

# ANALYSIS OF CLINICAL SYMPTOMS IN PATIENTS WITH ORAL SUBMUCOUS FIBROSIS

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<https://doi.org/10.51847/IRUEgUex6m>

## ABSTRACT

Oral submucous fibrosis is multifactorial, collagen metabolic disorder caused by chronic areca nut chewing. It is a 'Potentially Premalignant Oral Epithelial Lesion' (PPOEL) that could be regressed if diagnosed in the early stages. This study aimed to assess the prevalence of clinical symptoms in Oral Submucous Fibrosis (OSMF) patients who reported to a dental institution. The objective was to evaluate the association of clinical symptoms specific to OSMF with its grading of disease progression. One-year data of OSMF patients (N = 155) were retrospectively collected from the department. The prevalence of the lesion across gender and age was assessed using SPSS software. A Chi-square test was used to measure the association between gender and Chief complaints; grading and chief complaints. 91.89% of males and 8.11% of females had specific chief complaints related to OSMF. Among the symptoms, burning sensation (35.1%) and reduced mouth opening (35.1%) were more prevalent followed by pain in the cheeks (18.9%) and ulcers in the mouth (10.8%). The symptomatic cases were exclusively seen in grades 2, 3, and 4 (Kerr *et al.* classification). The association between gender and specificity of chief complaints was not statistically significant with a P-Value of 0.63 (P > 0.05). The association between the distribution of chief complaints and grading among OSMF patients was statistically significant with a P-Value of 0.0001 (P < 0.05). OSMF patients report clinical symptoms only at later stages of disease progression, increasing the burden of treatment care for the patient.

**Key words:** Oral submucous fibrosis, OSMF, OSF, Oral potentially malignant disorders, OPMD, Clinical symptoms.

## Introduction

Oral submucous fibrosis (OSMF) is a chronic, progressive, collagen metabolic disorder and scarring precancerous lesion of the oral cavity seen principally in the subcontinent of India and countries of South-eastern Asia [1]. The prevalence of oral submucous fibrosis in India has spiked over the past four decades from 0.03% to 6.42% [2]. The common etiology is areca nut products that are chewed and consumed as a form of quid with or without betel leaves. Arecoline and its metabolites stimulate the Transforming Growth Factor-Beta (TGF- $\beta$ ) and proliferative fibroblasts leading to excess collagen deposition. Oral submucous fibrosis is the result of an imbalance between collagen synthesis and degradation in the extracellular matrix [3]. This increased consumption of areca nut products among the younger population is due to a lack of awareness of its ill effects, peer pressure, low socioeconomic status [4], availability near school premises [5], and attractive advertisements targeting the younger population thereby making them addictive at an early age [6]. Among private school younger adults, academic performance pressure was common for habit onset [7].

OSMF is now one of the oral cavity's well-documented 'Oral Potentially Malignant Disorders (OPMDs)'. The incidence rate of OSCC in India is 12.6 per one lakh people [8] and the prevalence rate of OSCC in OSMF patients is 13.7% [9]. The

global malignant transformation rate of OSMF to OSCC is 2.3–7.6% [10] and in India, the malignant transformation rate is higher at 7 to 30% [11]. The clinical features of Oral submucous fibrosis include an oral mucosal smarting or burning sensation, pain in cheeks, ulcerations, tongue depapillation, blanching of the oral mucosa with leathery texture and marbled appearance, loss of pigmentation, limited jaw movements, restricted mouth opening, reduced tongue protrusion, palpable fibrotic bands, shrunken uvula [12]. The common sites of oral submucous fibrosis are buccal mucosa but can involve any part of the oral cavity including the pharynx [13]. The affected tissue will be symmetrical and progress to firm nature and paleness. This study aimed to evaluate the prevalence of the associated clinical symptoms in OSMF patients who reported to dental institutions retrospectively. The objective was also to evaluate the association of clinical symptoms with OSMF grading.

## Materials and Methods

The study was retrospectively conducted in the department of Oral Medicine and Radiology in our dental hospital, India from the period of March 2021 to March 2022 after acquiring institutional ethical clearance (IHEC/SDC/OMED-2002/22/457) from the research department. The study conformed to the ethical norms and standards of the Declaration of Helsinki. The clinical data

were collected from our Dental Information Archiving Software (DIAS) which had been stored with proper verbal and written informed consent from the patient. The internal validity of the study had been established as the collection was from the standardized database. The study's external validity had been established as this study design is reproducible in any outside clinical setting under adequate standardization.

Through the process of convenience sampling, the clinically diagnosed OSMF (N= 155) cases were rigorously screened for this study. The elicited chief complaint was scrutinized for the specificity of the clinical features of OSMF. The non-specific chief complaints were eliminated and specific chief complaints about OSMF were further categorized into functional disabilities like burning sensation, pain in the cheeks, reduced mouth opening, and ulcers in the mouth along with the measurable parameters of age and gender of the OSMF patients. The grading followed for OSMF was based on the Kerr and Warnakulasuriya classification [14] (Table 1) which is widely accepted for its conglomeration of clinical presentation, functional mouth opening, and histopathological analysis when compared to other numerous classifications reported across the literature. Grade 5 OSMF cases were not included in our data collection as oral squamous cell carcinoma when detected was subjected to oncology care for biopsy and further management without delay in treatment care.

**Table 1.** Kerr and Warnakulasuriya's classification of Oral Submucous Fibrosis

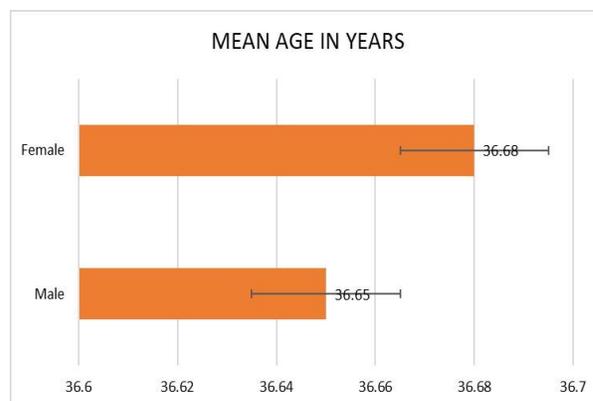
|          |   |
|----------|---|
| Grade 1  | Mild. Any features of Oral submucous fibrosis disease triad and interincisal opening of more than 35mm. |
| Grade 2  | Moderate. Above features of Oral submucous fibrosis with interincisal opening limited to 20-35mm.       |
| Grade 3  | Severe. Clinical features of Oral submucous fibrosis with an interincisal opening less than 20 mm.      |
| Grade 4A | Oral submucous fibrosis with other features of the oral potentially malignant disorder.                 |
| Grade 4B | Oral submucous fibrosis with any grade of epithelial dysplasia on biopsy                                |
| Grade 5  | Oral submucous fibrosis with oral squamous cell carcinoma   |

The collected data was entered in the Microsoft Office Professional Plus 2019 excel sheet and formatted. The statistical data analysis was processed using IBM's Statistical Package for the Social Sciences 23.0 software

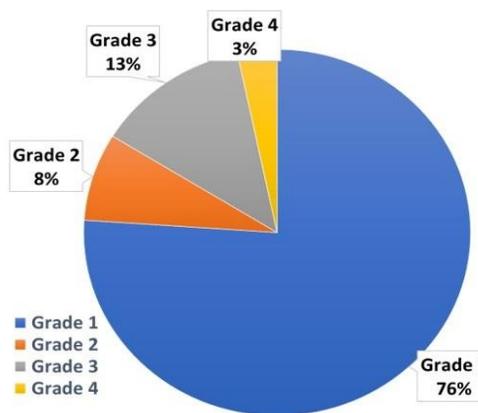
(SPSS Inc., Chicago, IL., USA). The Chi-square test was done to assess if there was any statistically significant difference in the distribution of complaints and grading among OSMF patients. The *P-value* < 0.05 was considered statistically significant.

**Results and Discussion**

Among our complete study participants (N=155), 145 were males (93.55%) and 10 were females (6.452%) with a mean age of 42.5 years in males and 52.4 years in females respectively (Figure 1) with a standard deviation of 11.8 and 9.4 in males and females. In the distribution of grading of the lesion in OSMF patients, 76% belonged to Grade I, 7.74 % belonged to Grade 2, 12.9% accounted for Grade 3 and Grade 4 accounted for 3.2% (Figure 2) and had the least number of participants (Table 2).



**Figure 1.** Graphical representation of age distribution according to gender



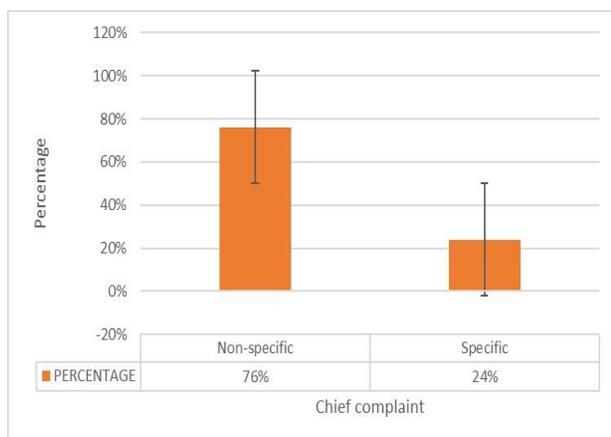
**Figure 2.** Distribution of grading of OSMF lesions in the study

**Table 2.** The chi-square test shows that there was a significant difference in the distribution of complaints and grading among OSMF patients

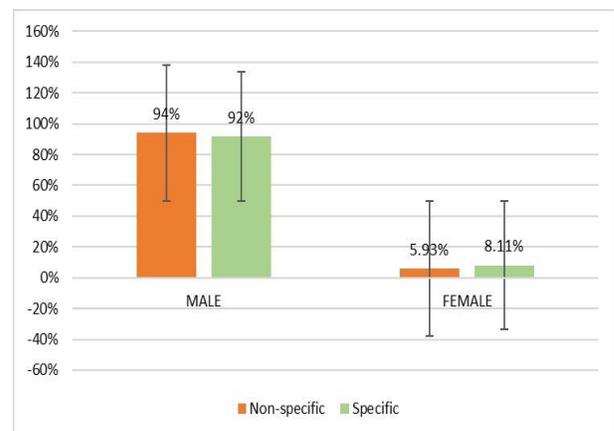
| Variable | Response | Not Specific to OSMF |         | Specific to OSMF |         | P value |
|----------|----------|----------------------|---------|------------------|---------|---------|
|          |          | Frequency            | Percent | Frequency        | Percent |         |

|                 |                       |     |       |    |       |        |
|-----------------|-----------------------|-----|-------|----|-------|--------|
| Gender          | Male                  | 111 | 94.1  | 34 | 91.9  | 0.63   |
|                 | Female                | 7   | 5.9   | 3  | 8.1   |        |
|                 | Total                 | 118 | 100.0 | 37 | 100.0 |        |
| Complaints      | Missing teeth         | 13  | 11.0  | 0  | 0     | 0.0001 |
|                 | Mobility of teeth     | 2   | 1.7   | 0  | 0     |        |
|                 | Stains on teeth       | 29  | 24.6  | 0  | 0     |        |
|                 | Toothache             | 74  | 62.7  | 0  | 0     |        |
|                 | Burning sensation     | 0   | 0     | 13 | 35.1  |        |
|                 | Pain in cheeks        | 0   | 0     | 7  | 18.9  |        |
|                 | Reduced mouth opening | 0   | 0     | 13 | 35.1  |        |
|                 | Ulcers in mouth       | 0   | 0     | 4  | 10.8  |        |
|                 | Total                 | 118 | 100.0 | 37 | 100.0 |        |
| Grading of OSMF | Grade I               | 118 | 100.0 | 0  | 0     | 0.0001 |
|                 | Grade II              | 0   | 0     | 12 | 32.4  |        |
|                 | Grade III             | 0   | 0     | 20 | 54.1  |        |
|                 | Grade IV              | 0   | 0     | 5  | 13.5  |        |
|                 | Total                 | 118 | 100.0 | 37 | 100.0 |        |

The patients with chief complaints or symptoms specific to OSMF were 23.87% and non-specific tooth-related complaints were 76.13 % (Figure 3). In the overall gender distribution in the study, 91.89% of males and 8.11% of females had specific and symptomatic chief complaints related to OSMF (Figure 4). Among the symptoms (Table 2), burning sensation and reduced mouth opening comprised 35.1% each followed by pain in the cheeks with 18.9%. Interestingly, the ulcers in the mouth were the least reported symptom with 10.8%.



**Figure 3.** Graphical representation of specificity of complaints among OSMF patients. 23.87 percent of the patients had complaints specific to the clinical presentation of OSMF



**Figure 4.** Gender distribution in the study specific to the Specificity of the lesions to OSMF

The Chi-Square ( $X^2$ ) test was used to compare the data sets to find the associations between parameters (Table 2). The association between gender and specificity of chief complaints was not statistically significant with a *P-Value* of 0.63 ( $P > 0.05$ ). The association between the distribution of chief complaints and grading among OSMF patients was statistically significant with a *P-Value* of 0.0001 ( $P < 0.05$ ). The symptomatic cases were exclusively seen in grades, 2, 3, and 4 where restriction of mouth opening and burning sensation was the common reporting parameter.

The etiology of Oral submucous fibrosis is multifactorial but areca nut components and metabolic by-products of betel quid play a vital role in the etiopathogenesis of oral submucous fibrosis [15]. Due to its alarming rise in the Indian population because of increased areca nut product chewing among younger generations, the prevalence documented was 0.6% in the southern zone, 0.03–0.2% in

the west zone, 2.7% in the east zone, 6.3–14.2% in the north-central zone and 30–42% in the northern zone [16]. Among south-eastern Asian countries, in the olden days, areca nut chewing was considered a popular traditional and cultural activity in social engagements which also extended to religious ceremonies. Arecanut was introduced in western countries during colonial rule for its therapeutic actions. Over the years, customary practices had declined due to social awareness but had been used ardently among the younger generation for their neuropsychological addictive effects. The acute effects are stimulative and pleasurable with euphoria, increased alertness, induced sense of well-being, a sensation of warmth over the body, and enhanced work capacity [17] which later leads to addiction.

Arecanut products and their metabolites are the main etiology of OSMF cases that are diagnosed clinically in habitual betel quid chewers. Further management is done by grading dysplasia through histopathological investigations. Comprehensive interventional therapy encompasses habit cessation with counseling, supportive or intralesional pharmacotherapy, jaw exercises physiotherapy, and if indicated, surgical excision of fibrotic bands with buccal flap repositioning or LASER fibrotomy. Treatment decision is based on clinicians' expertise taking into account histopathological grading, the patient's existing health status with comorbidities, willingness for the advised procedure, and follow-up.

In most situations, OSMF has become an incidental finding in screening camps for the public or those who visit the dental hospital for other teeth-related problems [18]. However, the characterization of those patients who reported pertaining symptoms needs to be understood clearly for understanding the progression of OSMF from the patient aspect. Hence this study was conducted aiming to understand the prevalence of clinical symptoms in OSMF cases reported in a dental institution. The data collected was done retrospectively for one year and statistical analyses were conducted.

Among the OSMF cases (N=155), the prevalence was more in males (93.55%) than females (6.452%) with a mean age of  $42.5 \pm 11.8$  and  $52.4 \pm 9.4$  years respectively. This prevalence is concurrent with previous studies where OSMF had been reported higher in males than females [19, 20]. This could also be due to the increased number of the male population who are chronic tobacco chewers when compared to females [21]. In the percentage of distribution in OSMF grading using Kerr *et al.* classification [14], 76% were Grade 1, 7.74 % were Grade 2, 12.9% were Grade 3, and 3.2% were Grade 4. Interestingly, the patients with chief complaints or symptoms specific to OSMF were only 23.87% comprising both males (91.89%) and females (8.11%). Burning sensation (35.1%) and reduced mouth opening (35.1%) comprised the most common clinical symptom. This is important as patients become conscious of

the presence of the effect of their deleterious habit only when these symptoms come to the limelight.

The association between gender and specificity of chief complaints was not statistically significant (P-Value 0.63) implying that gender does not influence the patients to report clinical symptoms. But there was a statistically significant association between OSMF complaint specificity and grading (P-Value of 0.0001). This signifies the fact that symptomatic cases are reported only in later stages with a pronounced reduction in mouth opening or burning sensation irrespective of gender. Grade 1 patients who are early OSMF, lack awareness of the presence of lesions as asymptomatic and are diagnosed only on routine oral screening. This is perturbing as the treatment plan gets complicated due to the lack of standard gold pharmacotherapy in OSMF and the burden of health care delivery again falls on the patient and community who are pre-existing with lower socioeconomic status. Also, the quality of life gets compromised when reported at later grades of OSMF involving low self-esteem, loss of weight, sleep disorders, malnutrition, social deprivation [22].

Our results could not be compared with previous studies as this was the first study to analyze the prevalence of symptomatic chief symptoms in OSMF patients in India. The rationale behind this study was that the disease onset should be understood from the patient's perspective as that becomes the driving factor for OSMF patients to approach oral medicine specialists for treatment care. In our study, the chief complaints of Burning sensation (35.1%) and reduced mouth opening (35.1%) made their report to our dental institution. Our study has highlighted the prevalence of OSMF in the south Indian population and the specific chief complaint that motivates them for treatment with detailed facts of age and gender. Also, the association between the specific chief complaints and grading had been well established.

The limitations of our study were that being a retrospective study, the cases analyzed were only those who reported to our institution. The results hence represent the demographics around the dental hospital or from areas accessible to our institution. Hence, Large-scale multicentric studies combining rural and urban populations covering broader geographic locations are needed to fathom the potency of the lesion and its variable presentation due to modified betel quid chewing habits. Also, the majority of the population reported OSMF were males and hence male prevalence had been concluded. This result needs to be understood with caution as the majority of the female population with OSMF might not have reported for treatment either due to lack of awareness or social stigma or lack of accessibility to treatment hospitals in approaching hospitals for interventional therapies.

## Conclusion

This study concludes that symptomatic OSMF cases are reported only after progression to grade 2 as patients are asymptomatic in grade 1. The most commonly reported symptoms were a burning sensation in the oral cavity and restricted opening of the mouth which along with other presenting features guides the diagnosis of Oral Submucous fibrosis in the general population during clinical examination by oral physicians. This highlights the lack of awareness of OSMF and its early clinical changes among chronic areca nut product chewers. There also exists research lacunae in the correlation of clinical symptoms of OSMF with the grading of dysplasia changes, location of fibrotic bands, and type of areca nut quid like self-made or commercial tobacco products used by the patient. The need for prevention of tobacco product consumption and early screening of habitual takers are again re-emphasized in establishing and upbringing a healthy disease-free society.

**Acknowledgments:** The article's authors would like to thank Saveetha Dental College and Hospital, Saveetha Institute of Medical and Technical Sciences, Chennai for their support in conducting this study.

**Conflict of interest:** None

**Financial support:** Saveetha Dental College and Hospital, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai, India.

**Ethics statement:** Institutional ethical clearance number: IHEC/SDC/OMED-2002/22/457

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