PREVALENCE OF ORAL SUBMUCOUS FIBROSIS AND PERIODONTAL HEALTH STATUS IN PATIENTS CHEWING GUTKA FROM BIHAR REGION

Dr Nikita Raman¹, Dr. Kumar Manish², Dr. Samir Jain³

¹Senior Resident, Department of Dentistry, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar
²Senior Resident, Department of Dentistry, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar
³Professor and Head, Department of Dentistry, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar.

Article Info: Received 20 December 2019; Accepted 11 January. 2020
DOI: https://doi.org/10.32553/ijmbs.v4i1.863
Corresponding author: Dr. Samir Jain
Conflict of interest: No conflict of interest.

Abstract
Smokeless tobacco (ST) chewing warrants special attention in India because of its popularity and widespread social acceptance. The major factors that persist to encourage people to use smokeless form of tobacco are its low price, ease of purchase, and the widely held misconception of purported medicinal value in curing toothache, headache, and in decreasing hunger. Furthermore, in contrast to smoking, there is no taboo against using ST. The lifestyle, socioeconomic status, and the standards of living of industrial workers are different from the rest of the population. Poverty, language barriers, and poor education contribute different lifestyle that encourages addictive tobacco habits. As there is a ban on smoking tobacco in most of the industrial premises, workers tend to consume more of ST products. Therefore, they form a special group who could be at a higher risk of periodontal breakdown. Hence the present study was planned for study of Prevalence of Oral Submucous Fibrosis and Periodontal Health Status in patients chewing Gutka from Bihar Region.

The present study was planned in Department of Dentistry, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar. Total 30 patients were enrolled in the present study. The patients were divided in three groups. The Group A included patients with a healthy periodontium. The Group B included patients with chronic periodontitis without OSMF, and Group C included patients with chronic periodontitis and OSIF. The data generated from the present study concludes that that chewing gutka leads to periodontal destruction in patients with OSIF. The cases illustrate the significant morbidity and mortality associated with OSF and emphasize the importance of close follow-up of such cases. Because of the significant cancer risk among these patients, periodic biopsies of suspicious regions of the oral mucosa are essential for the early detection and management of high-risk oral premalignant lesions and prevention of cancer.

Keywords: oral submucous fibrosis, periodontal destruction, gutka, Bihar region, etc.

Introduction
Oral submucous fibrosis is a chronic, complex, premalignant (1% transformation risk) condition of the oral cavity, characterized by juxta-epithelial inflammatory reaction and progressive fibrosis of the submucosal tissues (the lamina propria and deeper connective tissues). As the disease progresses, the jaws become rigid to the point that the person is unable to open the mouth. The condition is remotely linked to oral cancers and is associated with areca nut or betel quid chewing, a habit similar to tobacco chewing, is practiced predominantly in Southeast Asia and India, dating back thousands of years.

In 1952, Schwartz coined the term atrophiaciopathica mucosa oris to describe an oral fibrosing disease he discovered in 5 Indian women from Kenya. [1] Joshi subsequently coined the termed oral submucous fibrosis (OSF) for the condition in 1953. [2]

Oral submucous fibrosis is a chronic debilitating disease of the oral cavity characterized by inflammation and progressive fibrosis of the submucosal tissues (lamina propria and deeper connective tissues). Oral submucous fibrosis results in marked rigidity and an eventual inability to open the mouth. [3, 4] The buccal mucosa is the most commonly involved site, but any part of the oral cavity can be involved, even the pharynx. [5]

The condition is well recognized for its malignant potential and is particularly associated with areca nut chewing, the main component of betel quid. [6] Betel quid chewing is a habit practiced predominately in Southeast Asia and India that dates back for thousands of years. It is similar to tobacco chewing in westernized societies. The mixture of this quid, or chew, is a combination of the areca nut (fruit of the Areca catechu palm tree, erroneously termed betel nut) and betel leaf (from the Piper betel, a pepper shrub), tobacco, slaked lime (calcium hydroxide), and catechu.
(extract of the Acacia catechu tree). [3] Lime acts to keep the active ingredient in its freebase or alkaline form, enabling it to enter the bloodstream via sublingual absorption. Arecoline, an alkaloid found in the areca nut, promotes salivation, stains saliva red, and is a stimulant.

The ingredients and nomenclature of betel quid vary by region as detailed below [7, 8]:

Pan: This is freshly prepared betel quid (with or without tobacco).

Gutka (gutkha, guttkha, or guthka): This is a manufactured version of betel quid with tobacco sold as a single-use sachet. It is primarily used on the Indian subcontinent (ie, India, Pakistan, Bangladesh). Betel quid without tobacco is mostly used in Southeast Asian countries (ie, Taiwan, Myanmar, Thailand, China, Papua New Guinea, Guam).

Pan masala: This is a commercially manufactured powdered version of betel quid without tobacco used in the Indian subcontinent.

Pan Parag: It is a brand name of pan masala and gutka used in India.

Mawa (kharra): This is a crude combination of areca, tobacco, and lime.

Mainpuri tobacco: Popular in parts of northern India, Mainpuri tobacco is a mixture of areca nut, tobacco, lime, and various condiments. Depending on local preferences, sweeteners or spices (ie, cardamom, saffron, clove, anise seed, turmeric, mustard) are also added as flavorings.

In most patients with oral submucous fibrosis, areca nut was chewed alone more frequently than it was chewed in combination with pan (ie, betel leaf plus lime plus betel catechu, with or without tobacco) [4] or had a higher areca nut content. [9]

The pathogenesis of the disease is not well established, but the cause of oral submucous fibrosis is believed to be multifactorial. A number of factors trigger the disease process by causing a juxtaepithelial inflammatory reaction in the oral mucosa. Factors include areca nut chewing, ingestion of chilies, genetic and immunologic processes, nutritional deficiencies, and other factors.

The areca nut component of betel quid plays a major role in the pathogenesis of oral submucous fibrosis. [10, 11, 12, 13] In a 2004 study, a clear dose-dependent relationship was observed for both frequency and duration of chewing areca nut (without tobacco) in the development of oral submucous fibrosis. [14] Smoking and alcohol consumption alone, habits common to areca nut chewers, have been found to have no effect in the development of oral submucous fibrosis, [15] but their addition to areca nut chewing can be a risk for oral submucous fibrosis. [15] Commercially freeze-dried products such as pan masala, gutkha, and mawa have higher concentrations of areca nut per chew and appear to cause oral submucous fibrosis more rapidly than self-prepared conventional betel quid, which contains smaller amounts of areca nut. [9]

Arecoline, an active alkaloid found in betel nuts, stimulates fibroblasts to increase production of collagen by 150%. [16] In one study, arecoline was found to elevate the mRNA and protein expression of cystatin C, a nonglycosylated basic protein consistently up-regulated in a variety of fibrotic diseases, in a dose-dependent manner in persons with oral submucous fibrosis. [17]

In 3 separate but similar studies, keratinocyte growth factor-1, insulinlike growth factor-1, and interleukin 6 expression, which have all been implicated in tissue fibrogenesis, were also significantly up-regulated in persons with oral submucous fibrosis due to areca quid chewing, and arecoline may be responsible for their enhanced expression. [18, 19, 20] Further studies have shown that arecoline is an inhibitor of metalloproteinases (particularly metalloproteinase-2) and a stimulator of tissue inhibitor of metalloproteinases, thus decreasing the overall breakdown of tissue collagen. [21]

Insertion/deletion 5A polymorphism in the promoter region of the matrix metalloproteinase-3 gene, which results in alteration of transcriptional activities, has also been found in persons with oral submucous fibrosis but not in those with oral squamous cell carcinoma. [22] Conversely, insertion/deletion 2G polymorphism in the promoter of the matrix metalloproteinase-1 gene has been implicated in oral squamous cell carcinoma but not oral submucous fibrosis. [23]

Flavanoid, catechin, and tannin in betel nuts cause collagen fibers to cross-link, making them less susceptible to collagenase degradation. [24] This results in increased fibrosis by causing both increased collagen production and decreased collagen breakdown. [4] Oral submucous fibrosis remains active even after cessation of the chewing habit, suggesting that components of the areca nut initiate oral submucous fibrosis and then affect gene expression in the fibroblasts, which then produce greater amounts of normal collagen. [25] Chewing areca quid may also activate NF-kappaB expression, thereby stimulating collagen fibroblasts and leading to further fibrosis in persons with oral submucous fibrosis. [26]

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 that copper acts as an initiating factor in persons with oral submucous fibrosis by stimulating fibrogenesis through up-regulation of copper-dependent lysyl oxidase activity. [27, 28] Further, a significant gradual
increase in serum copper levels from precancer to cancer patients have been documented, [29] which may have a role in oral fibrosis to cancer pathogenesis.

The role of chili ingestion in the pathogenesis of oral submucous fibrosis is controversial. The incidence of oral submucous fibrosis is lower in Mexico and South America than in India, despite the higher dietary intake of chilies. [30] A hypersensitivity reaction to chilies is believed to contribute to oral submucous fibrosis. [4] One study demonstrated that the capsaicin in chilies stimulates widespread palatal fibrosis in rats, [31] while another study failed to duplicate these results. [32]

A genetic component is assumed to be involved in oral submucous fibrosis because of the existence of reported cases in people without a history of betel nut chewing [10, 33] or chili ingestion. [33] Patients with oral submucous fibrosis have been found to have an increased frequency of HLA-A10, HLA-B7, and HLA-DR3. [4]

An immunologic process is believed to play a role in the pathogenesis of oral submucous fibrosis. [34, 35] The increase in CD4 and cells with HLA-DR in oral submucous fibrosis tissues suggests that most lymphocytes are activated and that the number of Langerhans cells is increased. The presence of these immunocompetent cells and the high ratio of CD4 to CD8 in oral submucous fibrosis tissues suggest an ongoing cellular immune response that results in an imbalance of immunoregulation and an alteration in local tissue architecture. [36] These reactions may be the result either of direct stimulation from exogenous antigens, such as areca alkaloids, or of changes in tissue antigenicity that lead to an autoimmune response. [36]

Further, the major histocompatibility complex class I chain–related gene A (MICA) is expressed by keratinocytes and other epithelial cells and interacts with gamma/delta T cells localized in the submucosa. MICA has a triplet repeat (GCT) polymorphism in the transmembrane domain, resulting in 5 distinct allelic patterns. In particular, the phenotype frequency of allele A6 of MICA in subjects with oral submucous fibrosis is significantly higher and suggests a risk for oral submucous fibrosis. [37]

Some authors have demonstrated increased levels of proinflammatory cytokines and reduced antifibrotic interferon gamma (IFN-gamma) in patients with oral submucous fibrosis, which may be central to the pathogenesis of oral submucous fibrosis. [38]

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. [4] The resulting atrophic oral mucosa is more susceptible to the effects of chilies and betel nuts.

Some authors have found a high frequency of mutations in the APC gene and low expression of the wild-type TP53 tumor suppressor gene product in patients with oral submucous fibrosis, providing some explanation for the increased risk of oral squamous cell carcinoma development in patients with oral submucous fibrosis. [10] Other studies have suggested that altered expression of retinoic acid receptor-beta may be related to the disease pathogenesis. [39]

The term oral submucosal fibrosis derives from oral (meaning mouth), submucosal (meaning below the mucosa of the mouth), and fibrosis (meaning hardening and scarring). [4] Chewable agents, primarily betel nuts (Areca catechu), contain substances that irritate the oral mucosa, making it lose its elasticity. Nutritional deficiencies, ingestion of chilies, and immunologic processes may also have a role in the development of oral submucous fibrosis. [3] Oral submucous fibrosis is rare in the United States and is found only in the immigrant members of the South Asian population who chew betel nuts.

Worldwide, estimates of oral submucous fibrosis indicate that 2.5 million people are affected, with most cases concentrated on the Indian subcontinent, especially southern India. [3] The rate varies from 0.2-2.3% in males and 1.2-4.57% in females in Indian communities. [4] Oral submucous fibrosis is widely prevalent in all age groups and across all socioeconomic strata in India. A sharp increase in the incidence of oral submucous fibrosis was noted after pan parag came onto the market, and the incidence continues to increase. Oral submucous fibrosis also occurs in other parts of Asia and the Pacific Islands. [3]

Migration of endemic betel quid chewers has also made oral submucous fibrosis a public health issue in many parts of the world, including the United Kingdom, South Africa, and many Southeast Asian countries. [40]

Oral submucous fibrosis occurs on the Indian subcontinent, in Indian immigrants to other countries, and among Asians and Pacific Islanders as a result of the traditional use of betel quid endemic to these areas. [3]

The male-to-female ratio of oral submucous fibrosis varies by region, but females tend to predominate. In a study from Durban, South Africa, a distinct female predominance was demonstrated, with a male-to-female ratio of 1:1.3. [41] This was later confirmed by others, with a male-to-female ratio of 1:7. [42] In addition, a female predominance in areca nut chewing was also noted in this region. Studies in Pakistan reported a male-to-female ratio of 1:2.3. [4]

Conversely, a case-control study of 185 subjects in Chennai, South India revealed a male-to-female ratio 9.9:1. [15] In Patna, Bihar (also in India), the male-to-female ratio was 2.7:1. [43] With the onset of new commercial betel

Dr Nikita Raman et al.  International Journal of Medical and Biomedical Studies (IJMBS)
The age range of patients with oral submucous fibrosis is wide and regional; it is even prevalent among teenagers in India. In a study performed in Saipan, 8.8% of teenagers with a mean age of 16.3 years (± 1.5 y) were found to have oral submucous fibrosis. [44] Generally, patient age ranges from 11-60 years [4, 43] ; most patients are aged 45-54 years and chew betel nuts 5 times per day. [4]

Oral submucous fibrosis has a high rate of morbidity because is causes a progressive inability to open the mouth, resulting in difficulty eating and consequent nutritional deficiencies. Oral submucous fibrosis also has a significant mortality rate because of it can transform into oral cancer, particularly squamous cell carcinoma, at a rate of 7.6%. [4]

No treatment is effective in patients with oral submucous fibrosis, and the condition is irreversible. [45] Reports claim improvement of the condition if the habit is discontinued following diagnosis at an early stage. [46]

Patients with oral submucous fibrosis have an increased risk of developing oral cancer. The malignant potential and the origin of cancer are attributed to the generalized epithelial atrophy associated with oral submucous fibrosis. [45] Tobacco is the component of the quid believed to be most associated with cancer development. However, the carcinogenic property of the areca nut was discovered after noticing that cancer occurred in patients who chewed the nut without tobacco. [25] In vitro, betel nut extracts increase the rate of cell division, reduce cell cycle time, induce DNA strand breaks, and induce unscheduled DNA synthesis. [47] Whether the use of tobacco in addition to areca nuts is responsible for the increased risk of oral cancer is controversial because evidence is conflicting. [48, 49]

Patients should be instructed regarding the importance of discontinuing the habit of chewing betel quid and informed that eliminating tobacco from the quid product may reduce the risk of oral cancer. Patients should avoid spicy foodstuffs and eat a complete and healthy diet to avoid malnutrition. Also patients should be instructed regarding maintaining proper oral hygiene and scheduling regular oral examinations.

Intervention studies and public health campaigns against oral habits linked to oral submucous fibrosis may be the best way of controlling the disease at the community level. Educate the community regarding the local adverse effects of chewable agents, which although not inhaled, are still not harmless.

Smokeless tobacco (ST) chewing warrants special attention in India because of its popularity and widespread social acceptance. The major factors that persist to encourage people to use smokeless form of tobacco are its low price, ease of purchase, and the widely held misconception of purported medicinal value in curing toothache, headache, and in decreasing hunger. Furthermore, in contrast to smoking, there is no taboo against using ST. The lifestyle, socioeconomic status, and the standards of living of industrial workers are different from the rest of the population. Poverty, language barriers, and poor education contribute different lifestyle that encourages addictive tobacco habits. [46] As there is a ban on smoking tobacco in most of the industrial premises, workers tend to consume more of ST products. Therefore, they form a special group who could be at a higher risk of periodontal breakdown. Hence the present study was planned for study of Prevalence of Oral Submucous Fibrosis and Periodontal Health Status in Patients Chewing Gutka from Bihar Region.

Methodology:

The present study was planned in Department of Dentistry, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar. Total 30 patients were enrolled in the present study. The patients were divided in three groups. The Group A included patients with a healthy periodontium. The Group B included patients with chronic periodontitis without OSMF, and Group C included patients with chronic periodontitis and OSMF.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Inclusion Criteria: patients with chronic periodontitis were probing pocket depth (PPD) ≥3 mm, clinical attachment level (CAL) ≥3 mm, and habit of chewing gutka for at least 3 years >5 times per day.

Patients with any systemic disease, allergies or drug usage, smokers, history of periodontal treatment in the past 6 months, or pregnant and lactating women were excluded.

Results & Discussion:

Oral submucous fibrosis is predominantly caused by the use of areca-nut. Besides being regarded as precancerous condition, it is a serious debilitating and progressive disease. A causal association between areca-nut chewing habit and OSMF, and lichenoid lesion and oral cancer has been strongly established. In India, most of the habitualls of betel-nut used tobacco. The frequency of chewing was directly correlated with OSMF. The mutagenic and carcinogenic properties of areca-nut have been extensively studied in variety of experimental studies.] Areca-nut
contains 5%–40% polyphenols and alkaloids including arecoline, arecadine, guvacine, and guvacoline. [46-47] Gutkha is the commercial form of mixture of betel-nut and tobacco. Most of the habituuls were adapted to mixed habit of betel-nut chewing.

### Table 1: Demographic Details

<table>
<thead>
<tr>
<th>Groups</th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group of Case with</td>
<td>Healthy periodontium</td>
<td>Chronic periodontitis without OSMF</td>
<td>with chronic periodontitis and OSMF</td>
</tr>
<tr>
<td>No. of Cases</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Age (years)</td>
<td>28–45</td>
<td>32–43</td>
<td>31–48</td>
</tr>
<tr>
<td>Sex:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Females</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Frequency (times per day)</td>
<td>0</td>
<td>4.2–8.5</td>
<td>4.7–8.3</td>
</tr>
<tr>
<td>Duration</td>
<td>0</td>
<td>2–6</td>
<td>3–7</td>
</tr>
</tbody>
</table>

### Table 2: Clinical Parameters in Groups Enrolled

<table>
<thead>
<tr>
<th>Groups</th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group of Case with</td>
<td>Healthy periodontium</td>
<td>Chronic periodontitis without OSMF</td>
<td>with chronic periodontitis and OSMF</td>
</tr>
<tr>
<td>No. of Cases</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Gingival index</td>
<td>0.1–0.8</td>
<td>1.3–2.4</td>
<td>0.4–1.4</td>
</tr>
<tr>
<td>Plaque index</td>
<td>0.4–1.2</td>
<td>0.8–1.9</td>
<td>1.8–2.5</td>
</tr>
<tr>
<td>Probing pocket depth regional mm</td>
<td>1.3–1.9</td>
<td>3.9–4.6</td>
<td>2.8–4.1</td>
</tr>
<tr>
<td>Probing pocket depth overall mm</td>
<td>0.9–1.5</td>
<td>3.7–4.4</td>
<td>2.8–3.7</td>
</tr>
<tr>
<td>Clinical attachment level regional mm</td>
<td>0</td>
<td>3.9–5.0</td>
<td>4.2–5.9</td>
</tr>
<tr>
<td>Clinical attachment level overall mm</td>
<td>0</td>
<td>3.8–4.4</td>
<td>4.3–5.4</td>
</tr>
</tbody>
</table>

OSF was first described in the early 1950s.[48] It is a potentially malignant disease with 7–13% of OSF patients developing head and neck squamous cell carcinoma. It is regarded as a collagen metabolic disorder with an overall increased collagen production and decreased collagen degradation, resulting in increased collagen deposition in the oral tissues and fibrosis due to alkaloidal exposure. Clinical importance of OSF is due to two reasons, namely, (1) it is a disease that results from the use of betel-nut chewing in Indians as well as other nationalities adopting the oral habit of betel-nut chewing and (ii) it is generally accepted to be a premalignant condition of the oral cavity.[49]

The symptoms and signs of OSF are due to inflammation and, primarily, fibrosis. The most common initial symptoms and signs are a burning sensation, dry mouth, blanching oral mucosa, and ulceration. The burning sensation usually occurs while chewing spicy food.[48] Blanching of the oral mucosa is caused by impairment of local vascularity because of increasing fibrosis and results in a marble-like appearance.[50] Blanching may be localized, diffuse, or reticular. In some cases, blanching may be associated with small vesicles that rupture to form erosions. Patients complain that these vesicles form after they eat spicy food. These features can be observed at all stages of OSF. In the more advanced stage of the disease, the essential feature is a fibrous band restricting mouth opening and causing difficulty in mastication, speech, swallowing, and maintaining oral hygiene.[51] Development of fibrous bands in the lip makes the lip thick, rubbery, and difficult to retract or evert; a band around the lips gives the mouth an elliptical shape. Fibrosis makes cheeks thick and rigid. When a patient blows a whistle or tries to inflate a balloon, the usual puffed-out appearance of the cheeks is missing. In the tongue, depapillation of the mucosa around the tip and lateral margins may occur with blanching or fibrosis of the ventral mucosa. Fibrosis of the tongue and the floor of the mouth interfere with tongue movement. Hard palate involvement includes extensively blanched mucosa.

Fibrosis may extend posteriorly to involve the soft palate and uvula. The latter may appear shrunken and, in extreme cases, budlike. Gingival involvement is relatively uncommon and is characterized by fibrosis, blanching, and loss of normal stippling. In rare cases of extensive involvement, there may be loss of hearing due to blockage of eustachian tubes and difficulty in swallowing because of esophageal fibrosis.[48]

It is recommended from the current study that as the ST accounts for such a high proportion of oral mucosal lesions and periodontal disease, controlling tobacco use is of immense important if we are to make progress in reducing the burden of tobacco-related oral diseases. Regulatory actions are therefore warranted to control the manufacture, marketing, and the consumption of ST products that contain areca nut and/or tobacco, gutkha, khaini, etc.. People are aware about the health hazards of tobacco and merely that is not sufficient to stop them from...
starting or from continuing the habit. There is also a need to develop multifactorial tobacco quitting strategies focusing on early age intervention. Special efforts are needed to educate the adolescent population using available modalities such as oral health exhibition and oral health outreach programs.

According to Global Adult Tobacco Survey (GATS) India, there are an estimated 275 million tobacco users in India, of whom 25.9% are smokeless tobacco users, while 5.7% smoke cigarettes and 9.2% smoke beedis. Likewise after imposing a strict ban, it’s true that the tobacco cultivators and traders are bound to incur losses along with daily income based small scale industry labourers but it is indeed a need of the hour to curb the sale, supply and use of any form of these carcinogens since a casual intake opens the door for unbelievable un-restorable, irreversible changes by opening alternative options and avenues to those dependent. Importantly, just as a compensation to serve stomach, either as a substitute for food or means of income let’s not encourage this malignant entity to drive away smiles from our lives. Let us unanimously strive hard in creating a healthy disease free environment spreading awareness and smiles to one and all.

Conclusion:

The data generated from the present study concludes that chewing gutka leads to periodontal destruction in patients with OSMF. The cases illustrate the significant morbidity and mortality associated with OSF and emphasize the importance of close follow-up of such cases. Because of the significant cancer risk among these patients, periodic biopsies of suspicious regions of the oral mucosa are essential for the early detection and management of high-risk oral premalignant lesions and prevention of cancer.

References:

2. Joshi SG. Fibrosis of the palate and pillars. Indian J Otolaryngol. 1953. 4:1:
19. Tsai CH, Yang SF, Chen YJ, Chu SC, Hsieh YS, Chang YC. Regulation of interleukin-6 expression by arecoline in human buccal mucosal fibroblasts is related to
45. Murti PR, Bhonsle RB, Pindborg JJ, Daftary DK, Gupta PC, Mehta FS. Malignant transformation rate in oral


