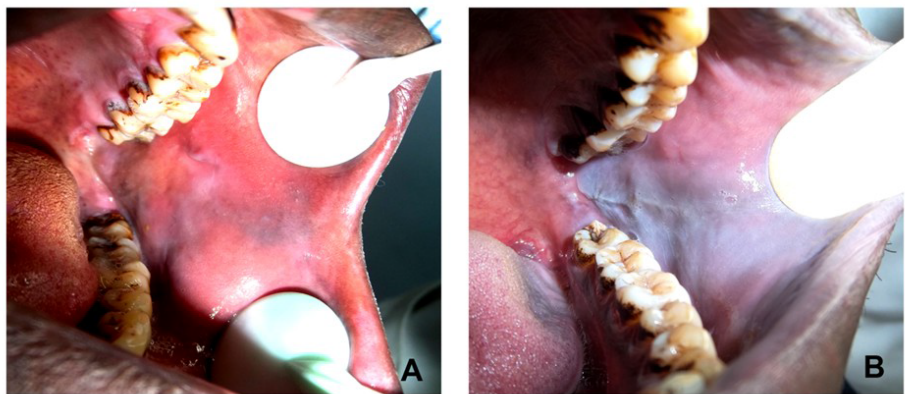
The pathological color changes of the oral mucosa in chronic khat chewers ranged from mild brown to dark brown or varying degrees of white discoloration (Figures 2 and 3). In both chronic khat chewers and chronic khat chewers who smoked tobacco, either white or brown or in most cases mixed white and brown discoloration of the mucosa was seen. Other than the localization of the lesions, there appeared to be no other differences in type and degree of discoloration among smokers and non smokers. Only four (9%) of the khat chewers presented with lesions that were classified as purely white lesions, and three of them were khat chewers who also smoked tobacco. Two (5%) of the khat chewers presented with purely brown pigmentation and both of them were nonsmokers. The rest of the khat chewers (86%) presented with mixed white and brown discoloration affecting various sites in the mouth. On further analysis done by grading of discolored lesions, the degree of white discoloration increased with the amount of khat chewed per day rather than the duration of khat chewing (Figure 4). However, the brown discoloration increased with increase in duration of khat use as well as increase in amount of khat used per day.

### ***Texture of the lesions***

The lesions also depicted varying changes in their texture. Most of the khat chewers (63%) presented with lesions that appeared smooth and



**Figure 2.** Clinical photographs of the oral mucosa in chronic khat chewers. Panel A shows widespread brown pigmentation affecting the labial mucosa in a non smoker who chewed more than 1 kg of khat per day. Panel B shows mixed brown and white color changes on the buccal mucosa of a man who chewed less than 1 kg of khat per day and also smoked between 10 and 20 cigarettes a day.

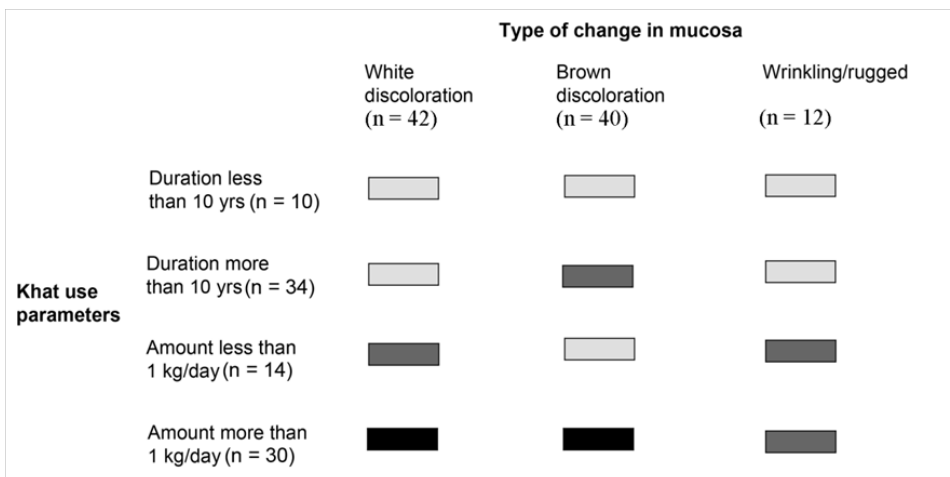


**Figure 3.** Clinical photographs of the oral mucosa in khat chewers. Panel A shows mild white and brown pigmentation on the buccal mucosa in a man who had used both khat and tobacco. Panel B shows extensive white color changes on the buccal mucosa of a man who chewed more than 2 kg of khat a day and also smoked more than 20 cigarettes. Notice the white lesion affecting the adjacent lateral border of the tongue.

plaque-like in texture. Twelve (27%) of them presented with lesions that were rough or wrinkled with rugged mucosa that appeared folded in some areas. Five of the non-smokers (36%) presented with wrinkling within the lesions whereas 7 of the smokers (23%) showed wrinkling within the lesions. Also, those using more than 1 kg of khat per day showed more wrinkled texture when compared to those using less than 1kg of khat per day. Severe forms of wrinkling were not noted even among heavy khat chewers, but the wrinkling was noted to be more pronounced among those using larger amounts of khat per day rather than the duration of khat use. These textural parameters were however not subjected to further analysis to determine the exact association because of the small sample sizes in each group.

**Discussion**

Khat use is widespread in certain parts of Kenya such as the Meru, coastal and Nairobi regions. In the present study, we sought to compare user characteristics and clinical changes seen on the oral mucosa of volunteers who were chronic khat chewers and chronic khat chewers who also smoked tobacco. Chronicity in khat chewing especially in relation to induction of oral white lesions has previously been defined as period of use exceeding 2 years as well as high frequency and not necessarily the amount of khat consumed per sitting (6, 7, 12). We therefore focused on chewers who had used khat for over 5 years. The typical chronic khat chewer in this study was an adult male aged above 30 years who often abused tobacco as well.



**Figure 4.** Variation in degree of white and brown discoloration as well as wrinkling with the duration and amount of khat use. The grade shown is the grade assigned to the majority of the participants in the specific group. (Light grey rectangles show mild changes, dark grey rectangles show moderate changes and black rectangles show severe changes)

This study demonstrated that khat induced oral lesions are often well localized in areas of the mouth that contact the khat bolus while chewing. These are found on the buccal mucosa and the tongue especially on the side of the mouth most often used for chewing khat. The study also demonstrated that the left side of the mouth was the most preferred side used for chewing khat. These results are comparable to those found in a number of previous studies where khat induced white lesions were mainly seen on the buccal and gingival mucosa and were more pronounced on the left side of the mouth which was most often the chewing side (12, 13, 14).

Use of tobacco alongside khat chewing was found to be a common practice, and all participants who used tobacco did so by smoking. Tobacco smoking was noted particularly in chronic khat chewers aged more than 35 years, and most of these smokers used between 1 and 10 cigarettes per day. In general, the clinical appearance of mucosal lesions was found to be similar in khat chewers who smoked tobacco and those who did not smoke tobacco. This agrees with findings in a recent study among chronic khat chewers in Yemen which found that water-pipe smoking and cigarette smoking did not cause significant change in clinical presentation of oral lesions in the chronic khat chewers (14). In yet another study, even though tobacco use was found to correlate with presence of oral lesions in khat chewers, the lesions were clearly well localized in the sites used for khat chewing, indicating that khat use was the major factor in the induction of the oral lesions (6). However,

the observations in all these studies are contrary to the expectation that concomitant tobacco use would essentially worsen the clinical appearance of khat induced white lesions. Indeed, contrary to our findings, a study by Ali *et al* found that the risk for developing oral white lesions is especially high among khat chewers who also use tobacco products (7). More studies with larger samples sizes are needed to provide a clearer picture on this issue.

With regard to color of the lesions, only a small proportion of khat chewers (less than 10%) presented with lesions that could be classified as purely white or brown lesions. Most of the khat chewers presented with lesions that showed a mixed white and brown discoloration. In both chronic khat chewers and chronic khat chewers who smoked tobacco, either white or brown or in most cases mixed white and brown discoloration of the mucosa was seen. The degree of whitening increased with increase in amount of khat chewed per day. Brown discoloration increased with both amount of khat chewed per day and duration of khat use in years. In this study, most of the oral lesions appeared smooth particularly among khat chewers who were also smokers. However, mild wrinkling in texture was observed in about a third of the khat chewers. These findings are similar to those in a previous study which found that mucosal lesions resulting from khat use vary in relation to the duration of khat chewing. The lesions included whitening, whitening with mild corrugation, frictional keratosis and frictional keratosis with mild corrugation of the mucosa (15). Brown pigmentation related

to khat use has also been described in a separate study (16) in which the pigmentation was found to be independent of pigmentation associated with tobacco use even among khat chewers who were heavy smokers.

A recent systematic review ranked oral mucosal white lesions as the most prominent of all oral conditions associated with chronic abuse of khat (17). In spite of its limitations, this study does bring out additional information with regard to the clinical nature of oral mucosal lesions associated with long term use of khat. In addition, the study describes user characteristics such as duration of khat chewing, amount of khat chewed and other factors that could influence the various clinical presentations of the oral lesions induced by khat chewing.

## Conclusion

The findings of this study identify mucosal white and brown discoloration as key clinical features of chronic khat chewing. From the findings here, it appears that concomitant smoking of tobacco has limited effect on the clinical appearance of khat induced oral mucosal lesions.

## Study limitations

One key limitation of the study was the small sample sizes particularly in the control group, occasioned by failure to get adequate numbers of volunteers. Inclusion of a fourth group of participants consisting of tobacco smokers who do not chew khat could also have provided additional information. Most of the comparisons between groups were not subjected to statistical tests because of low sample sizes and use of non numerical measures. Larger studies



with adequate sample sizes are recommended to confirm the findings in this study.

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