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RESEARCH ARTICLE

A REVIEW ON ORAL SUBMUCOUS FIBROSIS

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ABSTRACT

Oral sub mucous fibrosis is a chronic, progressive, and irreversible disease of unknown aetiology. Oral submucous fibrosis (SMF) is a potentially malignant disease caused by chewing of areca nut and is associated with both significant morbidity and an increased risk for malignancy. The habit has a major social and cultural role in communities throughout the Indian subcontinent which explains the high prevalence of SMF in people of Indian subcontinent and South Asian ethnicity. Epidemiological studies have identified a variety of oral mucosal lesions and conditions in association with betel quid and tobacco use. It is a heterogeneous disease with complex molecular abnormalities with a malignant transformation rate ranging from 3-19%.

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INTRODUCTION

Oral submucous fibrosis (SMF) is a potentially malignant disease caused by chewing of areca nut and is associated with both significant morbidity and an increased risk for malignancy. Oral sub mucous fibrosis is a chronic, progressive, and irreversible disease of unknown aetiology. It affects oral, oropharyngeal. (Johnson *et al*., 2000)

Synonyms

The earliest description of the disease was by Schwartz in 1952, who coined the term atrophica idiopathic mucosa oris to describe an oral fibrosing disease. Joshi subsequently termed the condition as oral sub mucous fibrosis (OSF) in 1953. (Schwartz, 1952)

- Lal (1953): Diffuse Oral submucous fibrosis
- Su (1954): Idiopathic scleroderma of the mouth
- Behl (1962): Sclerosing stomatitis
- Rao (1962): Idiopathic palatal fibrosis
- Pindborg (1966): Juxta epithelial fibrosis
- Ramanathanan (1981): Asian Sideropenic Dysphagia. (Joshi, 1953)

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Historical review

Can be dated back to ancient times where SUSHRUTHA: described a condition called "VIDARI" of oral condition in patients chewing pan and betelnut.

Schwartz (1952): reported the 1st case into the literature, entitled "Atrophia idiopathica Tropica mucosae oris" occurring in Indians in East Africa

Lal and Joshi (1953): first described this condition in India

Joshi (1953): coined the term oral submucous fibrosis.

Sue (1954): described 3 cases of 'Idiopathic scleroderma of the mouth' and reported dysphagia as one of the symptom. (Meghji *et al*., 1987)

Epidemiology

The disease occurs mainly in Indians between 0.2%and 1.2% The first Indian cases were reported from Bombay and Hyderabad.

Etiology

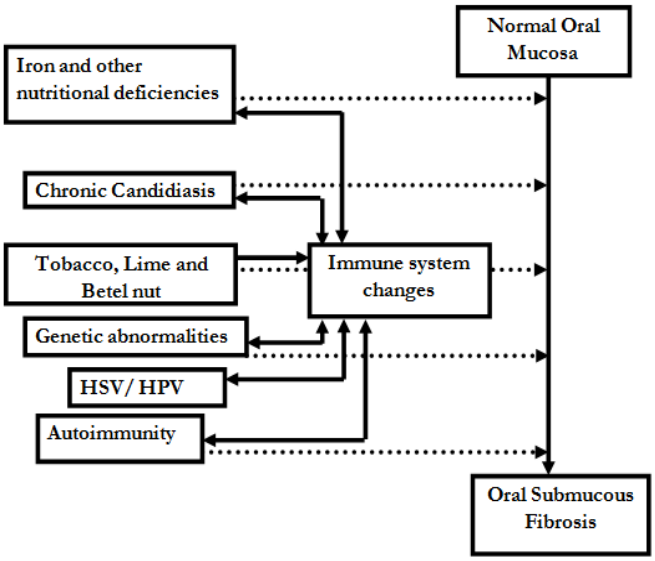
It is considered to be Multifactorial (Tilakaratne *et al*., 2006)
LOCAL FACTORS: are as follows

- Arecanut
- Chilli
- Misi

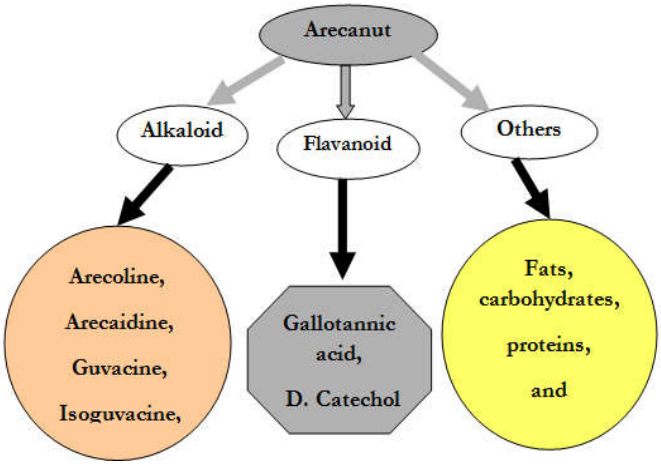
SYSTEMIC FACTORS: are as follows

- Nutritional deficiency
- Autoimmunity
- Genetic susceptibility

Multifactorial model for pathogenesis of OSMF (Pillai *et al*., 1992)



Ariyawardana A, Athukorala ADS, Arulanandam A (2006) strong association of betel quid chewing (including tobacco as an ingredient) with the causation of OSMF (Abhinav Kumar *et al*., 2007)



KHANNA JN, ANDRADE NN (1995)

Pindborg JJ, Chawla TN, Srivastava AN, Gupta D, Mehrotra ML (1964) increased blood eosinophils and connective tissue eosinophils in the biopsy specimen: allergen probably due to chillies (Pindborg *et al*., 1980)

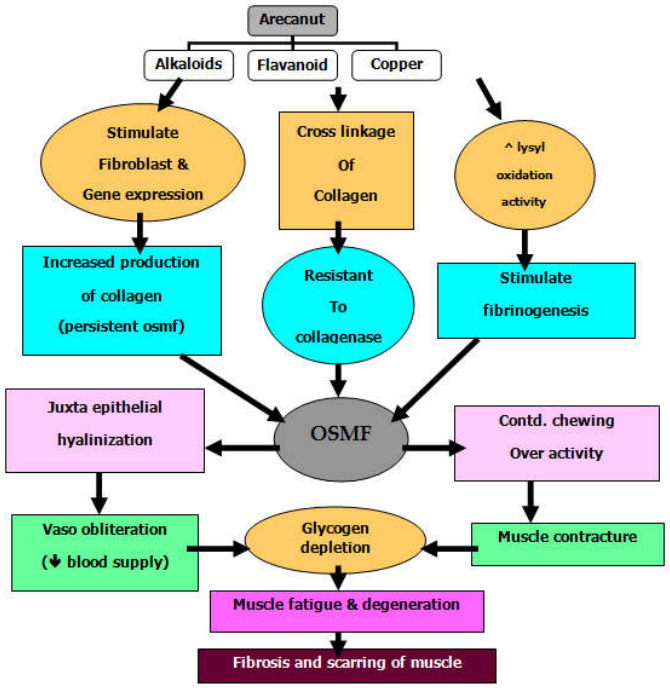
NUTRITION DEFICIENCY (Johnson *et al*., 2000)

Malnutrition

Wahi PN, Kapur VL, Luthra UK, Srivastva MC (1966): defcy of Vit A, B & C

Ramanathan K (1981): Iron & Vit B complex deficiency

McGurk M, Craig GT (1984) : serum Iron deficiency



Cox SC, Walker DM (1996): Nutritional+Chillies+ Immnlogical processes & OSMF

Autoimmunity

Considered as one of the etiologic factors by various authors based on the following observations Certain clinical similarities of OSMF with other collagen disorders namely Scleroderma Ultrastructural changes like presence of fibrinoid in connective tissue as seen in Scleroderma, Rheumatoid arthritis etc and also demonstrated in OSMF.

Clinical features

Clinical presentation of SMF varies from person to person depending on their habit history, generalized health status and level of involvement of oral tissues. Development of clinical symptoms of SMF shows significant intra individual variation depending on the type of areca nut consumed, duration and practice of the habit, individual susceptibility and other factors. Initial presenting features of SMF include; burning sensation especially on eating hot and spicy foods, dry mouth and blanching. Progressive fibrosis causes impairment of local vascularity of oral mucosa leading to blanching and a marble-like appearance. (Gupta *et al*., 2004) As the disease progresses,

individual fibrous bands or a generalised fibrosis of oral mucosa will be palpable with marked rigidity. The most frequently affected locations are the buccal mucosa and the retromolar areas. Sometimes, circum-oral bands will be palpable restricting mouth opening and causing difficulty in mastication, deglutition and maintaining oral hygiene. Tongue shows depapillation of mucosa with blanching or fibrosis of the ventral mucosa and floor of the mouth. Fibrosis of the tongue and the floor of the mouth will be associated with restricted tongue movement and protrusion. Another key feature noted in SMF is epithelial atrophy. Atrophic areas along with poor oral hygiene (due to reduced moth opening) predisposes these areas to candidiasis. Studies of various populations have recently linked the use of betel quid to the presence of candidal species. In patients who swallow the areca nut juice and the quid, fibrosis may extend posteriorly to involve the soft palate, uvula, palatal faucesand oropharynx. Uvula usually appear shrunken and, in extreme cases, referred to as budlike/ hockey stick like. In rare cases of extensive involvement, there may be hoarseness of voice (with laryngeal involvement), difficulty in swallowing because of oesophageal fibrosis and occasionally, mild hearing loss due to blockage of Eustachian tube (Anila *et al*., 2011).

Symptoms

- Burning senasation
- Inability to open the mouth
- Inability to blow the cheeks
- Difficulty in swallowing
- difficulty in protruding tongue

Signs

- diffuse blanching of the mucosa
- palpable bands
- Hyperpigmented areas adjacent to zones with loss of pigment
- loss of tongue papillae and a leathery consistency of the mucosa

Clinical differential diagnosis

Anaemic Stomatitis: because of presence of Dysphagia concomitant with OSMF, patient will have reduced diet and hence nutritional deficiency and finally resulting anemia

Scleroderma: a connective tissue disorder resulting in trismus and stiffness of mucosa

Radiation Fibrosis: if the patient gives history of radiation therapy

Vertical Scar Band: if patient gives history of minor or major surgical procedures

Chronic Infections: Actinomycosis also may result in trismus

TMJ Bony Ankylosis & Fibrous Ankylosis: result in Trismus (Schwartz, 1952; Meghji *et al*., 1987)

Classification

Wahi PN, Kapur VL, Luthra UK, Srivastva MC (1966)

Group I : no symptoms referable to the mucosal involvement

- Lesions affected one or other commonly involved anatomical site focal in character
- Showed pallor or whitish coloration, wrinkling of mucosa and minimal induration

Group II : symptoms of soreness of the mucosa or increased sensitivity to chillies

- Lesions: diffuse, white, extensive and indurated involving one or more anatomical sites.

Group III : Symptomatic mainly due to restricted mobility such as Trismus

- Stretching at angles of mouth and altered pronunciation
- Firm mucosal bands could be palpated, the surface might be fissured or ulcerated.

Pindborg (1989) divided OSMF into three stages based on clinical features. (Pindborg and Sirsat, 1966)

Stage 1: Stomatitis includes erythematous mucosa, vesicles, mucosal ulcers, melanotic mucosal pigmentation and mucosal petechiae

Stage 2: Fibrosis occurs in healing vesicles and ulcers, which is the hallmark of this stage. Early lesions demonstrate blanching of the oral mucosa. Older lesions include vertical and circular palpable fibrous bands in the buccal mucosa and around the mouth opening or lips, resulting in a mottled marble like appearance of the mucosa because of the vertical thick, fibrous bands associated with blanched mucosa.

Specific findings include the following

- Reduction of the mouth opening (trismus)
- Stiff and small tongue
- Blanched and leathery floor of the mouth
- Fibrotic and depigmented gingiva
- Rubbery soft palate with decreased mobility
- Blanched and atrophic tonsils
- Shrunken bud like uvula
- Sinking of the cheeks, not commensurate with age or nutritional ststus

Stage 3: Sequelae of OSMF

Leukoplakia, a precancerous lesion, and is found in more than 25% of individuals with OSMF. Speech and hearing deficits may occur because of involvement of the tongue and the eustachian tubes. Haider SM, Merchant AT, Fikree FF, Rahbar MH (1999) have staged the disease clinically and functionally depending on the location of bands as well as the maximum mouth opening: (Khanna *et al*., 1995; Haider *et al*., 2000)

Clinical staging

Faucial bands only
Faucial and buccal bands
Faucial, buccal and labial bands

Functional staging

Mouth opening > 20 mm

Mouth opening < 19 mm
Mouth opening < 10 mm

Staging/grading of SMF

Various authors have proposed grading of SMF based on: Clinical features Histopathological features Clinical and histopathological features Inter-incisal distance I.Utsunomiya *et al* (2005) havehistologically divided SMF based on the concept of Sirsat M and Pinborg J J with minor modifications (Utsunomiya *et al*., 2005)

Early stage: Large number of lymphocytes in subepithelial connective tissue zone along with myxedematous changes.

Intermediate stage: Granulation changes close to the muscle layer and hyalinization appeares in subepithelial zone where blood vessels are compressed by fibrous bundles.Reduced inflammatory cells in subepithelial layer.

Advanced stage: Inflammatory cell infiltrate hardly seen. Number of blood vessels dramatically small in subepithelial zone. Marked fibrous areas with hyaline changes extending from subepithelial to superficial muscle layers. Atrophic, degenerative changes start in muscle fibres.

II. Kiran *et al.* (2007) divided SMF based on mouth opening as follows (Kiran Kumar *et al*., 2007):

Grade I: Only symptoms with no demonstrable restriction of mouth opening
Group II: Limited mouth opening 20 mm and above
Group III: Mouth opening < 20 mm
Group 1V: SMF advanced with limited mouth opening. Precancerous and cancerous changes seen throughout the mucosa

III. Chandramani More *et al* (2011) gave a clinical as well as functional staging of SMF: (More *et al*., 2012)

Stage 1(S1): Stomatitis and / blanching of mucosa.
Stage 2 (S2): Presence of palpable fibrous bands in buccal mucosa and / oropharynx with/ without stomatitis.
Stage 3 (S3): Presence of palpable fibrous bands in buccal mucosa and /oropharynx and in any other parts of oral cavity with / without stomatitis.
Stage 4(S4):

a. Any one of the above stages along with other potentially malignant disorders. Eg: oral leukoplakia, oral erythroplakia etc
b. Any one of the above stage with oral carcinoma

Functional staging:

M1: Interincisal mouth opening equal to or greater than 35mm.
M2: Interincisal mouth opening between 25 and 35mm
M3: Interincisal mouth opening between 15 and 25mm
M4: Interincisal mouth opening less than 15mm

IV. Staging of SMF proposed by AR Kerr, S Warnakulasuriya *et al.* (2011)

Proposed disease Grading System – Oral submucous fibrosis

- Grade 1 –Mild: Any features of the disease triad for SMF (burning, depapillation, blanching or leathery mucosa) may be reported – and inter-incisal opening >35 mm
- Grade 2 –Moderate: Above features of SMF + inter-incisal limitation of opening 20–35 mm
- Grade 3 – Severe: Above features of SMF + inter-incisal opening <20 mm
- Grade 4A – SMF + other potentially malignant disorder on clinical examination
- Grade 4B – SMF with any grade of oral epithelial dysplasia on biopsy
- Grade 5 – SMF + oral squamous cell carcinoma (SCC)

Investigation

Hematological abnormalities reported in oral submucous fibrosis include:

- Increased erythrocyte sedimentation rate
- Iron-deficiency anemia
- Decrease in serum iron and increase in total iron binding capacity (TIBC)
- Eosinophilia
- Increased gamma globulin

Hematological

1) Complete hemogram

Anemia : which might be concomitant to presence of burning sensation, dysphagia and restricted mouth opening.
ESR: is found to be raised in most of the cases.

2) Serological

- IgM, IgG, IgA: are found increased in number, particularly IgG
- HLA typing: can be done estimate familial predisposition
- β2 microglobulin: a serological marker used for squamous cell carcinoma, is found to be increased in oral submucous fibrosis, suggesting premalignant potential.

3) Biochemical

- Iron
- Copper

4) Histopathology

- The epithelial changes in OSMF, as described by many investigators varies from Normal to Atropic or Hyperplastic
- Dense bundles & sheets of Collagen immediately beneath the epithelium
- Thick band of hyalinised subepithelial collagen shows varying extension into subepithelial tissues (Tilakaratne *et al*., 2006; Pillai *et al*., 1992)

Management (Haque *et al*., 2001)

Preventive measures
Nutritional support
Physio therapy:
Muscle stretching exercises

Heat –Short wave diathermy
Micro wave diathermy

Surgical management

- Cutting the fibrotic bands under anesthesia
- Submucosal resection and replacement with a partial thickness skin or mucosal grafts
- Bilateral temporal myotomy
- New treatment regimen : composed of surgical excision of the fibrotic bands with submucosal placement of fresh human placental grafts, followed by local injections of dexamethasone, recommended for advanced cases

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