

Epidemiology of Oral Submucous Fibrosis: A Review

Madhushree Das¹, Manjunath C², Ankit Srivastava³, Malavika J⁴, Ameena Musareth V.M.⁵

1,3,4-Post graduate student, Public Health Dentistry 2-Professor, Public Health Dentistry.

Correspondence to:
Dr. Madhushree Das, Post graduate student, Public Health Dentistry 2-Professor, Public Health Dentistry
Contact Us: www.ijohmr.com

ABSTRACT

Oral submucous fibrosis (OSF) is now accepted globally as an Indian disease, having highest malignant potential than any other oral premalignant lesions. Epidemiological data and intervention studies suggest that areca nut is the main aetiological factor for OSMF. Other etiological factors suggested are chillies, lime, tobacco, nutritional deficiencies such as iron and zinc, immunological disorders, and collagen disorders. The male-to-female ratio of OSMF varies by region, but females tend to predominate. Many therapeutic and surgical treatment modalities for relieving the symptoms have been advocated, but no definitive and widely accepted treatment is currently available. Moreover, recent data suggests that prevalence of OSMF in India has increased from 0.03% to 6.42%. The researchers should evolve to unexplored the clear mechanism behind the OSMF and its treatment further the work is also required in the field of drug designing and for neutralizing the effects of Areca nut a nature base therapy could be developed.

KEYWORDS: Oral Submucous Fibrosis, epidemiology, areca nut

INTRODUCTION

Oral submucous fibrosis (OSF) is a chronic debilitating disease and a premalignant condition of the oral cavity. The pathogenesis of the disease is not well established. Epidemiological evidence strongly indicate the association of the betel quid (BQ) habit and OSF.¹

The hallmark of the disease is submucosal fibrosis that affects most parts of the oral cavity, pharynx and upper third of the esophagus leading to dysphagia and progressive trismus due to rigid lips and cheeks.²

Despite its association with a significantly increased risk of cancer, the etiology is still not clear. An epidemiological assessment showed a prevalence of 0.4% for OSMF in Kerala, South India, which is among the highest recorded.³ No relationship to any community or religious group has been suggested, but an ethnic basis is indicated because OSMF is found mostly in Asians or Asians settled in other countries.⁴

The treatment of patients with oral submucous fibrosis depends on the degree of clinical involvement. If the disease is detected at a very early stage, cessation of the habit is sufficient.

Medical treatment is symptomatic and predominantly aimed at improving mouth opening and tongue movements. The principal actions of drug therapy include anti-fibrotic, anti-inflammatory, and anti-oxygen radical mechanisms. Potential new drugs are on the horizon. Surgery may be necessary in advanced cases of trismus. Prevention is most important, as no healing can be achieved with available treatments.⁵

Back ground: In ancient medicine, Shushruta described a condition, “vidari” under mouth and throat diseases. He noted progressive narrowing of mouth, depigmentation of oral mucosa, and pain on taking food. These features precisely fit in with the symptomatology of oral submucous fibrosis. (Mukharjee and Biswas 1972).⁶

Schwartz (1952) for the first time reported a case of “atrophica idiopathica tropica mucosae oris” occurring in Indians in East Africa.

Lal and Joshi (1953) first described this condition in India. Joshi coined the term “oral submucous fibrosis”.⁷

Pindborg JJ, Sirsat SM (1966) described histologically, the four consecutive stages of the OSMF.⁸

Seedat HA, Van Wyk CW (1988) have reported about irreversible nature of the disease i.e., once OSMF induced by the habit of chewing betel nut, the reversal of the disease after cessation of the habit could not occur.⁹

Definitions:

Schwartz in 1952: “An insidious chronic disease characterized by the deposition of fibrous tissue in the submucosal layer of pharynx, palate, fauces, cheeks, pharynx and esophagus and in the underlying muscles of mastication.”¹⁰

Pindborg and Sirsat in 1964: “An insidious chronic disease affecting any part of the oral cavity and sometimes the pharynx. Although occasionally preceded by and or associated with vesicle formation, it is always

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associated with a juxta epithelial inflammatory reaction followed by a fibroelastic change of the lamina propria with epithelial atrophy leading to stiffness of the oral mucosa and causing trismus and inability to eat.^{9,11}

ETIOLOGY

Epidemiological data and intervention studies suggest that areca nut is the main aetiological factor for OSF. Other etiological factors suggested are chillies, lime, tobacco, nutritional deficiencies such as iron and zinc, immunological disorders, and collagen disorders.

1) Areca nut: The term areca nut is used to denote the unhusked whole fruit of the areca nut tree and term betel nut is exclusively referred to the inner kernel or seed which is obtained after removing husk.

Arecoline, an active alkaloid found in betel nuts stimulates fibroblasts to increase production of collagen by 150%. Areca nuts have also been shown to have a high copper content, and chewing areca nuts for 5-30 minutes significantly increases soluble copper levels in oral fluids. This increased level of soluble copper supports the hypothesis as an initiating factor in individuals with OSMF.²

2) Immune system: Betel quid affects the immune system. The levels of transforming growth factor (TGF)- β and interferon (IFN)- γ are lower in mononuclear cells among OSF patients.

Many of the connective tissue diseases like Rheumatoid Arthritis, Scleroderma and Systemic lupus erythematosus are associated with unique HLA-DR antigens.²⁸ A similar association has been sought for OSMF.¹²

3) Antioxidant status and cytokines: Glutathione S-transferases (GST) are part of the antioxidant system. GSTT1 and GSTM1 null phenotypes increase the risk of OSF.

4) Chillies: Capsaicin, which is vanillylamide of 8-methyl-6-nonenic acid, is the active ingredient of chillies, play an etiological role in oral submucous fibrosis (Rajendran, 1994).

5) Nutritional deficiency:- A subclinical vitamin B complex deficiency has been suspected in cases of OSF with vesiculations and ulcerations of oral cavity.¹³

Iron deficiency anemia, vitamin B complex deficiency and malnutrition are promoting factors that derange the repair of the inflamed oral mucosa, leading to defective healing and resultant scarring.¹⁴

6) Genetic and Immunologic Processes: A genetic component is assumed to be involved in OSF Patients with increased frequency of HLA-A10, HLA-B7, and HLA-DR3 reported in people without a history of betel nut chewing or chilli ingestion.⁴

7) Defective iron metabolism: Microcytic hypochromic anemia with high serum iron has been reported in submucous fibrosis (Rajendran, 1994).¹³

8) Immunological disorders: Raised ESR and globulin levels are indicative of immunological disorders. Serum immunoglobulin levels of IgA, IgG and IgM are raised significantly in oral submucous fibrosis.

PATHOGENESIS

I. Collagen accumulation:

a) **Increased Collagen Production:** Under the influence of areca nut, fibroblasts differentiated into phenotypes that produce more collagen. Arecoline gets converted into arecadine which is the active metabolite. There is dose dependent increase in production of collagen by fibroblasts.

b) **Stabilization of collagen structure and decreased collagen breakdown:** One of the mechanisms that can lead to increased fibrosis is by reduced degradation of collagen by forming a more stable collagen structure. Betel nut contains tannin. Tannin has ability to stabilize collagen by cross-linking it.

II. Increased expression of fibrogenic cytokines: The most important finding in the various studies was the demonstration of increased expression of fibrogenic cytokines namely TGF β -1, PDGF and bFGF in OSF tissues compared to normal.

III Genetic polymorphisms predisposing to OSF:

Polymorphisms of the genes coding for TNF- α has been reported as a significant risk factor for OSF. TNF- α is known to stimulate fibroblastic proliferation in vitro. Evidence suggest that collagen-related genes are altered due to ingredients in the quid. The transcriptional activation of the procollagen genes by TGF- β suggests that it may contribute to increased collagen levels in OSF.¹⁵

MANAGEMENT

Many therapeutic and surgical treatment modalities for relieving the symptoms have been advocated, but no definitive and widely accepted treatment is currently available. The first step of preventive measure should be in advising the patient to discontinue the habit, which can be encouraged through education, counselling and advocacy. Medical treatment includes steroids, placental extracts, IFN γ , lycopene, pentoxifylline, surgical excision, laser removal, etc. These have proved to be symptomatic and are predominantly aimed at improving mouth movements. Treatment modalities both medical and surgical, for relieving the symptoms have been advocated, but have not been successful so far. Therefore, the search for an effective treatment modality still continues.¹⁶

REGIONAL PREVALENCE OF OSMF IN INDIA

The disease predominantly occurs mostly in India and in South East Asia, but the cases have been reported worldwide like Kenya, China, UK, Saudi Arabia and

other parts of the world as Asians are migrating to these parts. Moreover, recent data suggests that prevalence of OSMF in India has increased from 0.03% to 6.42%.

Northern Zonal Council: According to an epidemiological survey conducted on the geriatric Indian population Jodhpur, 64% of the patients presented with one or more oral lesions, among which it accounted 30% of oral submucous fibrosis.¹⁷

Whereas according to a cross-sectional study conducted on the younger age group in the rural area of Jaipur, Rajasthan. The prevalence of OSMF in the study population was 231 (3.39%). Majority of subjects were males 188 (81.38%). The prevalence of OSMF was maximum in 15 to 24 years of age group 98 (42.42%).¹⁸

North-Central Zonal Council: According to an etiological and epidemiological study done in Patna, Bihar it was observed that Male: Female ratio was 2.7: 1. A maximum number of cases belonged to 21-40 years of age. Most of the OSMF cases used heavy spices and chillies, and gutkha was most commonly used by the OSMF cases.¹⁹

In a study conducted to evaluate the prevalence of use of tobacco & its associated products & Oral Sub Mucous Fibrosis among teenagers, it showed that 34.1% of the study subjects used tobacco and among them, 14.2% of Oral Sub Mucous Fibrosis cases were identified.²⁰ Similarly, according to a population-based case control study in rural and urban Lucknow, it was found that patients who use pan masala were at higher risk of developing oral submucous fibrosis.²¹

In a study done among habitual gutkha, areca nut and pan chewers of Moradabad, India, between the ages of 11-40 years. The prevalence of OSMF was 6.3% (63/1000), and gutkha chewing was the most common abusive habit amongst OSMF patients.²²

In a study conducted in a dental institute in Modinagar, Uttar Pradesh, India, the overall prevalence of OML was (16.8%), the most prevalent being smoker's palate (10.44%) followed by leukoplakia (2.83%), oral submucous fibrosis (1.97%), oral candidiasis (1.61%), recurrent aphthous stomatitis (1.53%), oral lichen planus (0.8%) and others (0.78%).²³

North Eastern Zonal Council: There are no studies done to evaluate the prevalence of OSMF in north eastern zone. Whereas a study was done to obtain baseline information about the prevalence of tobacco use among school children in eight states in the north-eastern part of India.

Eastern Zonal Council: In a study done in the villages of two districts of the West Bengal state to detect early oral premalignant, it was found that oral submucous fibrosis showed the highest prevalence (2.7%) among the various OPLs detected.²⁴

Western Zonal Council: According to an extensive epidemiologic house-to-house survey conducted in Poona

district, Maharashtra it was found that oral submucous fibrosis had a prevalence of 0.03%. It was found that for oral submucous fibrosis prevalence depends on sex if tobacco habits are taken into account.²⁵ Similarly, a house to house epidemiological survey was conducted in Bhavnagar district, Gujarat state among 5018 men who reported the use of tobacco or areca nut, 164 were diagnosed as suffering from OSMF with a prevalence of 3.2%. A prevalence of 0.16% was noted in a survey carried out in the same district in 1967. It was found that there was a significant increase in the prevalence of OSMF.²⁶

According to a study conducted in the semi-urban district of Sangli in Western Maharashtra. Among 623 patients who had significant mucosal lesions, 152 had oral submucous fibrosis.²⁷

Southern Zonal Council: According to a case-control study conducted within the framework of an on-going randomized oral cancer screening trial in Kerala, India. An inverse dose-response relationship was seen between BMI and the risk of oral submucous fibrosis.²⁸

According to a hospital based cross-sectional study oral soft tissue lesions were found in 4.1% of the study subjects. The prevalence of OSMF was 0.55%. The prevalence of smoking, drinking alcoholic beverages and chewing was 15.02%, 8.78% and 6.99% respectively.²⁹ From the study conducted to evaluate the prevalence of oral mucosal lesions in Manipal, Karnataka State, India the result showed the presence of one or more mucosal lesions in (41.2%) of the population. The prevalence of oral submucous fibrosis was 2.01%.³⁰

According to an epidemiological survey conducted among alcohol misusers attending a rehabilitation center in Chennai, south India. A total of 25% of the study group had at least one OML. The common oral lesions were smoker's melanosis (10.2%), oral submucous fibrosis (8%), and leukoplakia (7.4%).³¹

CONCLUSION

Oral submucous fibrosis (OSF) is now accepted globally as an Indian disease, having highest malignant potential than any other oral premalignant lesions.

The hallmark of the disease is submucosal fibrosis that affects most of the parts of oral cavity, pharynx and upper third of the esophagus. Various available data suggests that the main causative agents for OSF are the constituents of areca nut, mainly arecoline, whilst tannin may have a synergistic role.

Intervention studies and public health awareness program linked with OSMF condition & habits may prove the best way to control disease process at the community level.

It is an urgent need to educate people about the adverse effects regarding oral cavity. However, crucial steps were also been taken by the Supreme court, Government of India and other state governments by placing ban on such

commercial products, but still there are several local or branded manufacturers who are sailing such products with different names or in different formulation type.

The researchers should evolve to unexplore the clear mechanism behind the OSMF and its treatment, further work is also required in the field of drug designing and for neutralizing the effects of areca nut a nature base therapy could be developed.

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