

Oral submucous fibrosis: study of 1000 cases from central India

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BACKGROUND: Very few reports have been published on the gender specificity of oral submucous fibrosis (OSF) in relation to habit patterns and the severity of disease in the world literature. The purpose of the study was to ascertain the gender specificity for different habits and severity of OSF.

METHODS: A hospital-based cross-sectional study on various habit patterns associated with OSF was performed in Nagpur over a 5-year period. A total of 1000 OSF cases from 266 418 out patients comprised the study sample.

RESULTS: The male-to-female ratio of OSF was 4.9:1. Occurrence of OSF was at a significant younger age group (<30 years) among men when compared with women (OR = 4.62, 3.22–6.63, $P = 0.0001$). Reduced mouth opening, altered salivation and altered taste sensation were found to be significantly more prevalent in women when compared with men. Exclusive areca nut chewing habit was significantly more prevalent in women (OR = 44.5, 25.4–79.8, $P = 0.0001$). Whereas significant increase for *Gutkha* (Areca quid with tobacco) (OR = 2.33, 1.56–3.54, $P = 0.0001$) and *kharr/Mawa* (crude combination of areca nut and tobacco) (OR = 6.8, 4.36–11.06, $P = 0.0001$) chewing was found in men when compared with women.

CONCLUSIONS: There is a marked difference in literacy, socioeconomic status, areca nut chewing habits, symptoms and disease severity in women when compared with men in the central Indian population.

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Keywords: oral submucous fibrosis; descriptive study; gender; pan masala; oral cancer

Introduction

Oral submucous fibrosis (OSF) is a high risk precancerous condition characterized by changes in the connective tissue fibers of the lamina propria and deeper parts leading to stiffness of the mucosa and restricted mouth opening. OSF has been reported almost exclusively among Indians living in India and among other Asiatics, with a reported prevalence ranging up to 0.4% in Indian rural population (1). Epidemiological and *in vitro* experimental studies have shown that chewing areca nut (*Areca catechu*) is the major aetiological factor for OSF (2).

Although there are regional variations in the type of areca nut products used in India, the betel quid (BQ) was the most popular and prevalent habit in ancient Indian culture. But in 1980, both areca quid products such as *Pan masala* (Areca quid) and *Gutkha* (AQ + tobacco) were introduced in Indian market as commercial preparations. Since then there has been an increase in the use *Pan Masala* (Areca quid) and *Gutkha* (AQ + T) in the younger age groups, which had led to increased incidence of OSF (3).

Pan Masala (Areca quid) includes areca nut, catechu, lime, flavours and spices. Our previous hospital-based case-control study has proved strong association of *Pan Masala* (AQ) with highest relative risk (489.1) of development of OSF (4). *Gutkha* (AQ + T) contains all ingredients of *Pan Masala* (AQ) plus tobacco and other contents, that are closely guarded secretes and is a commercial substitute to local preparation popularly known as *Kharr/Mawa* (5).

Recently, it has been documented that the habit of chewing *Gutkha* (AQ + T) had gained considerable popularity among the younger men in this region. The rapidly increasing prevalence of this habit can be judged from the reports that the Indian market for *Pan masala* (AQ) and *Gutkha* (AQ + T) is worth 25 billion (US\$ 500 million) (6).

Many epidemiological studies on OSF have been published in world literature (1, 2, 5, 17, 19, 20, 23–25). However, very few reports have been published on the

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gender specificity of OSF in relation to habit patterns and the severity of disease (7). Given this paucity of information, a hospital-based cross-sectional study was performed to ascertain the gender specificity for different habits associated with OSF and the prevalence of oral cancer among these patients controlling for tobacco chewing habits.

Materials and methods

A total of 266 418 patients visited the outpatient department of Government Dental College and Hospital, Nagpur, central India, in a 5-year period (from January 2000 to December 2004). Out of these, 1000 patients were diagnosed for OSF and they comprised the study sample. Criteria for diagnosis of OSF were the presence of palpable fibrous bands in the labial and/or buccal mucosa, loss of elasticity of the buccal/labial mucosa and inability to open the mouth wide (1, 6). The clinical diagnosis was confirmed by biopsy in a subgroup of cases, using established criteria: submucosal dense and avascular collagenous connective tissue, variable number of chronic inflammatory cells and epithelial atrophy (8).

Complete clinical history, including demographic details, various oral habits – the frequency (number of times per day), duration (years of consumption) and type [Areca nut, *kharra/Mawa*, *Pan Masala* (AQ), *Gutkha* (AQ + T), BQ] along with tobacco use were recorded in case record forms.

Data management and analysis

For the purpose of data entry, storage and retrieval, clinician-friendly graphical software programme 'SOFPro 1.0' was specially designed and developed with the help of a qualified software programmer. Graphical user interface (GUI) screens were developed using Visual Basics 6.0 and database in MS Access. Designing of a suitable 'form' for data entry and 'format' for storage of information (computer screens) was done as per the structure of case record form for OSF.

All statistical analyses were performed using 'Intercooled STATA Version 8.0' (STATA corporation, Lakeway, TX, USA) software. Descriptive measures like mean values and standard deviations for continuous variables and percentage for categorical variables were calculated. The OSF cases were classified by gender for comparison purposes. Estimation of odds ratio (OR) along with 95% confidence intervals was made for comparing risk of OSF by gender. Tests of significance like unpaired *t*-test for comparing means and chi-squared test of association were performed for comparing percentages of two independent samples (men vs. women). A value of $P < 0.05$ was considered statistically significant.

Results

Year-wise prevalence of OSF in the study population is shown in Table 1. The overall prevalence of OSF was found to range from 2.42 in 2000 to 6.42 per 1000 per

Table 1 Year-wise prevalence of oral submucous fibrosis

Year	Cases	Sample size	Prevalence (per 1000 cases)
2000	152	62 587	2.42
2001	167	59 973	2.78
2002	168	48 848	3.43
2003	203	46 753	4.34
2004	310	48 257	6.42

year in 2004. Fig. 1 highlights the increasing trend in prevalence of OSF since 2000.

Demographics

Table 2 shows the demographics of 1000 OSF cases. The mean age for men ($n = 830$) was 27.60 ± 9.58 (range 12–75) years and for women ($n = 170$) it was 34.78 ± 12.21 (range 9–75) years. Thus, occurrence of OSF was at a significantly younger age (< 30 years) among men when compared with women (OR = 4.62, 3.22–6.63, $P = 0.0001$). Prevalence of OSF in men (83%) was significantly ($P < 0.0001$) more than in

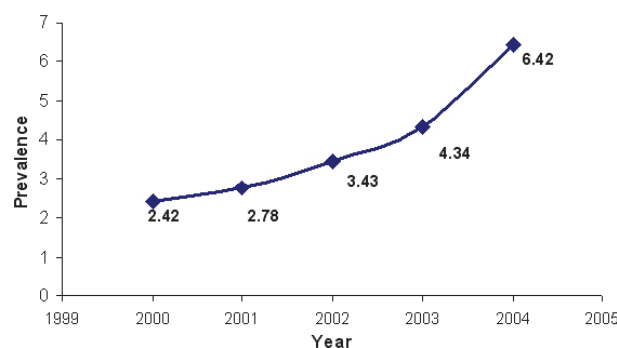


Figure 1 Prevalence of oral submucous fibrosis (per 1000 population) for 5 years.

Table 2 Demographics of oral submucous fibrosis

Variable	Male (<i>N</i> = 830)		Female (<i>N</i> = 170)		Total (<i>N</i> = 1000)	
	No.	%	No.	%	No.	%
Age group						
0–9	–	–	1	0.6	1	0.6
10–19	180	21.7	23	13.5	203	35.2
20–29	439	52.9	42	24.7	481	77.6
30–39	131	15.8	59	34.7	190	50.5
40–49	55	6.6	30	17.6	85	24.3
> 50	25	3.0	15	8.8	40	11.8
Educational status						
Graduate	161	19.4	12	7.1	173	17.3
Non-graduate	567	68.4	103	60.6	670	67
Illiterate	51	6.1	44	25.8	95	9.5
Not-mentioned	51	6.1	11	6.5	62	6.2
Socio-economic status						
Low	281	33.8	72	42.3	353	35.3
Middle	520	62.6	93	54.7	613	61.3
Higher	13	1.5	2	1.1	15	1.5
Not-mentioned	16	1.9	3	1.7	19	1.9

Table 3 Symptoms and risk/distribution of OSF by gender

Symptom*	Male (N = 830)		Female (N = 170)		OR (95% CI)	P-value
	No.	%	No.	%		
Reduced mouth opening	747	90.0	161	94.7	1.98 (0.97–4.5)	0.053
Burning sensation	734	88.4	157	92.3	1.57 (0.85–3.15)	0.135
Ulceration	545	65.7	117	68.8	1.15 (0.80–1.67)	0.427
Altered salivation	307	36.9	86	50.6	1.41 (0.99–1.99)	0.043
Taste change	268	32.2	74	43.5	1.61 (1.13–2.29)	0.004
Dysphagia	205	24.7	53	31.2	1.38 (0.94–2.00)	0.078

*Some patients had more than one symptoms of OSF.

women (17%) with male-to-female ratio being 4.9:1. Significantly higher proportions of women belonged to low socioeconomic status when compared with men (OR = 1.43, 1.00–2.04, *P* = 0.035). Proportion of illiterate women was significantly higher when compared with illiterate men (OR = 5.46, 3.38–8.74, *P* = 0.0001).

Table 3 shows the gender-wise distribution of symptoms in OSF cases at first presentation. Reduced mouth opening (OR = 1.98, 0.97–4.5, *P* = 0.053), altered salivation (OR = 1.41, 0.99–1.99, *P* = 0.043) and altered taste sensation (OR = 1.61, 1.13–2.29, *P* = 0.004) were found to be significantly more prevalent in women when compared with men.

Chewing habits

Out of 1000 patients, 77.8% (*n* = 778) patients were having multiple (more than one) habits, whereas 20.5% (*n* = 205) patients were having exclusive habits (only one habit), 1.7% (*n* = 17) patients did not give history of any habit. Average length of chewing for all cases was 21.5 ± 22.6 min with a mean frequency of chewing 1.28 ± 4.03 per day and mean duration of chewing 1.4 ± 3.59 years.

Exclusive habits

Table 4 gives the distribution and risk of OSF cases having exclusive habits (*n* = 192). Females have shown statistically significant increase in exclusive areca nut chewing habit (OR = 44.5, 25.4–79.8, *P* = 0.0001)

Table 4 Gender-wise risk/distribution of oral submucous fibrosis with exclusive habits

Variables	Male (N = 830), n (%)	Female (N = 170), n (%)	OR (95% CI)	P-value
Areca nut				
Yes	20 (2.40)	89 (52.35)	44.5 (25.4–79.8)	0.0001
No	810 (97.59)	81 (47.64)		
Kharra				
Yes	38 (4.57)	0 (00)	— ^a	— ^a
No	792 (95.42)	170 (100)		
Gutkha				
Yes	35 (4.21)	02 (1.17)	3.69 (0.93–32)	0.0557
No	795 (95.78)	168 (98.82)		
Tobacco				
Yes	05 (0.60)	03 (1.76)	2.96 (0.45–15.3)	0.1212
No	825 (99.39)	167 (98.23)		

^aOR values cannot be calculated because of zero cell frequency.

when compared with men, but significant increase for *Gutkha* (AQ + T) (OR = 3.69, 0.93–32, *P* = 0.055) and *kharra/Mawa* chewing was found in men when compared with women.

Multiple habits

Table 5 gives the distribution and risk of OSF patients with multiple habits (*n* = 791). There was a statistically significant increase in areca nut chewing (OR = 24, 12.10–54.17, *P* = 0.0001), *Kharra/Mawa* chewing (OR = 6.8, 4.36–11.06, *P* = 0.0001), *Gutkha* (AQ + T) chewing (OR = 2.33, 1.56–3.54, *P* = 0.0001) and smoking habits (OR = 12.8, 5.3–40.6, *P* = 0.0001) in men when compared with women. Although BQ chewing and the use of snuff for teeth cleaning were proportionately higher in men, they were not found to be statistically significant.

Associated lesions

In the present sample, major pre-malignant lesions associated with OSF were leukoplakia (4.8%) and lichen planus (0.7%) followed by erythroplakia (0.2%) and Betel chewer's mucosa (0.7%).

Table 5 Gender-wise risk/distribution of OSF with multiple habits

Variables	Male (N = 830), n ^a (%)	Female (N = 170), n ^a (%)	OR (95% CI)	P-value
Areca nut				
Yes	476 (57.34)	09 (5.29)	24 (12.10–54.17)	0.0001
No	354 (42.65)	161 (94.70)		
Kharra				
Yes	459 (55.30)	26 (15.29)	6.8 (4.36–11.06)	0.0001
No	371 (44.69)	144 (84.70)		
Ghutka				
Yes	345 (41.56)	37 (21.76)	2.33 (1.56–3.54)	0.0001
No	531 (63.97)	133 (78.23)		
Tobacco				
Yes	275 (33.13)	41 (24.11)	1.55 (1.05–2.34)	0.0213
No	555 (66.86)	129 (75.88)		
Snuff				
Yes	230 (27.71)	37 (21.76)	1.37 (0.91–2.10)	0.1104
No	600 (72.28)	133 (78.23)		
Smoking				
Yes	233 (28.07)	05 (2.94)	12.8 (5.3–40.6)	0.0001
No	597 (71.92)	165 (97.05)		
Betal quid				
Yes	108 (13.01)	16 (9.41)	1.43 (0.81–2.68)	0.1944
No	722 (86.98)	154 (90.58)		

^aAll of these patients had more than one habit.

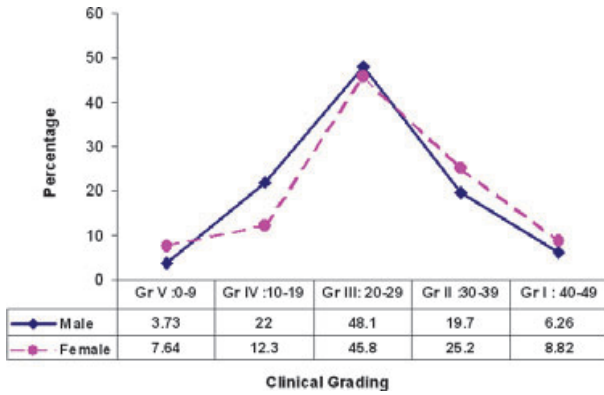


Figure 2 Gender-wise distribution of clinical grading by interincisal opening.

Clinical grading

Fig. 2 depicts the gender-wise distribution of clinical grading of OSF (mouth opening in millimetres), where men and women were equally (48.3%) affected with grade III (20–29 mm) severity.

Pattern of oral cancer in OSF

Out of a total of 33 malignant cases, 28 cases (2.8%) were squamous cell carcinomas and five cases (0.5%) were verrucous carcinomas. This accounts for 3.3% malignancy potential in the present study. Table 6 gives the comparison of all the habits between malignant and non-malignant OSF cases. We have found that malignancy in OSF cases was significantly associated ($P < 0.05$) with increased frequencies of BQ chewing and smoking as well as increased durations of tobacco chewing, BQ chewing and smoking habits.

Discussion

Oral submucous fibrosis is a pre-malignant condition, which has been described in detail in Asians and Asians settled in other countries. Describing the condition in five Indian women, Schwartz (9) called it ‘atrophia idiopathica mucosae oris’. Subsequently, Joshi called it submucous fibrosis (10). Various aetiological factors have been suggested for OSF, which include local irritant such as capsaicin (11), pungent and spicy food

(12) and areca nut use (1). In addition to the local factors, systemic factors have also been suggested to play a role in the development of OSF. These include anaemia, chronic iron and vitamin B deficiency (13) and genetic pre-disposition (14).

Chewing areca nut in its various forms is widely prevalent in the Indian subcontinent, giving rise to increased prevalence of OSF, from an estimated 250 000 cases in 1980 (15) to an estimated 5 million people in 2002 (16).

In present study, an increasing trend in prevalence for OSF was observed since 2000 (2.42 in 2000 to 6.42/1000/year in 2004). The period prevalence rate for 2004 was comparable with other Indian and Malaysian studies (17, 18), and less when compared with studies from China and Taiwan (19, 20). This striking difference between the prevalence rates may be attributable to long history of chewing habits, and an important role of areca/BQ in Taiwanese cultural activities (20).

The mean age of all cases affected with OSF was 28.8 ± 10.4 years, which is relatively a younger age when compared with south Indian (32.4 ± 10.4 years) and north Indian (30.42 ± 10.86) OSF cases (21, 22). There are very few reported cases of children affected with OSF (23, 24). In the present study, we have found OSF in the youngest, 9-year-old girl and 12-year-old boy.

Our study showed a high preponderance of OSF in men (4.9:1), which is similar to a male preponderance, reported by various authors (5, 21, 22). However, few studies have reported female preponderance (25–28). Inability to open the mouth wide was the chief complaint (90.8%), which clearly suggests that one of the diagnostic signs of the disease, is restricted mouth opening (29–31). In the present study, there were 17 cases with no history of areca nut chewing, tobacco chewing or smoking habits. Seedat and Van Wyk (32) from South Africa made similar observations in OSF patients.

In the present study, posterior one-third of oral cavity (both buccal mucosae, retromolar area and soft palate) was predominantly affected, which is similar to the observations from Pune group from Maharashtra state and in contradiction with findings from Ernakulam group from Kerala state, where labial mucosa was

Table 6 Comparison of mean frequencies (per day) and durations (years) of different habits in malignant and non-malignant oral submucous fibrosis cases

Habits	Frequency (per day)			Duration (years)		
	Malignant (n = 33)	Non-malignant (n = 967)	P-value	Malignant (n = 33)	Non-malignant (n = 967)	P-value
Areca nut	2 ± 3	1.8 ± 4.1	0.901	3.6 ± 7.3	2.85 ± 6.0	0.507
Tobacco	2.3 ± 4.1	1.9 ± 3.7	0.544	4.2 ± 7.1	2.23 ± 5.2	0.033
Kharra	3 ± 3.1	2.8 ± 6.8	0.995	4.2 ± 5.9	2.50 ± 3.4	0.015
Betel quid	1.2 ± 2.7	0.3 ± 1.3	0.001	2.4 ± 6.2	0.74 ± 3.2	0.006
Gutkha	4 ± 8.4	3.6 ± 6.3	0.752	2.6 ± 4.6	2.35 ± 3.6	0.731
Snuff	0.4 ± 0.9	0.2 ± 0.9	0.181	1.8 ± 4.3	1.21 ± 4.1	0.384
Smoking	3.4 ± 6.9	1.0 ± 3.6	0.001	2.9 ± 7.3	1.07 ± 3.5	0.005

Values are given as mean ± SD.

significantly affected, which represents a regional variation with respect to various chewing habits practised in different parts of India (33).

Women have shown statistically significant increase for exclusive areca nut chewing habit when compared with men, which is mainly attributable to the local cultural practices and easy availability of areca nut. Similar finding had been reported by several studies in Asian and South African population (25, 34). Inversely, men have shown statistically significant increase in *Gutkha* (AQ + T) and *Kharra/Mawa* chewing habits. This finding justified that the commercial product *Gutkha* (AQ + T) have equated with the local preparation *Kharra/Mawa*. Negligible number of female smokers ($n = 5$) was found in our study as it was in Yang's study (27).

In the present study, majority of OSF (48.3%) cases were in grade III (20–29 mm) severity with an average mouth opening of 24.62 mm, which is in contrast with Cox's study (35), who found an average mouth opening of 34 mm in the Nepalese OSF cases. Our study also revealed a strong association between the incidence of leukoplakia (4.8%) and OSF, which might be attributed to BQ chewing and smoking habits (36).

Although this study was not designed as a case-control study, we tried to evaluate by calculating OR with group comparisons, the association between OSF and other baseline characteristics, which highlighted the significant association of OSF with younger age, illiteracy, low socioeconomic status and various chewing products.

In this study, a malignant potential of 3.3% was noted. These malignant OSF cases have shown statistically significantly increased frequencies and duration of BQ, tobacco chewing as well as smoking habits when compared with non-malignant cases. This finding confirms that tobacco plays a modifying effect on malignant transformation in OSF. A similar malignant potential (3.6%) was noted by Caniff in Durban, South Africa (37).

The present study also confirms the fact that the increased *Gutkha* (AQ + T) chewing habit, which has substituted the BQ and *Kharra/Mawa* use in this region has not only given rise to increased prevalence of OSF but also can give rise to increased incidence of oral cancer among these patients mainly because of its tobacco and other carcinogenic additives.

We hypothesize from the present epidemiological study that there is a marked difference in habits, their frequency and duration, signs and symptoms and disease severity in women when compared with men seeking dental care for OSF at tertiary level in the central Indian population. The present cross-sectional study, to the best of our knowledge, is the single largest report on OSF so far published from India.

Conclusion

The impression of emerging prevalence of OSF since 2000 (0.42–0.64%), in relatively younger population in India seems to be justified by the data observed in the

present study. Urgent regulatory actions are therefore warranted to control the manufacture, marketing and the consumption of products that contain areca nut and/or tobacco, especially *pan masala* and *Gutkha*. Special efforts are needed to educate the adolescent population using available modalities such as oral health exhibition and camps.

Endorsement

I, the undersigned, Dr (Mrs) S.M. Ganvir, hereby endorse that, the data used for the research titled 'Oral submucous fibrosis: study of 1000 cases from central India' are hospital based and were obtained from patients who visited the Department of Oral Pathology and Microbiology, Government Dental College and Hospital, Nagpur, Maharashtra, India, during the period January 2000 to December 2004.

I have verified the claimed conclusions and found them correct as per the results obtained from this study.

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