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Evaluation of Oral Submucosal Fibrosis and Related Factors in Areca Nut Users

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Abstract

***Background*:** Oral Submucousal Fibrosis (OSF) is a precancerous condition often created in consumers of different products containing arecanut. These products are commonly used in countries like India and Pakistan. In Iran, it is commonly consumed in cities which are in proximity of Pakistan border including Chabahar. The present study is done in order to study OSF and other relating factors in consumers of products containing areca nut.

***Materials and Methods*:** In this descriptive-analytical and cross-sectional study, 362 consumers of products containing areca nut (pan, supari, gutka and etc.) were studied in order to examine the incidence of OSF. The diagnostic criteria were mouth-opening limitations, mucosa stiffness and touching the intramucous fibrotic bands. Information about the consumption amount, alternation, the type of consumed material and time of consumption was mentioned in the questionnaire. Finally, the data was analyzed using SPSS-14 and χ^2 test.

***Results*:** Of 362 consumers of areca nut (227 men (62.7%) and 135 women (37.3%)) in the age group 7-71 and average age of 27 years old, 61 person (16.9%) including 33 men (54.1%) and 28 women (45.9%) were suffering OSF. There was a significant relationship between OSF incidence and time, dose and alternation of consumption ($p<0.05$). Age and sex didn't have a certain correlation with OSF.

***Conclusion*:** The recent study indicated a strong correlation between consumption of products containing areca nut and OSF.

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Introduction

Oral Submucousal Fibrosis (OSF) is a chronic, progressive and precancerous condition usually seen in Indian immigrants and south-east Asian residents [1-3]. This condition is specified with reduction of blood vessels and epithelium surface atrophy. Its clinical perspective including paleness and mucous stiffness results in mouth-opening limitation, impaired tongue movement and disorder of cheek elasticity. Swallowing disorder (dysphagia) is seen in severe cases. Experimental and epidemiological studies indicated that chewing acre nut is an important factor for creating OSF [2, 3].

Different products of acre nut are available such as Betel quid (betel leaf, slaked lime, acre nut) with or without tobacco and pan masala. There are regional differences in consumption of different products of acre nut in India. Nut contains alkaloid and acrolein. The material is a strong stimulus for collagen synthesis through fibroblasts [3, 4].

Many consumers of acre nut products use also other products such as tobacco and etc. which can play an important role in initiation and progress of the precancerous condition [2, 5]. In the study of Ranganathan et al. in Chennai, 185 OSF-afflicted individual and 185 healthy individual were studied for 3 years. In this study, women were more prone to OSF (9:1); all acre nut products were influential in creating OSF and pan users were more affected with OSF. The time of consumption had more effect in creating OSF rather than times of chewing material. The studies indicated that chewing acre nut has a strong correlation with creation of OSF [2].

In a case-control study conducted in India by Sinor et al. on 60 OSF-afflicted patients, 98% of the individuals were regularly chewing one of acre nut products and with an increase in times of consumption and the time of chewing acre nut, the risk of affliction to OSF and as a result oral cancer increased [6]. Recently, consumption of acre nut products (pan and gutka) is common at early ages resulting to an increase of OSF incidence in the youth [7]. Richart et al. studied a 31-year old Indian woman living in Germany since 1997 and was suffering from OSF. At the age of 17 (up to now), the patient accustomed to chewing acre nut products (pan and gutka) and referred to clinic while complaining of mouth-opening limitation. Surgical treatment was not useful (effective) for him. They stated that regarding OSF prevalence in children and youth, the primary objectives in treatment of the disease is to prevent the disease progress via physiotherapy [8]. In the study of Gao et al. with the aim of epidemiological investigation of betel nut chewing among the students in Loudi, it was specified that betel nut consumption as one

of acre nut products can also result in the incidence of OSF. All the OSF-afflicted individuals in this study were male [9].

In a study by Maher et al. with the aim of investigating the relationship between acre nut consumption and OSF incidence in Karachi, Pakistan, OSF incidence was the same in both sexes (male and female) and OSF incidence didn't have significant difference in different age groups. In the study, it was specified that the amount of acre nut consumed per day has more effect on OSF than the years of consuming the substance [10].

There is no effective treatment for complete removal (elimination) of this disease. OSF will gradually brings about severe limitations in mouth opening, dental caries (tooth decay), poor oral health, periodontal problems and disorders/difficulties in chewing (dysmasesis), in swallowing (dysphagia) and in speaking (dysphonia/ dysarthria/ dysphrasia/ dyslogia/ dysorthographia). Given that OSF is a precancerous lesion, prevention of creation and progress of the lesion as well as training about the disadvantages of consuming materials containing acre nut must be put on top of the health agenda [11]. Few epidemiological studies have been carried out in Iran about consumption of different acre nut products (such as pan and gutka) and OSF incidence and there is no report indicating the incidence of the disease in Chabahar (South of Iran). Therefore, OSF incidence and its relevant factors are evaluated in this study.

Materials and Methods

In this experimental study we used recombinant In this descriptive-analytical and cross-sectional study which was conducted in 2009 in Chabahar, 362 consumers of acre nut products (pan, supari, gutka, etc.) were selected among the visitors of the city Health Centers through multi-stage random sampling method and were examined using headlight and dental mirror in order to examine the OSF incidence by oral disease specialist. Considering 60%, sample size was estimated to be 362 [11]. Having coordinated with Chabahar Health Center authorities and dividing the city into 4 geographic regions- north, south, east and west, a health center was selected of each region and the desired samples were collected randomly among the visitors of these centers.

The study was conducted in a certain period (about 6 months); information form was completed for each person including demographic data, types of oral habits, consumption amount, consumption period (years of consumption), consumption frequency (number of times per day), type of consumable product (acre nut, pan, gutka, etc).

Those who had at least one year experience in consumption of acre nut products (current user) were entered into the study and those who sometimes consumed the product (less than 2 times per month) or in lifetime (life span) were excluded from the study [4].

Clinical criteria for the diagnosis of OSF included difficulty in opening the mouth and the existence of fibrous bands in labial-buccal mucosa and lack of elasticity in buccal-labial mucosa [2]. Clinical diagnosis with biopsy was proved in all patients. The criteria for proving diagnosis were dense submucosal layer, collagen vascular in connective tissue, chronic inflammatory cells, and epithelial atrophy [1, 3].

Mouth-opening amount was evaluated based on interincisal distance according to millimeter. OSF was divided into 3 clinical stages according to mouth-opening amount as follows:

Stage I: mouth- opening amount $\leq$ 45 mm; Stage II: mouth-opening amount about 21-44 mm; Stage III: mouth-opening amount $\geq$ 20 mm.

After completing the written letter of satisfaction (testimonial), all the subjects took part in the study knowingly and without force and left the study in case of unwillingness to cooperation. Finally, all the information obtained based on information forms and tables were analyzed using SPSS-14 and χ^2 (Chi-squared) method.

Results

In this study, 362 consumer of acre nut products including 227 men (62.7%) and 135 women (37.3%) in the age group 7-71 and average age 27±13.6 were analyzed; among them 61 individuals (16.9%) including 33 men (54.1%) and 28 women (45.9%) were suffering OSF. Based on χ^2 test, there was not a significant relationship between sex variable and OSF. The average age of OSF-afflicted individuals and healthy persons was 29 and 27, respectively. The incidence amount of OSF in different age groups was not significantly different (Table 1).

In this study, the most frequently used substance was supari (85.4%) and 53 individuals consumed other materials such as cigarette, gutka and pan beside supari. 14.6% of those who only consumed supari were suffering OSF. 30.1% of those who consumed other materials with supari were also suffering OSF. There was a significant statistical relationship between OSF prevalence and simultaneous consumption of supari and other materials. So that, in those who consumed other materials beside supari, OSF prevalence was lower (p=0.0008) (Table 2).

The consumption time of acre nut products had also a significant relationship with the incidence of OSF, so that most of the individuals who were suffering OSF (93.5%) had consumed these products more than 24 months (2 years) (p=0.004) (Table 3).

Lesion severity in 4.9% (3) of the afflicted individuals was less than 10 mm; in 57.3% (35 persons) was 10-20 mm, in 36.1% (22 persons) was 20-30 mm, and in 1.7% (1 person) of the individuals was more than 30 mm. Accordingly, of 61 person suffering from OSF, 38 of them (62.3%) were in Stage III and 23 of them (37.7%) were in Stage II (Maximum mouth-opening in the afflicted people was less than 45 mm).

In the current study, there was a significant difference between the consumption amount of supari and affliction to OSF so that most (90.2%) of those who were suffering

OSF were in the group who consumed more than 3 pockets of supari per day (p=0.003) (Table 5). In the present study, those who were suffering OSF had symptoms such as mouth-opening limitation, mucosal stiffness and fibrotic bands. Among them 45 person (73.7%) had all the 3 symptoms in the oral mucosa at the same time (Fig. 1).

Table 1. Frequency distribution of OSF in the subjects of study based on age

OSF age (year)	Affected N(%)	Normal N(%)
<10	0(0)	7(2.3)
11-20	16(26.2)	100 (33.2)
21-30	21(34.4)	79 (26.2)
31-40	15(24.6)	69(23)
41-50	7(11.5)	36(12)
51-60	2(3.3)	8(2.6)
>61	0(0)	2(0.7)

Table 2. Frequency distribution of OSF in the subjects of study based on the type of consumable material

OSF consumable material	Affected N(%)	Normal N(%)
Supary	45(73.8)	264(87.8)
Supary & pan	1(1.6)	8(2.6)
Supary, pan & guthka	6(9.8)	4(1.3)
Supary, pan, guthka & cigar	5(8.2)	3(1)
Supary & guthka	2(3.3)	13(4.3)
Supary & cigar	0(0)	4(1.3)
Supary, guthka & cigar	2(3.3)	5(1.7)

Table 3. Frequency distribution of submucous fibrosis in the subjects of study based on the duration of consumption (mounth)

OSF duration consumption (mounth)	Affected N(%)	Normal N(%)
0-6	0(0)	4(1.3)
6-12	1(1.6)	23(7.7)
12-24	3(4.9)	60(19.9)
>24	57(93.5)	214(71.1)

Table 4 Frequency distribution of submucous fibrosis in the subjects of study based on the times of consumption per day

OSF times of consumption per day	Affected N(%)	Normal N(%)
1 time	0(0)	19(6.3)
2 times	3(4.9)	25(8.3)
3 times	2(3.3)	56(18.6)
4 times>	56(91.8)	201(66.8)

Table 5. Frequency distribution of OSF in the subjects of study based on the consumption amount per day

OSF consumption amount per day	Affected N(%)	Normal N(%)
1 pack	2(3.3)	20(6.6)
2 pack	1(1.6)	23(7.6)
3 pack	3(4.9)	57(19)
> 3 pack	55(90.2)	201(66.8)

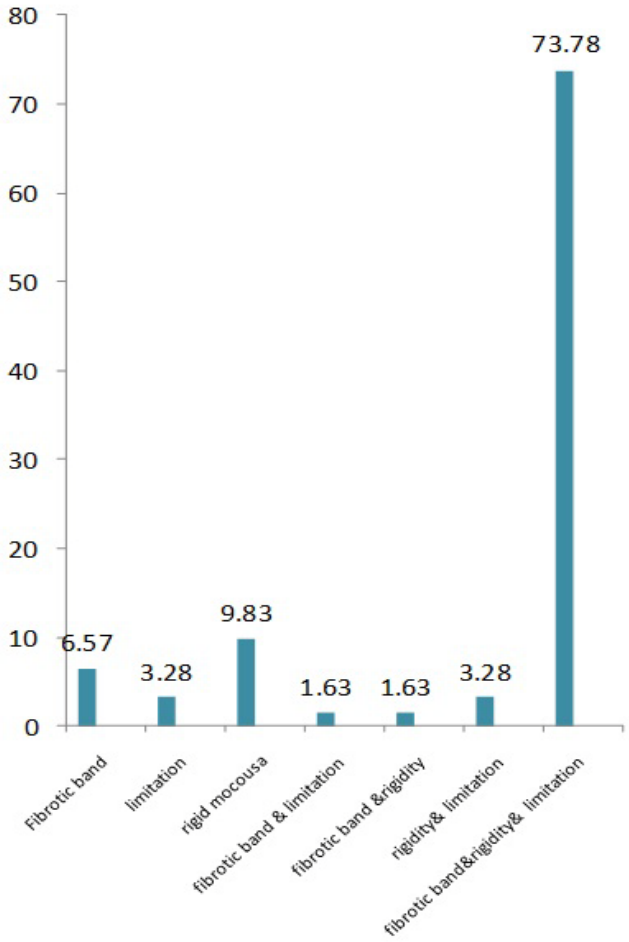

Figure 1. Frequency of Oral Submucosal Fibrosis in the subjects of the study

Discussion

In the current study, 16.9% of individuals were suffering from OSF. Prevalence of the disease in men (54.1%) has been more than women (45.9%) and amount, alternation, and consumption time of acre nut products had a significant relationship with incidence of the disease.

Submucosal fibrosis is a precancerous condition most commonly found in residents of Southeast Asians, Sri Lanka, Bangladesh [12] and Indian immigrants. Consumption of acre nut products is a common habit which can be observed in these people and has strong relationship with OSF incidence [2, 5]. The characteristic of OSF is that it is restricted to certain geographic areas, so it is assumed that it is probably restricted to certain eating (nutritional) habits and diets [4].

Several factors such as local factors (Capsacin, consumption of hot foods and acre nut) are suggested for OSF incidence [2]. In addition to local factors, systemic factors also play an important role in creating OSF including anemia, vitamin B complex deficiency and genetic predisposition [13, 14]. Chewing acre nut in different ways is common in India. OSF prevalence in India is increasing so that 250000 cases in 1980 and 2 million cases in 1993 were reported [15, 16].

Consumption of acre nut products is also very common in Pakistan and Iran which is in its vicinity (south of Sistan & Baluchistan province).

In the current study, 16.9% of consumers of acre nut products in Chabahar were suffering from OSF. The incidence of the disease in this region was less compared to Jacob study in Kerala, India that 56% of the people were suffering from OSF [17]. While in studies of Reichart in Vietnam and Sarswathi in South India, 13% and 0.55% of the people were suffering the disease, respectively [18, 19]. The difference in diets, certain oral habits and etc can be influential in the incidence rate of the disease. For example, in some regions of India in which hot foods are commonly used [2], the incidence of the disease is also higher. Likewise, consumption of acre nut products may have a great influence in increasing the risk of OSF. It seems that the prevalence of the disease in Chabahar is more than other regions of Iran because the consumption of acre nut is common in this region which has a strong relationship with OSF incidence.

In the present study, 54.1% of the sufferers were men and 45.9% were women; while in the study of Kumar et al. in Chennai [4], of 75 OSF cases 86% were men and 14% were women. In several studies, age and gender of OSF patients has been very extensive. In some epidemiological studies in India, it is reported that OSF incidence is more common in women, but in another study in this country Sinor has stated that the incidence of the disease is more common in men [6]. In a study in Vietnam [18] and in study of Kumar [4], it is reported that the ratio of men affliction to women is 6:1. Also, in the present study OSF incidence in men was more, although there was no significant difference between the two groups.

In the current study, OSF rate in different age groups was not significantly different. In Maher study in Karachi, there was no relation between age and OSF incidence, too [10]. However, different studies point out that the age of OSF incidence has decreased a lot and the rate of this precancerous disease is increasing in the young and teenager group [2]. In the present study, the most acre nut consumers were also of age group 11-20 and 26.2% of the patients were in this age group. Epidemiological studies on Indian immigrants living in South Africa have indicated that chewing acre nut is an important risk factor for OSF incidence [20]. In recent years, consumption of commercial products containing acre nut such as pan, gutka and supari has been common in India, Pakistan, and border regions of neighboring countries and many OSF patients have a long-term history of chewing acre nut [4, 5].

The result of the recent study indicated that the probability of OSF incidence in those who repeatedly chew acre nut during the day is more and there was a significant relationship between the two variables. Kumar also came to the same conclusion. Shah believes that the consumption time of the substance is a more powerful risk factor for creating OSF and its duration of consumption is less important [21]. However, in the present study, most of OSF patients were those who used acre nut more than 24 months.

There is also a direct relationship between the consumption dose and OSF incidence. In Jacob study in India, dose of consumption, alternation and its duration had also a positive effect on OSF incidence [17]. In their studies, Maher and Shah concluded that as the consumption of acre nut products increases, OSF prevalence will also increase [10, 21].

Classic symptoms of OSF include intensive mouth-opening limitation, paleness; mucosal stiffness and existence of fibrotic bands within the patient mucosa [3]. In the present study, the most common symptoms of OSF were intensive mouth-opening limitation, stiffness and formation of submucosal fibrotic bands. In Ranganathan study, the average mouth opening in healthy Indian men and women was 47.5 and 44.5 mm, respectively [2].

The level of mouth opening in those who are suffering from OSF depends on the lesion severity. The more the lesion severity, the less the mouth opening and based on this the lesion severity is divided into 3 stages (stages I, II, III). In Kumar study, 75% of men and 80% of women were in stage II and their mouth opening amount was about 21-30 mm [4]. In the present study, 37.7% of the patients were in stage II and 62.3% were in stage III and intensive mouth opening limitation (below 20 mm).

The recent finding confirms that treatment of OSF patients in Chabahar is done with delay and many people don't refer for treatment even in advanced stages of the disease due to their poor knowledge in this regard. But in Kumar study 75% of the individuals were in stage II and referred to doctor for treatment in early stages of the disease [4]. Early treatment will prevent the lesion from progress.

In OSF, collagen metabolism is affected and in the early stages of the disease collagen fibers will settle in (precipitate) the submucosal tissues, then as the disease progresses, dense collagen fibers will substitute leading to increased stiffness of the mucosa. In this stage, the tissue will lose its elasticity, so the patient will become afflicted with severe mouth-opening limitation. Finally, mucosa tissues will get involved with atrophy and will be prone to premalignant changes. The risk of oral cancer in OSF lesions equals 30% [4].

The study indicated that chewing acre nut has strong relationship with OSF and with an increase in dose, alternation the consumption amount of the products, OSF incidence rate will increase. In the current study, most of the OSF patients were the youth and teenagers. In other studies it is also pointed out that the age of OSF incidence has decreased compared to the past [3, 6].

It should be mentioned that the probability of malignant changes is very high is young people who suffer from OSF, so for the purpose of decreasing the incidence of oral cancer in the young people of the society, their knowledge about the disadvantages of acre nut products such as pan, supari and gutka should increase. Conducting case-control studies in this field and comparing the effective factors in creating OSF in case and control

groups may naturally be an effective help in reducing the incidence rate of the disease.

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Authors' Contributions

All authors had equal role in design, work, statistical analysis and manuscript writing.

Conflict of Interest

The authors declare no conflict of interest.

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