

Clinico-Pathological Study of 170 Cases of Oral Sub-Mucous Fibrosis

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Abstract

Introduction: Oral sub-mucous fibrosis (OSMF) is a chronic, irreversible, disease of the oral cavity characterized primarily by burning sensation in the mouth particularly while eating spicy food and progressive development of the inability to open mouth (trismus). Very few clinico-pathological study of OSMF has been published from India and the Indian subcontinent.

Materials and Methods: We carried out a retrospective hospital-based clinico-pathological study of 170 patients diagnosed with OSMF attending the outpatient department of Oral and Maxillofacial Surgical Hospital, Rajkot, India and compared our findings with those findings published in earlier studies.

Results: In our study of 170 patients with OSMF, male:female ratio was 23.28:1. The highest incidence of OSMF was in the age group 21-30 years (mean 22.70 years), the youngest patient being 8 years old and the oldest 60 years. Inter-incisal distance (IID) varied between 00.00 CM (complete trismus) and 3.70 CMS, average IID being 2.70 CMS. The burning sensation in the mouth was the most common complaint (94.11% patients) followed by vesiculations and ulcerations (83.52% patients). Duration of disease was 2-5 years Buccal mucosa was involved bilaterally in 98.82% patients and palatal mucosa in 92.94% patients. No correlation was found between histopathological and clinical findings.

Conclusions: Incidence of OSMF is rising with the younger population getting involved into pathological oral habits such as tobacco and supari (Areca nut) chewing. This article gives an insight into OSMF and adds to its clinico-pathological profile.

Key words: Mouth diseases, Mouth neoplasms, Oral pathology, Oral sub-mucous fibrosis, Retrospective study

INTRODUCTION

Oral sub-mucous fibrosis (OSMF) is a chronic, progressive, irreversible, scarring disease, which predominantly affects the people of South-East Asian origin. This condition was described first by Schwartz¹ while examining five Indian women from Kenya, to which he ascribed the descriptive term “atrophia idiopathica (tropica) mucosae oris.” Later in 1953, Joshi² from Bombay (Mumbai) redesignated the condition as OSMF, implying predominantly its histological nature.

Described for the first time in detail in the year 1966 by Pindborg and Sirsat,³ OSMF is now definitely being

recognized as a disease of the Indian subcontinent occurring more commonly in countries such as India, Pakistan, Sri Lanka, Nepal, China, and few countries where Indians have migrated like Europe and North America. Very few publications and possibly none clinico-pathological study, on OSMF, has emanated from Western Countries because of the paucity of cases. Until 2008, only 39 cases have been reported from Europe and Canada, including 3 cases reported by Auluk *et al.*⁴

Recent epidemiological data indicates that the number of cases of OSMF has raised rapidly in India from an estimated 250,000 cases in 1980 to 2 million cases in 1993. That figure has crossed 10 million in the year 2013.⁵ In future, this figure is likely to increase many folds.

The number of gutkha consumers in India is, also, rising alarmingly. Prior to 2000, the incidence of OSMF in patients visiting dental surgeons was 0.2-1%, mostly in the age group of 45-54 and sex ratio of 1:3 (male-female).

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After 2000, there has been a 2-5% jump in the incidence of OSMF, mostly in the age group of 15-35 years.

Patients present themselves to the clinician treating OSMF with two major complaints: Burning sensation in the mouth, particularly while eating spicy food and progressive inability to open mouth fully (Trismus).

Epidemiological data and intervention studies suggest that areca nut (Supari) is the main etiological factor for OSMF.⁶⁻¹⁶ Areca nut is believed to be the fourth most addictive substance in the world¹⁷ and is also associated with dependency syndrome.¹⁸ Other etiological factors suggested are chillies, lime, tobacco, nutritional deficiencies such as iron, zinc, and copper, immunological disorders, collagen disorders, and genetic predisposition.

MATERIALS AND METHODS

In this retrospective hospital-based study, patients attending the outpatient Department of Oral and Maxillofacial Surgery Hospital, Rajkot, Gujarat State, India were screened for the presence of OSMF based on pre-determined clinical criteria mainly, burning sensation in the mouth particularly while eating spicy hot food and progressively increasing inability to open mouth (Trismus). Complete records were maintained detailing, apart from routine information such as name, age, and sex, areca nut and tobacco chewing or any other tobacco habit, duration of habit, how long areca nut and tobacco was kept in the mouth, other oral hygiene conditions, the amount of consumption of tobacco and areca nut per day, age since habit was initiated. Inter-incisal distance (IID) (mouth opening) was measured with calipers. All cases of OSF were classified into four stages based on IID.

Very early stage (Stage 1): IID = >3.50 CMS

Early stage (Stage 2) IID = 2.5-3.5 CMS

Moderately advanced stage (Stage 3) IID = 1.5-2.5 CMS

Advanced stage (Stage 4) IID = <1.5 CMS

Radiological examinations were carried out whenever found necessary. Blood and urine examination were carried out for all patients with particular attention to anemia, iron and B-complex deficiency, and protein deficiency.

Inclusion Criteria

1. Patient with chief complaint of burning sensation in the mouth while eating spicy foods and progressive inability to open mouth fully
2. Positive history of consumption or chewing of tobacco or related products
3. Clinical examination shows ulcerations and vesiculations

of the oral mucosa and / or fibrous bands running across buccal mucosa in the vertical direction or horizontal direction in the palate

4. Confirmation of OSMF by biopsy.

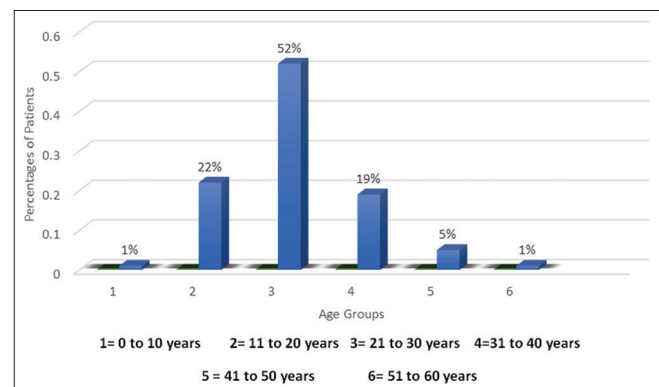
Exclusion Criteria

1. Presence of frank oral squamous cell carcinoma (OSCC)
2. The presence of severe systemic disease.

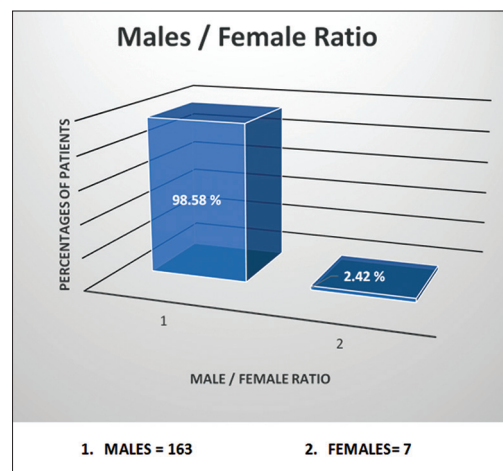
RESULTS

Age and Sex (Graphs 1 and 2)

Totally 170 patients were included in this study, out of which 163 patients were found to be males while only 7 patients were found to be females. Out of 170 patients, the youngest patient was 8 years old while the oldest patient was 60 years old, the average age of the patient being 22.70 years. Percentage wise patients between 0 and 10 years was 1%, 11 and 20 years old patients were 22%, 21 to 30 years patients were 52%, 31 to 40 years old patients were 19%, 41 to 50 years old patients were 5% while 51 to 60 years patients were 2%.



Graph 1: Percentages of patients in each age group



Graph 2: Male to female ratio

Sites of Involvement (Graph 3)

In 170 patients examined, 168 patients showed the bilateral involvement of buccal mucosa, lip mucosa was involved in 108 patients while palatal mucosa was involved in 158 patients. The floor of the mouth was seen to be involved in 109 patients while tongue was involved in 98 patients. The most patients showed multiple sites of involvement in the disease process.

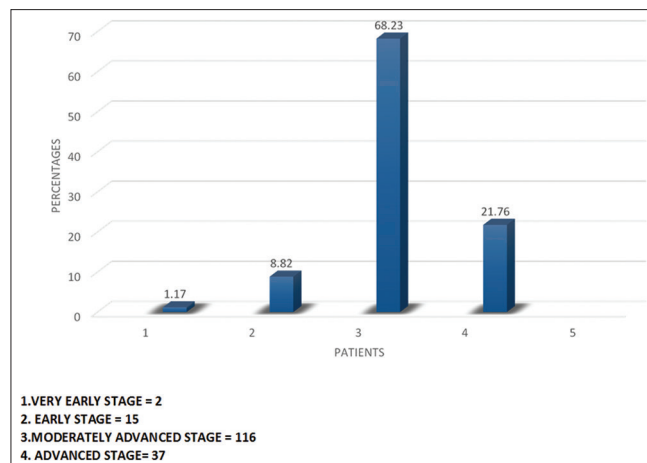
IID

When clinically examined, IID, maximum mouth opening was 3.70 CMS while minimal IID was found to be 0.00 CMS (total trismus). The average mouth opening was 1.79 CMS.

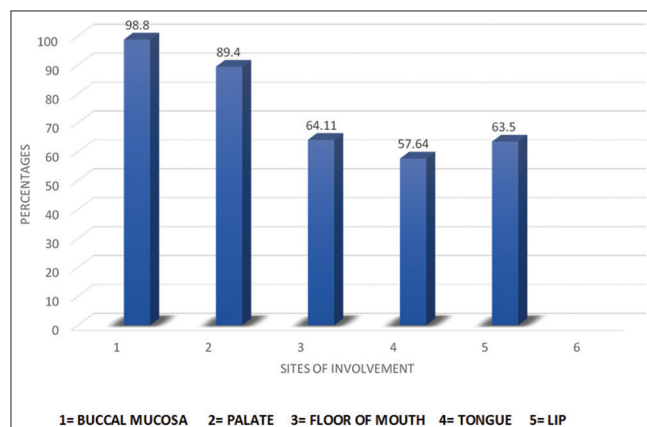
Clinical Presentations (Graph 4)

Two patients were seen to be in very early stage, early stage of disease was seen in 15 patients. OSMF was seen moderately advanced stage in 116 patients while advanced stage of disease was noticed in 37 patients.

Duration of disease refers the time lapse that occurs between patient noticing the first symptoms of OSF



Graph 3: Percentages of patients in each clinical grading



Graph 4: Sites of involvement

and subsequent consultation with the treating clinician. Duration of disease among 170 patients was found to be between 2 and 5 years with average being 3.5 years.

Presenting Symptoms (Graph 5)

Out of 170 patients, 160 patients had a chief complaint of burning sensation in the mouth and inability to open mouth fully. Vesications and ulcerations were found in 142 patients while dryness of mouth was the chief complaint in 102 patients. Surprisingly stiffness of the cheek was chief complaint only in 11 patients. Most patients had multiple complaints.

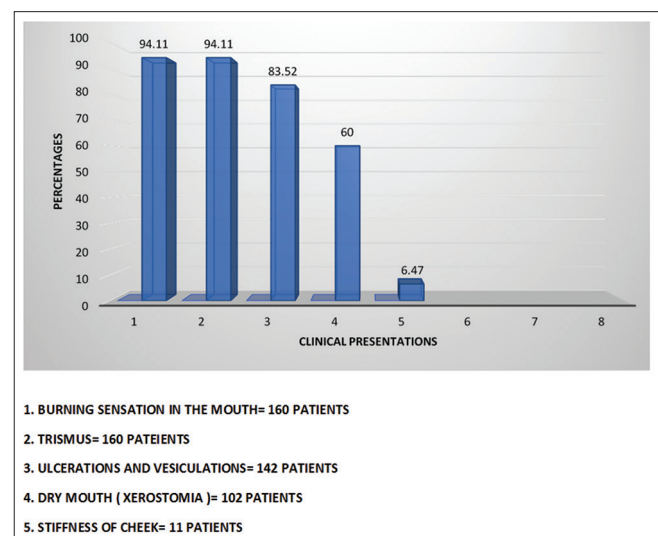
Histopathology (HP) (Graph 6)

On HP examination, all 170 patients ($n = 100\%$) showed various degrees of fibrosis. 36 patients showed no inflammatory changes in the sub-mucosa while 82 patients had mild inflammatory changes in sub-mucosa, moderate inflammation was present in 32 patients, and severe inflammation was present in 20 patients.

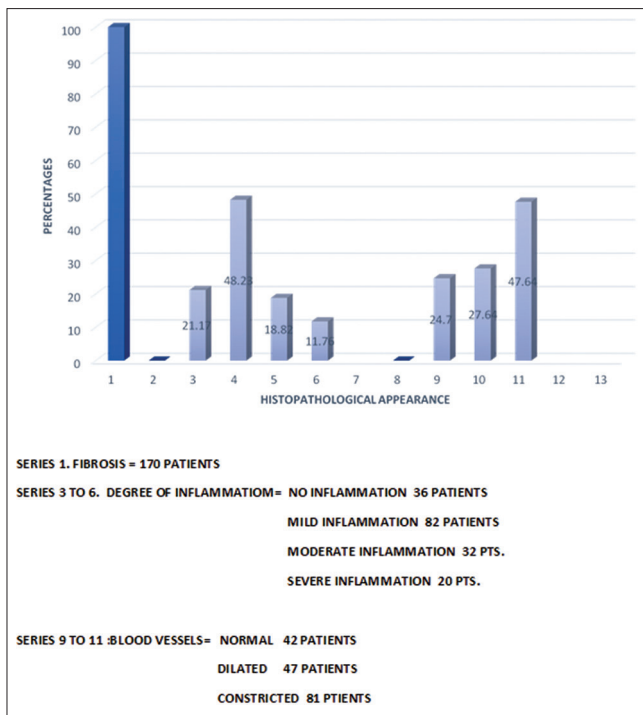
42 patients showed the normal size of the blood vessel while 47 patients had dilated blood vessels. 81 patients showed constricted blood vessels.

Almost all patients belonged to low socio-economic strata and had very low or no education to understand consequences of areca nut or tobacco chewing.

165 patients had habit of chewing mixture of areca nut, tobacco, and lime (known as gutkha or Mava). One patient, the youngest 8 years old had habit of chewing areca nut only while remaining 4 had habit of taking areca nut, tobacco, and lime in green leaf known as paan.



Graph 5: Percentages of patients with various clinical presentations



Graph 6: Percentages of patients showing various histopathological findings

Laboratory tests were carried out in all patients to rule of iron and b-complex deficiency. Since the most patients belonged to low socio-economic strata, the results showed one or more of the following findings:

- Decreased hemoglobin levels
- Decreased iron levels
- Decreased protein levels
- Increased erythrocyte sedimentation rate
- Decreased Vitamin B complex levels.

DISCUSSION

OSMF has also been called as “diffuse OSMF,” “idiopathic scleroderma of mouth,” “idiopathic palatal fibrosis,” sclerosing stomatitis” and “juxta-epithelial fibrosis.” Pindborg and Sirsat³ gave definition for OSMF as “As an insidious chronic disease affecting any part of the oral cavity and sometimes pharynx, although occasionally preceded by and/or associated with juxta-epithelial inflammatory reaction followed by fibroelastic changes of lamina propria with epithelial atrophy leading to stiffness of oral mucosa and causing trismus and inability to eat”. The WHO definition for an oral precancerous condition is a generalized pathological state of oral mucosa associated with a significantly increased risk of cancer accords well with characteristics of OSMF.¹⁹

It is now unequivocally established fact that OSMF is a disease of India and Indian subcontinent where chewing of areca nut and tobacco is almost endemic, and it is pre-

malignant condition leading to OSCC if the habit is not discontinued. In spite of very high prevalence of OSMF in India and Indian subcontinent very few clinico-pathological studies are available in the literature.^{10,20-30}

The discussion on OSMF will be done under following headings:

1. Age
2. Male-female ratio
3. Sites of involvement
4. Presenting clinical symptoms
5. HP.

Age

Study of age is an important prognostic parameter in the clinical study of OSMF because it gives three important informations:

1. Age at which patient was initiated into pathological oral habits such as beetle-nut or gutkha chewing
2. Age at which the patient developed first signs of OSMF and reported for treatment
3. Age at which patient is likely to develop OSCC and accordingly follow-up plan can be charted out.

There is a wide variation in the range of ages as reported by various authors; however, if one studies these reports in details a definite pattern in the incidence of OSMF emerges. Some of the earlier workers have reported the incidence of OSMF within the age group of 30-40 years. As a matter of fact, Pindborg *et al.*³¹ reported average age range as 53.6 years for males and 37.7 years for females. Recent authors, however, report incidence of OSMF mostly in the younger population age ranging from 20 to 30 years.^{2,15,20,22,23,28,32}

In India, OSMF has already been reported in children. In a study reported by Babu *et al.*²⁹ and Trivedy *et al.*³³ on OSMF, 23% of patients were of ages between 14 and 19 years. In separate studies children as young as 4 years³⁴ and 5 years³² old have been diagnosed with OSMF.

In the study reported by us of 170 patients with OSMF, the youngest patient was only 8 years old while the oldest patient was 60 years old, with mean age as 22.70 years (Figures 1 and 2).

Male-Female Ratio

Though earlier studies on OSMF reported female preponderance,^{2,8,9,36-41} more recent publications show male preponderance.^{7,12,20,24,25,27,28,30,40,42-46}

In the present study carried out in Rajkot, Saurashtra region, Gujarat state, there was male preponderance with 163 males and only 7 female patients. The M:F ratio was 23.28:1.



Figure 1: 8-year-old child with oral sub-mucous fibrosis white blanching of oral mucosa of lower lip is visible



Figure 2: 8-year-old child with oral sub-mucous fibrosis. Notice difficulty in opening mouth

Our study corroborates with the findings of Sinor *et al.*⁷ who reported male to female ratio as 29:1 from the city of Bhavnagar, Saurashtra region, Gujarat State. There seems to be a definite preponderance for male patients from Saurashtra region of Gujarat State, where gutkha chewing is almost endemic, and incidence of oral cancer is the highest in India and therefore in the world.

Male predisposition in recent studies could be due to easy accessibility of gutkha and other products to males than females in the Indian Society and probably females feel uncomfortable in purchasing gutkha products. Furthermore, the financial administration is not in the hands of most females limiting their access to such gutkha products, and most females shy away from medical treatment due to various reasons including financial crunch and societal and cultural traditions. One reason for occurrence of OSMF in female patients could be explained on the grounds that most females in the Indian sub-continent suffer from deficiency of iron and B-complex.⁴⁷ However, it needs to be confirmed whether iron and B-complex deficiency is the cause of OSMF in

female patients or it is effect of OSMF as eating ability reduces considerably in OSMF.

Sites of Involvement

It seems the various sites of the oral cavity involved in OSMF depends on many factors such as the type of material chewed, duration of habit, the way material is chewed and finally on the age of initiation of habit. Involvement of the whole of the oral cavity (pan or total involvement) is common in the advanced cases of OSMF.

Most of the clinicians have reported maximum involvement of buccal mucosa followed by palatal mucosa in OSMF.^{28,38,43,48-50} Occasionally floor of the mouth and tongue may get involved in the disease process as in our study in which 64.11% of the patients showed the involvement of floor of the mouth while 57.64% showed the involvement of tongue.

The involvement of buccal mucosa is the most common observation in most studies, including ours, because most of the patients are habituated to keep beetle-quid or gutkha in the buccal vestibule. In such patients next two commonly involved sites are soft palate and uvula. On the other hand, it was observed that those patients who chewed gutkha and other products for longer time and spat it out; fibrosis mostly got developed in the whole of buccal mucosa, parts of labial mucosa, and also the floor of the mouth. Most of the clinicians including Canniff³⁵ have reported OSMF in which fibrosis was in both sides of buccal mucosa or it was extended into soft palate, uvula, pharynx and root of the tongue. But no one has reported fibrosis on very localized on one side of buccal mucosa and other side completely normal.

Presenting Symptoms

The most common complaints which bring patients to clinicians for treatment are two:

1. Burning sensation in the mouth particularly while eating spicy hot food
2. Progressive inability to open mouth fully (trismus).

Most of the patients are not aware of the presence of the disease until they are told about OSMF and its consequences. Patients become aware of the trismus once they fail to put large size food bolus into their mouth. With advancing trismus, patient shift to a liquid diet or tend to push food into their mouth in small amounts by forcefully pushing it between teeth with their fingers. Such patients are known to develop indentations of teeth on their fingers, particularly thumbs.

According to Sabharwal *et al.*,⁵¹ specific presentations by patients with OSMF include the following:

1. Reduction of the mouth opening (trismus)
2. Stiff and small tongue

3. Blanched and leathery floor of the mouth
4. Fibrotic and depigmented gingiva
5. Rubbery soft palate with decreased mobility
6. Blanched and atrophic tonsils
7. Shrunken budlike uvula
8. Sinking of the cheeks, not commensurate with age or nutritional status.

Most investigators reported trismus as the main clinical presentation by the patients.^{3,38,43,52,53} Sitheeque *et al.*⁵⁴ have suggested depigmentation of oral mucosa as an earliest feature to develop in the natural history of OSMF in their study of Sri Lankan preschool children aged 2-3 years.

According to Hayes,³⁴ the most characteristic feature of OSMF is the marked vertical fibrous ridge formation within the cheeks, and board like stiffness of the buccal mucosa³⁴ leading to trismus and difficulty in blowing cheeks. The fibrosis in the soft tissue leads to trismus, difficulty in eating, and even dysphagia as reported by Pundir *et al.* in the year 2010.⁵⁵

Fibrous bands run vertically in the buccal mucosa while they run across the palate horizontally. Fibrous bands, in advanced stages, are visible to naked eyes and palpable under fingers.

Reduced mouth opening, altered salivation, and altered taste sensation were found to be significantly more prevalent in women when compared with men as reported by Hazarey *et al.* in the year 2007.²⁴

Goel *et al.*³⁰ also found that the patients who used pan masala with a greater frequency per day developed OSMF earlier. In other words, daily consumption (frequency) was more significant than the total duration of the habit.

According to Rajendran,⁴⁷ the exact site and extent of the fibrosis and its role in the causation of trismus are determined by several factors. For example, the anatomical and physiological integrity of the underlying musculature is vital for the degree of mouth opening. Based on electron microscopic observations el-Labban and Canniff⁵⁶ reported muscle degeneration in OSMF, the extent of which may significantly affect the already existing trismus in these patients. Equally important is the involvement of the pterygomandibular raphe, a site commonly reported to accentuate the extent of trismus. Another factor is the duration of the disease in the affected individuals, which depends on the subjective evaluation of signs and symptoms. Current views of a protracted and insidious onset of OSMF and its very slow progression make any sort of objective diagnostic criterion difficult, at least in the earlier stages.⁴⁷

HP of OSMF

HP study does not seem to play a much significant role in the diagnosis of OSMF as most clinicians diagnose OSMF based on clinical findings, and it is likely that facilities to carry out HP diagnosis may not be possible under certain adverse circumstances and in under-resourced countries. However, this does not undermine in any way importance of HP studies. Though most clinico-pathological studies did not find any correlation between HP findings and clinical grading, HP studies of OSMF patients is an important diagnostic and prognostic parameter so far as malignant transformation of OSMF is concerned as high percentages of OSMF patient land into frank OSCC, the incidence of OSMF being degraded to OSCC being reported as high as 7-13%.

According to Mukherjee *et al.*,⁵⁷ currently one of the greatest challenges to oral oncobiologists is to determine and identify the degree of tissue damage or stages of various precancerous states of oral tissue and to detect the exact transition of normal tissue to precancerous state. In this current scenario in which clinicians depend more on clinical findings rather than on HP studies, improved immunohistochemical techniques and morphometric analysis of HP images may go help to provide a better diagnosis and early detection of oral cancer.

In our study, we studied three parameters during the HP study of 170 patients.

1. Inflammation
2. Condition of blood vessels
3. Fibrosis.

Mild to moderate inflammation was present in 114 patients while constricted blood vessels were more common, present in 81 patients. All the patients showed an advanced degree of fibrosis. There was no correlation found between HP grading and clinical grading in our study as well.

Since HP of OSMF is non-specific and no correlation has been found between HP grading and clinical grading, possibly ultrasonographic studies may prove to be more reliable diagnostic tool than biopsy in the future.^{58,59}

CONCLUSIONS

In conclusion:

1. OSMF is mainly disease of the Indian sub-continent where chewing areca nut is rampant; however, it is likely to spread in Western countries like the USA and Europe because of migration of areca nut and tobacco chewing people from the Indian sub-continent to these countries

2. There is an urgent need to initiate public health education measures to educate people about these debilitating oral pre-malignant condition before it is too late, particularly in western countries
3. OSMF is definitely established as a pre-malignant oral condition, the range of OSMF degenerating into OSCC is 7-13%
4. OSMF has male pre-ponderance
5. Most patients of OSMF are within age group between 20 and 30 years, but even children as young as 4-5 years are not immune to OSMF
6. There is no correlationship between clinical findings and HP gradings
7. Burning sensation in the mouth while eating spicy hot food and progressively developing inability to open mouth are hallmark of clinical pictures of OSMF
8. Areca nut and its constituents are chief etiological factors in development of OSMF, while other etiological agents such as lime, tobacco, chillies, genetic predisposition act as co-factors
9. Oral Screening for oral pre-cancer and oral cancer should be part of periodic oral examinations.

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