

Oral Submucous Fibrosis: Benign or Malignant

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ABSTRACT

Introduction: Oral submucous fibrosis (OSMF) is a premalignant disorder, mainly caused by betel nut chewing in various forms. It is found in the Asian subcontinent. **Aim:** The purpose of the study is to evaluate the OSMF as benign or malignant by evaluating aggravating factors in detail to avoid unnecessary intervention in OSMF as well as for the better treatment plan. **Materials and Methods:** Total numbers of 61 cases of clinically diagnosed OSMF which include 22 cases of OSMF alone and 22 cases of OSMF with associated like chronic traumatic ulcer, speckled leukoplakia or any other red or erosive lesions (Aggravating factors) were included for this study. This study was done on the basis of age group, sex, habit duration, types of habit, aggravating factor, investigation, treatment plan and follow up according to group of OSMF. After collecting data, they were analyzed statistically. **Results:** From 61 OSMF cases, 42.5% of group 1 patients were in 20-29 years age and 33.3% of group 2 in 30-39 years age with M:F ratio of 2.6:1 in group 1 and 9.5:1 in group 2. In both the groups, maximum no of patients had habit of betel nut with tobacco. Cytological smear was done in 5 (23.8%) and biopsy was done in 6 (28.5%) patients of group 2. According to the grade of OSMF treatment was decided. **Conclusion:** When aggravating factors like smoking + smokeless tobacco habit, pouching tobacco habit, chronic irritating factors (sharp teeth/ restorations) and partially impacted/ buccally placed 3rd molar were associated with OSMF, there was more chances of converting into malignancy with the malignant potential of 28.57% which was underestimated before.

Key words: OSMF, Potentially Malignant, Benign

Oral Submucous fibrosis (OSMF) is a premalignant 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 that has received considerable attention because of its chronic debilitating and resistant nature. The epidemiological assessment of the prevalence of OSMF among Indian villagers, based on baseline data, recorded a prevalence of 0.2% in Gujarat, 0.4% in Kerala, 0.04% in Andhra Pradesh, and 0.07% in Bihar [1]. OSMF may cause atrophy in the epithelium, increasing carcinogen penetration [2,3].

Areca nut has been proven as an etiologic agent for OSMF and Class 1 carcinogen which might contribute to early development of oral squamous cell carcinoma (OSCC) in younger age group. Epithelial dysplasia has been reported to occur in 7%–43% of OSMF in different studies. The rate of transformation to malignancy varies from 3% to 19%. The incidence of OSCC concomitant with OSMF was found to be 25.77% in a recent study from India [4], and it is evident that the malignant potential of OSMF is underestimated. After comparing the risk ratio, it has been estimated that people with OSMF are 19.1 times more likely to develop oral cancer than those without it.

Nonhealing traumatic ulcer is the most common cause for malignant transformation in oral submucous fibrosis patients [2,5]. Purpose of this study is to evaluate the OSMF as benign or malignant by evaluating aggravating factors in detail to avoid unnecessary intervention in OSMF as well as for the better treatment plan.

MATERIAL AND METHOD

This study includes 61 cases of OSMF which include 22 cases of OSMF alone and 22 cases of OSMF with associated like chronic traumatic ulcer, speckled leukoplakia or any other red or erosive lesions (Aggravating factors). Permission to undertake this study was obtained from the institutional ethics committee. Written informed consent obtained from all the patients before enrolling them in the study.

Selection criteria:

1. All 61 cases were selected clinically on the basis of clinical criteria shown in **Table 1**
2. Patient having OSMF with other habit related lesions like leukoplakia, Tobacco Quid Lesion (TQL), smoker's palate, chronic traumatic ulcer, minor/major aphthous ulcer as well as local lesions related to teeth, gingiva and periodontium were included.
3. Patients having OSMF with any systemic diseases were included.

Once the patients were selected for the study, each subject was interrogated in detail regarding age, gender, occupation, past medical history, past dental history and family history. History of habit of both smoking and smokeless was evaluated in detail. Along with the chief complaint related to OSMF, associated complaint was also asked. Extraoral examination includes general body examination like stature, built, vitals, nail, hair, lip, lymph node, TMJ and mouth opening measurement were done. Intraoral examination includes hard and soft tissue examination in detail.

Local examination pertained to OSMF and associated lesions were done in detail. After thorough clinical examination, clinical diagnosis was given along with grading of OSMF and grouping of patients. Patients were grouped into two groups as follows:

Group 1- patient with only OSMF

Group 2 - Patient has OSMF with other lesions such as speckled and nodular leukoplakia, chronic traumatic ulcer, erosive type of TQL (which has malignant potential)

Radiographic (OPG) evaluation was carried out in patients with complete trismus either due to severe OSMF or OSMF with pericoronitis or chronic traumatic ulcer in posterior retromolar region to rule out status of impacted tooth & alteration in bony trabeculae or irregular bone loss. Histopathological investigations (incisional/punch biopsy) were done in OSMF patients with erosive lesions like speckled leukoplakia, and smoker's palate (Group 2) [**Table 10**].

All group 1 patients were treated for OSMF according to the grade. In group 2 patients, after radiographic interpretation, if there was irregular bone loss or floating tooth appearance noted, exfoliative cytology was carried out from ulcer to know malignant changes. No malignant changes were noted in cytology, ulcer was considered to be traumatic ulcer and treated with local application of lignocaine and salicylate to reduce inflammation and kept in follow up. Once the ulcer heals, OSMF treatment was started as per grade. If ulcer was not healed in 15 days, incisional biopsy was done. If biopsy report of chronic traumatic ulcer showed no dysplastic changes, ulcer was treated with local application.

If biopsy report of speckled or nodular leukoplakia showed no dysplastic changes or mild to moderate dysplasia, patient was managed with topical application of vit A and biopsy was repeated after 3 months in dysplastic cases. If biopsy showed no dysplasia or mild to moderate dysplasia in erosive type TQL, topical application of lignocaine and salicylate was given to reduce inflammation followed by topical application of vit A and biopsy was repeated after 3 months in dysplastic cases. If biopsy report showed severe dysplasia or carcinoma in situ or carcinoma, patient was referred to cancer hospital as considering it as malignancy. All details were regarded in detail, tabulated and analyzed as shown in table and result.

RESULTS

Total of 61 cases were examined in this study, of which 40 (65.57%) cases were in group 1 and 21 (34.42%) cases in group 2. Grade wise distribution of group 1 cases [**Fig 1**] and associated lesion wise distribution of grade 2 were described in **Table 2**.

Table 1: Clinical criteria for selection of participants

Grades	Chief Complaint	Clinical Examination	Mouth Opening	Treatment
Grade I Very Early	Burning sensation on hot and spicy food;	Blanching (white fibrotic band) at the junction of hard & soft palate; Pale & blanched buccal mucosa; No palpable fibrosis	Normal	Counselling for discontinuation of habit Local application of topical anaesthetic gel for burning sensation Nutritional supplements
Grade II Early	Burning sensation on hot and spicy food;	Blanching, and palpable fibrosis of buccal mucosa faucial pillars, pterygomandibular raphe & soft palate; Thick, mottled & marble like buccal mucosa	25-35mm	Treatment of Grade 1+ Topical application of Betamethasone gel 0.5%, Mouth opening exercise with wooden key, ice cream stick No need of vigorous exercise
Grade III Moderate	Burning sensation on hot and spicy food;	Palpable fibrosis of buccal mucosa, faucial pillars, pterygo-mandibular raphe & soft palate fibrosis extending anteriorly to involve labial mucosa, floor of the mouth & tongue; Restriction of tongue movements to some extents; Loss of flexibility of buccal mucosa;	15mm to 25mm	Treatment of Grade 1+ Mouth opening near to 25mm Mild stage just converting into moderate stage - Treat like Grade II (mild osmf) Mouth opening near to 15mm Moderate stage near to converted to severe stage Treat like Grade IV (severe OSMF) Vigorous Mouth Opening Exercise
Grade IV Severe	Burning sensation even in absence of stimuli; Difficulty in swallowing & deglutition; Difficulty in speech & nasal voice	Severe fibrosis of entire oral cavity; Severe restriction of tongue movements; Severe loss of flexibility of buccal mucosa; Circular band (fibrotic rim) around lips & mouth; Fibrosis of soft palate & shrunken uvula;	less than 15mm	Treatment of Grade 1+ Intra-lesional/submucosal injection therapy. Dexamethasone (4 mg/2 ml) Hydrocortisone (25 mg/ml) Placental extract (2 ml) In combination with Enzyme therapy (Hyaluronidase (1500 IU)
Grade V Extreme severe	Burning sensation even in absence of stimuli; Difficulty in swallowing & deglutition; Difficulty in speech & nasal voice;	All findings of severe OSMF are present along with Loss of puffiness of face & Loss of vertical dimension.	Complete trismus;	1 st rule out for any other cause of the trismus, any ulcerative growth in mandibular posterior region, as most common cause of trismus is pericoronitis, peri coronal abscess with impacted mandibular 3 rd molar. OPG should be done to evaluate impacted 3 rd molar or any bone loss in mandibular posterior area. If patient has peri coronal abscess, first give treatment of abscess by giving antibiotic & anti-inflammatory. After 5days of this therapy, perform exfoliative cytology from posterior 3 rd molar area. If cytology showing nuclear enlargement take incisional biopsy. If non-dysplastic - Topical application of betamethasone 0.5% and Mouth

				opening exercise with ice cream sticks. Once the mouth opening is accessible for intra lesional injection Intra-lesional/Submucosal Injection therapy and treat as severe osmf If dysplastic - patient should be advised for further investigations like CECT to check lymph node status and extension of lesion.
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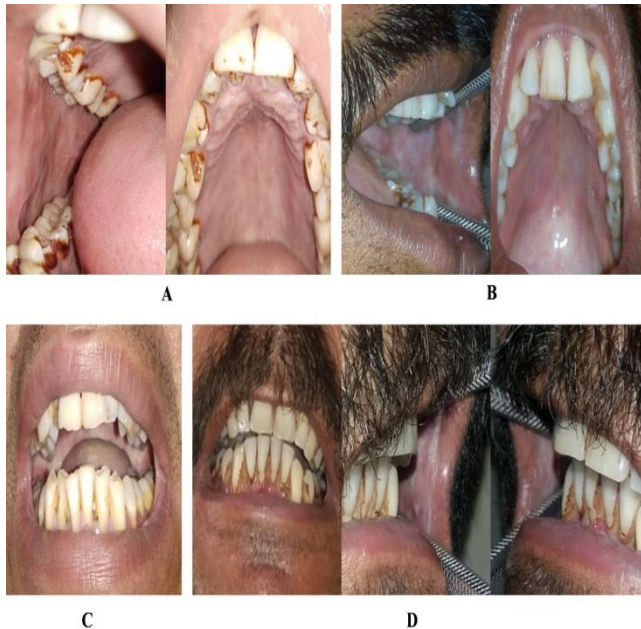


Figure 1: OSMF; Early stage [A], Moderate stage [B], Severe stage [C], Extreme severe stage [D]

Maximum [17 (42.5%)] number of patients were in 20-29 years age group in group 1 and 30-39 years [7 (33.3%)] in group 2 [Table 3]. Male: female ratio for group 1 was 2.6:1 and for group 2 was 9.5:1[Table 4]. In both the groups, maximum number of patients had habit of betel nut with tobacco [30 (75%) vs 13 (61.9%)] which was highly significant [Table 5]. Duration and frequency wise distribution of patient was mentioned in [Table 6 & 7]. Most common complaint was related to teeth [Table 8].

Aggravating factor wise distribution of group 1 & 2 cases [Table 9] was statistically significant. Cytological smear was done in 5 (23.8%) and biopsy was done in 6 (28.5%) patients of group 2. Only 1 (2.5%) patient underwent for tzanck smear in group 1 as OSMF was associated with pemphigus. According to the grade of OSMF treatment was decided. 22 cases in group 1 and 6 cases in group 2 were responded with various treatments.

Table 2: Group wise distribution of patients

Groups		Total no
Group 1	Grade 1	2 (5%)
	Grade 2	3 (7.5%)
	Grade 3	26 (65%)
	Grade 4& 5	9 (22.5%)
	Total	40(65.57%)
Group 2	Speckled leukoplakia	2 (9.5%)
	Nodular leukoplakia	1 (4.76%)
	TQL	3 (14.3%)
	Chronic traumatic ulcer	12 (57.1%)
	Carcinoma	3 (14.3%)
Total	21 (34.42%)	

Table 3: Age wise distribution of patients

Age group	Group 1(n= 40)	Group 2(n=21)
10-19 yrs.	1 (2.5%)	-
20-29 yrs.	17 (42.5%)	5 (23.8%)
30-39 yrs.	14 (35%)	7 (33.3%)
40-49 yrs.	4 (10%)	4 (19%)
50-59 yrs.	3 (7.5%)	4 (19%)
≥60 yrs.	1 (2.5%)	1 (4.7%)

Table 4: Sex wise distribution of patients

Sex	Group 1(n= 40)	Group 2(n=21)
Male	29 (72.5%)	19 (90.47%)
Female	11 (27.5%)	2 (9.5%)

Table 5: Habit wise distribution of patients

Habit	Group 1(n= 40)	Group 2 (n=21)	P value
Betel nut Alone	9 (22.5%)	-	0.000 (H.S)
Betel nut +Tobacco	30 (75%)	13 (61.9%)	
Betel nut +Smoking	-	4 (19.04%)	
Tobacco alone	1 (2.5%)	4 (19.04%)	

Table 6: Frequency of habit wise distribution

Frequency/day	Group 1(n= 40)	Group 2 (n=21)	P value
1-2	12 (35%)	5 (23.8%)	0.701 (N.S)
3-5	15 (37.5%)	9 (42.85%)	
6-10	10 (25%)	5 (23.8%)	
11-15	3 (7.5%)	1 (4.7%)	
>15	-	1 (4.7%)	

Table 7: Duration of habit wise distribution of patients

Duration (in years)	Group 1 (n= 40)	Group 2 (n=21)	P value
1-2	9 (22.5%)	1 (4.7%)	0.033 (S)
3-5	6 (15%)	6 (28.57%)	
6-10	18 (45%)	3 (14.28%)	
11-15	5 (12.5%)	6 (28.57%)	
>15	2 (5%)	5 (23.8%)	

Table 8: Signs and symptom of the patients

Signs and symptom	Group 1 (n= 40)	Group 2 (n=21)	P value
Fibrosis of OM	40 (100%)	21 (100%)	0.926 (N.S)
Vesiculation/Ulceration	4 (10%)	4 (19%)	
Burning Sensation	4 (10%)	2 (9.5%)	
Restricted Mouth opening	13 (32.5%)	5 (23.8%)	
Difficulty in tongue movement	8 (20%)	2 (9.5%)	
Nasal Twang	2 (5%)	2 (9.5%)	
Pain/other complaint in teeth	23 (57.5%)	10 (47.6%)	
White discoloration	-	1(4.76%)	
Growth	-	1 (4.76%)	

Table 9: Aggravating factors in the study\ patients

Aggravating factor	Group 1(n= 40)	Group 2 (n=21)	P value
Habit (smoking + smokeless tobacco)	-	4 (19.04%)	0.002 (S)
Habit of pouching tobacco	-	5 (23.8%)	
Chronic irritating factors (sharp teeth/ restorations)	-	5 (23.8%)	
Partially impacted / buccally placed 3 rd molar	9 (22.5%)	7(33.3%)	

Table 10: Histopathological investigation of patients

Clinical lesion	Cytology [Dysplasia]		Histopathology [Dysplasia]		Malignant potential
	yes	no	yes	no	
Chronic traumatic ulcer(n=12)	-	5	-	-	28.57%
Ulcer with growth (n= 1)	-	-	1	-	
Speckled leukoplakia (n=2)	-	-	2	-	
Nodular leukoplakia (n=1)	-	-	1	-	
TQL (n=3)	-	-	-	-	
Carcinoma (n=2)	-	-	2	-	



Figure 2: OSMF with traumatic ulcers on right buccal mucosa

DISCUSSION

Tobacco is addictive, and its use is harmful to health in many ways. Lack of awareness of the effects of tobacco use and the difficulty to discontinue the habit (psychology and nicotine dependence of an individual) has led to the increased incidence of tobacco use mainly in the form of tobacco smoking, tobacco chewing, and tobacco snuff use [6]. OSMF is a pre-malignant condition, which has been described in detail in Asians or Asians settled.

Various etiological factors have been suggested for OSMF, which include local irritant such as capsaicin,

pungent and spicy food and areca nut use. In addition to local factors, systemic factors have also been suggested to play a role in the development of OSMF. These include anemia, chronic iron and vitamin B deficiency and genetic pre-disposition [3]. Betel nut is the main etiological factor for the development of OSMF but tobacco acts as an addictive ingredient [5,8-10]. Same findings were noted in the present study (75% in group 1 and 61.9% in group 2). This was in accordance with other studies [6,7].

In present study, OSMF was more reported in males (2.6:1 in group 1 and 9.5:1 in group 2) in comparison to females. This was in accordance with other studies [6,7]. Male predominance can be due to easy accessibility due to their field or other works for the stress burst. There was more prevalence of OSMF in 20–29 years age group in group 1 and 30-39 years in group 2. Similar findings were also observed by other studies [6,7]. Prevalence of OSMF in the younger age group which is strongly related to increase availability, advertisement and marketing strategies of betel nut containing products force the youth to accept it as sign of modernity and fashion. This could be also because of increased social encounters and economic liberty they get at this age. Therefore, during this age, they indulge in various chewing habits either to relieve stress, as a fashion or due to peer pressure.

In this study, high prevalence was noted in patients with 6–10 years habit duration in group 1 and 11-15 years in group 2 with 3–5 packets/day frequency. These findings were in accordance with findings of other studies [6]. In the present study, it was found that the severity was more in subjects who were chewing for a longer duration and swallowing. The majority of patients present with an increased severity of disease with Grade III inter-incisal mouth opening which suggests a lack of awareness among patients and delayed diagnosis.

When OSMF alone was present, there is no chances of converting into malignancy and it is considered as benign. It has malignant potential due to various aggravating factors like smoking + smokeless tobacco habit, pouching tobacco habit, chronic irritating factors (sharp teeth/restorations) and partially impacted / buccally placed 3rd molar. Radiographic investigation like OPG is useful to detect the status of partially impacted teeth which is one of the main causes of trauma in OSMF patients. OSMF is reversible when patient is cooperative, quitted habit, having only OSMF and on periodic regular follow up. In

our study, out of 40 group 1 cases, 2 cases in grade 1, 3 cases in grade 2, 14 cases in grade 3 and 3 cases in grade 4 were responded with treatment and reduced the grade. Other patients were uncooperative and didn't came for follow up. Out of 21 group 2 cases, 2 cases of speckled, 1 case of nodular leukoplakia, 3 cases of traumatic ulcer were responded to the treatment but didn't continue for OSMF treatment.

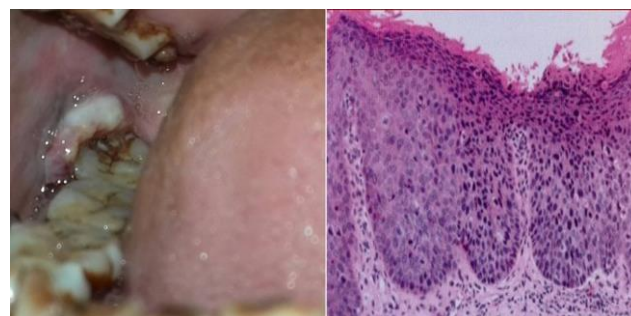


Figure 3: OSMF with chronic hyperplastic growth on right buccal mucosa showing carcinoma in situ histologically

Histopathological investigations like cytological smear or biopsy are mandatory in patients with chronic traumatic ulcer, other associated premalignant lesion or ulceroproliferative growth in association with OSMF. Cytological smear was done in 6 cases of traumatic ulcer and biopsy was done in 2 speckled [Fig 4 A], 1 nodular leukoplakia [Fig 4B] and 3 cases of ulceroproliferative growth [Fig 5B] to rule out malignant changes.

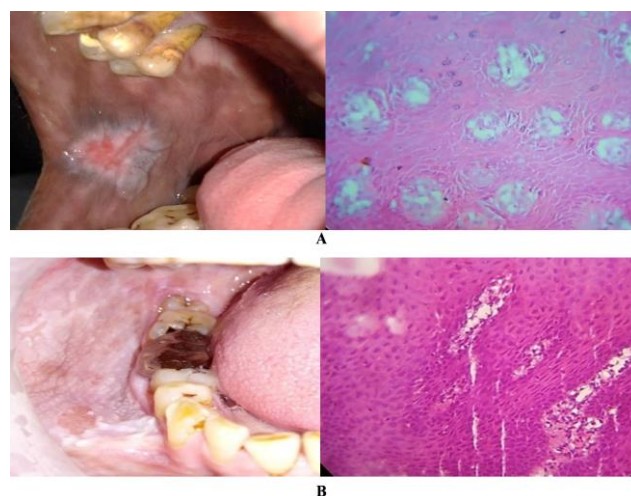


Figure 4: OSMF with leukoplakia on right buccal mucosa showing moderate dysplasia histologically; Speckled leukoplakia [A], Nodular leukoplakia [B].

TQL patients [Fig 5A] doesn't turnout for follow up in present study. Out of 12 traumatic ulcer patients [Fig 2], 7 were treated by conservative management and 5 patients underwent cytological smear due to chronic nature, unresponsiveness to conservative management. But in all 5 cases, dysplastic changes were not noted in cytology even though it was associated with complete trismus. Hence continued with routine treatment and kept under follow up.

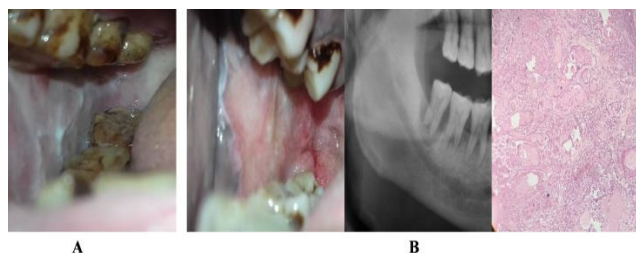


Figure 5: OSMF with tobacco quid lesion on right buccal mucosa [A], OSMF with presence of ulceroproliferative growth on right buccal mucosa which showed well differentiated squamous cell carcinoma histologically and bony changes in OPG [B].

In one case of traumatic fibroma [Fig 3], excisional biopsy showed carcinoma in situ changes. This suggested that, the malignant potential of chronic traumatic ulcer associated with OSMF was less compared to any growth or hyperplasia in OSMF. Out of 21 cases, 3 cases of non-homogeneous leukoplakia, 2 ulceroproliferative growth and 1 traumatic fibroma cases showed dysplastic changes. OSMF with associated non-homogenous leukoplakia or traumatic fibroma or ulceroproliferative growth cases should be considered for radiographic and histologic investigations as malignant potential of 28.57% was found in present study which was more than other studies 3% to 19%.⁷ It indicates the underestimation.

CONCLUSION

All the necessary steps should be taken towards prevention of the disease through public awareness rather than waiting for futile effort to treat the same ineffectively. When aggravating factors like smoking + smokeless tobacco habit, pouching tobacco habit, chronic irritating factors (sharp teeth/ restorations) and partially impacted/ buccally placed 3rd molar were associated with OSMF, there was more chances of converting into malignancy with the malignant potential of 28.57% which was underestimated before.

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