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## A Study On Integrating Technology In Down Staging Approach

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### ABSTRACT

The global burden of Oral cancer accounts for 200,000 deaths annually, encompassing eighty percent of occurrence in low and middle-income countries. Globally, India accounts for highest number of oral cancer cases, reporting 83,000 new cases and 46,000 deaths annually. The major causes of oral cancer include tobacco use, areca nut chewing and heavy alcohol drinking; avoiding these can prevent the disease. Preceded by precancerous lesions, early oral cancers present as red or white patch, small painless ulcers or growths that can be detected, by careful visual examination, and effectively treated. Prevention, early detection and treatment are effective interventions to reduce the worldwide burden of oral cancer.

Oral cancers form a significant portion of the cancer burden seen in our country. Typically, they tend to be preceded by a premalignant state for a long time. This study discusses the various types of premalignant disorders commonly seen in daily practice. Also, it is important to screen patients for these conditions so as to detect malignant changes early. Previously, the screening of patients for oral cancer and precancerous lesions has relied mainly on conventional oral examination. Nowadays, many newer techniques are available to potentially assist in the screening of healthy patients for evidence of oral cancer. This study attempts to review the current literature for screening methods and integrating technology into screening methods and adjuncts such as toluidine blue, brush cytology, tissue chemiluminescence and auto fluorescence.

### 1. INTRODUCTION

Oral cancers are one of the leading cancers in India today, with an age standardized incidence rate of 12.6 per 100 000 population. It is one of the leading cancers in Indian males accounting for approximately 30% of the cancer burden. A significant number of

these cases would present initially with precursor lesions that are further classified as precancerous lesions and precancerous conditions.

A precancerous lesion is a morphologically altered tissue in which oral cancer is more likely to occur than in its apparently normal counterpart, for example, Leukoplakia, Erythroplakia etc. A precancerous condition is a generalized state associated with a significantly increased risk of cancer, for example, submucous fibrosis, Lichen planus etc. However, in a World Health Organization (WHO) Workshop, held in 2005, it was decided to use the term "potentially malignant disorders (PMD)" as it conveys that not all disorders described under this term may transform into cancer. [\[1\]](#)

The following were identified as Potentially Malignant Disorders by the World Health Organisation's working group on Oral Cancer. [\[2\]](#)

- Leukoplakia
- Erythroplakia
- Palatal lesion of reverse cigar smoking
- Oral lichen planus
- Oral submucous fibrosis (SMF)
- Discoid lupus erythematosus
- Hereditary disorders such as dyskeratosis congenita and epidermolysis bullosa.

### ➤ **Leukoplakia**

The term "leukoplakia" was coined by Schwimmer of Budapest in 1877, for white changes on the tongue, seen prior to lingual cancer development in tertiary syphilis. It is the most common premalignant lesion and the most studied PMD. The WHO working group defines leukoplakia as "a keratotic white patch or plaque that cannot be scraped off and cannot be characterized clinically or pathologically as any other disease." Therefore, a process of exclusion establishes the diagnosis of the disease.

### **Incidence**

The estimated prevalence of oral leukoplakia, worldwide, is approximately 2%. [\[3\]](#) Petti, [\[3\]](#) in a systematic review, summarized the world prevalence of leukoplakia based on 23 studies from 17 countries published between 1986 and 2002. Using statistical

techniques, he calculated a global prevalence of 2.6%. In India, a striking variation has been observed with 0.2% in Bihar and 4.9% in Andhra Pradesh. <sup>[4]</sup>Gujarat has shown a prevalence rate of 11.7% owing to the high prevalence of tobacco or guthka chewing practices. The systematic review by Petti <sup>[3]</sup> also confirmed that oral PMD affects males at least three times as often as females.

### **Etiopathogenesis**

The etiology of leukoplakia remains unknown. Many physical agents have been proposed, including tobacco, alcohol, chronic friction, electro galvanic reaction between unlike restorative metals, and ultraviolet radiation. <sup>[5],[6]</sup> Tobacco smoking is by far the most accepted factor and smokers are six times more prone to leukoplakia than nonsmokers. There are conflicting results of studies related to the possible role of human papilloma virus infection. <sup>[7]</sup>

Clinically, leukoplakia can be subdivided into a homogeneous type (flat, thin, uniform white in color) and a nonhomogeneous type. The nonhomogeneous type has been defined as a white lesion, that may be either irregularly flat (speckled) or nodular. Verrucous leukoplakia is yet another type of non-homogeneous leukoplakia. Although verrucous leukoplakia usually has a uniform white appearance, its verrucous texture is the distinguishing feature from homogeneous (flat) leukoplakia. Verrucous leukoplakia is clinically indistinguishable from the clinical aspect of verrucous carcinoma. <sup>[8]</sup> Proliferative verrucous leukoplakia (PVL) is a subtype of verrucous leukoplakia, being characterized by multifocal presentation, resistance to treatment and a high rate of malignant transformation. <sup>[9],[10]</sup> PVL seems more prevalent among elderly women.

Leukoplakias are known to occur at almost all places in oral cavity. However, they are most frequent in buccal mucosa. Two-third of the oral leukoplakias occurs at the vermillion, buccal mucosa and gingival surface. In Gujarat, where smoking is common, 43.9% of leukoplakias occurred on the buccal mucosa while 35.4% at the commissure, whereas in Kerala where tobacco chewing is common, 64.8% were on the buccal mucosa, 24.3% at the commissures and 6% on the tongue. In Andhra Pradesh, where smoking is common, 71.3% were on palate, 8.1% on the commissure, 16.9% on the buccal mucosa and 2.7 on tongue. <sup>[4]</sup> In a Swedish study, the buccal mucosa or commissure was involved

in 90% of cases. <sup>[11]</sup> In a Hungarian study, the tongue was involved in 36.5%, buccal mucosa in 27.9%, alveolar ridge in 13.6% and commissure in 12.5%.

### **Prognosis and malignant transformation**

The prognosis of leukoplakia varies. In a study conducted in Mumbai, 42.5% untreated leukoplakias disappeared in 5 years and 45.3% in 10 years in the tobacco chewing group. <sup>[12]</sup> In Gujarat, 11% of leukoplakias re-examined after 2 years had increased in the size, 31.6% had decreased in size or disappeared and 57.3% had remained unchanged. <sup>[13]</sup> In a study from developed world only 20.1% had disappeared, 17.8% had reduced in size and 3.3% had increased at 10 years follow up. <sup>[14]</sup>

The frequency of dysplastic or malignant alterations in oral leukoplakia has ranged from 15.6 to 39.2% in several studies. In Indian studies, the rate of malignant transformation ranges from 0.13% to 2.2% per year. <sup>[12],[13]</sup> In a Swedish study, 0.2% developed oral cancer in 2 years, 0.4% in 5 years in tobacco users while in non tobacco users the transformation rate was 1.15 and 3.1% at 2 and 5 years respectively. <sup>[15]</sup> In systematic review, Petti has calculated a global transformation rate for oral leukoplakia of 1.36% per year. <sup>[3]</sup> The lesions that are present in the floor of mouth, lateral tongue and lower lip are more likely to show dysplastic or malignant changes.

The possibility of malignant transformation of leukoplakias depends on multiple factors:

- gender
- Long duration of leukoplakia
- Leukoplakia in nonsmokers (idiopathic leukoplakia)
- Location on the tongue and/or floor of the mouth
- Size > 200 mm<sup>2</sup>
- Nonhomogeneous type
- Presence of *Candida albicans*
- epithelial dysplasia.

Erythroplakia is not as common as leukoplakia and has an incidence reported between 0.02% and 0.83%. <sup>[17]</sup> It mainly occurs in the middle aged and the elderly. There is no distinct gender preference. This lesion signals a significant alteration in oral mucosa

because it typically presents as carcinoma in situ, severe epithelial dysplasia or superficially invasive carcinoma under the microscope. In very high risk settings, such as floor of mouth lesions in heavy smokers and alcohol abusers, 80% of these red patches already may contain focal areas of microinvasive cancer at the time of initial biopsy. Any site of the oral and oropharyngeal cavity may get involved, usually in a solitary fashion. This solitary presentation is often helpful in clinically distinguishing erythroplakia from erosive lichen planus, lupus erythematosus and erythematous candidiasis, since these lesions occur almost always in a bilateral, more or less in a symmetrical pattern.

In other study, to their large series of leukoplakia cases, Shafer and Waldron also analyzed their biopsy experience with 65 cases of erythroplakia. <sup>[18]</sup> All the erythroplakia cases showed some degree of epithelial dysplasia; 51 % showed invasive squamous cell carcinoma, 40% were carcinoma in situ or severe epithelial dysplasia, and the remaining 9% demonstrated mild-to-moderate dysplasia. Therefore, true clinical erythroplakia is a much more worrisome lesion than leukoplakia.

#### ➤ **Oral Submucous Fibrosis**

Oral submucous fibrosis (OSMF) is a chronic disorder characterized by fibrosis of the lining mucosa of the upper digestive tract involving the oral cavity, oropharynx and frequently the upper third of the oesophagus. Except in early forms of the disease, the clinical presentation is characteristic due to fibrosis of lamina propria and submucosa with an increasing loss of tissue mobility. OSMF is particularly associated with areca nut chewing, the main component of betel quid. <sup>[19]</sup> Hence, it is the most common precancerous lesion that is a unique problem in South East Asia especially India. Factors including areca nut chewing, ingestion of chillies, genetic and immunologic processes, nutritional deficiencies, and other factors have been incorporated in causation of OSMF. Patients with OSMF have been found to have an increased frequency of HLA 10, DR3, and DR7. <sup>[20]</sup>

Clinically, OSMF is characterized by a burning sensation, blanching and stiffening of the oral mucosa and oropharynx, and trismus. The most characteristic feature is the marked vertical fibrous ridge formation within the cheeks, and board like stiffness of the buccal mucosa. The fibrosis in the soft tissue leads to trismus, difficulty in eating, and even dysphagia. In advanced stages vertical fibrous bands appear in the cheeks, faucial pillars,

and encircle the lips. Through an as yet unknown process, fibrosis and hyalinization occur in the lamina propria, which results in atrophy of the overlying epithelium. The atrophic epithelium apparently predisposes to the development of a squamous cell carcinoma in the presence of carcinogens. Biopsy of the tissue is rarely performed due to the observation that such investigation results in further fibrous scar formation and worsening of the symptoms.

The clinical presentation can be summarized into early and forms:

- Early forms are characterized by burning sensation exacerbated by spicy foods, vesiculation, blanching of mucosa, and leathery mucosa.
- Late forms are characterized by fibrous bands within the mucosa, limitation of mouth opening, narrowing of the oropharyngeal orifice with distortion of uvula and woody changes of the mucosa and tongue.

In India, it affects between 0-2% and 1.2% of an urban population attending dental clinics. [\[21\]](#) There is a positive association between the incidence of leukoplakia and oral cancer with OSMF. The frequency of malignant change has been reported from 3% to 6%. The possible precancerous nature of OSMF was first described by Paymaster, who observed the occurrence of squamous cell carcinoma in one third of his patients with OSMF. [\[22\]](#) In a long-term follow-up study over a period of 17 years by Murti *et al.*, [\[23\]](#) the annual malignant transformation rate was approximately 0.5% or 7.6% over 17 years. [\[23\]](#)

### ➤ **Oral Lichen Planus**

Lichen planus is an immune related – T cell mediated disorder of the skin and/or oral mucosa which usually affects middle-aged persons but may occur at any age with a strong female predilection (M:F = 1:2). Persons with oral lesions may be associated with skin lesions. Oral lichen planus is a T-cell-mediated autoimmune disease in which autotoxic CD8<sup>+</sup> T cells trigger apoptosis of oral epithelial cells. [\[24\],\[25\]](#) Oral mucosal lichenoid lesions may occur after the administration of systemic drugs such as nonsteroidal anti-inflammatory drugs (NSAIDs), sulfonylureas, antimalarials, beta-blockers, and some angiotensin-converting enzyme (ACE) inhibitors. The period between the commencement of the drug therapy and the clinical appearance of oral lichen planus-like disease varies.

The buccal mucosa, tongue, and gingiva are the most common sites, whereas palatal lesions are uncommon; with intertwining white streaks forming a reticular pattern similar to a spider web, any oral area can be affected. The background membrane may be red, and some persons might have blisters and ulcers with the white lines. There may be a metallic taste, and ulcers may be tender. The lesions tend to be bilateral and symmetrical that distinguishes them from erythroleukoplakia. Andreasen [\[26\]](#) divided oral lichen planus into six types: reticular, papular, plaque-like, erosive, atrophic, and bullous. The reticular, papular, and plaque-like forms are usually painless and appear clinically as white keratotic lesions. The erosive, atrophic, and bullous forms are often associated with a burning sensation and in many cases can cause severe pain.

There is still no consensus in the literature whether patients with oral lichen planus (OLP) may carry an increased risk of developing squamous cell carcinomas. Most of the assumptions are based on retrospective studies with only few prospective studies. [\[27\],\[28\],\[29\],\[30\]](#) The reported annual malignant transformation rate is usually well below 1%. There is no data to conclude which variety of OLP would eventually develop into squamous carcinoma, though some studies attribute a higher rate in specially the atrophic and erosive-ulcerative types. [\[31\],\[32\]](#) The present lack of clinicopathologic correlation in the diagnosis also adds to the confusion. [\[33\],\[34\]](#) Another entity, described as lichenoid dysplasia [\[35\]](#) adds to the confusion. As there is no particular treatment to prevent the malignant transformation, some authors [\[36\]](#) recommend keeping patients on close surveillance.

### **Nicotine Stomatitis**

Nicotine stomatitis is a thickened, hyperkeratotic alteration of the palatal mucosa that is most frequently related to pipe smoking or reverse smoking. The palatal mucosa becomes thickened and hyperkeratotic, sometimes developing a fissured surface. The surface often develops papular elevations with red centers, which represent the inflamed openings of the minor salivary gland ducts. The term nicotine stomatitis is actually a misnomer because it is not the nicotine that causes the changes; the changes are caused by the intense heat generated from the smoking. Although nicotine stomatitis is a tobacco related it is not considered to be premalignant and it is readily reversible with discontinuation of the tobacco habit.

### ➤ **Palatal Lesions in Reverse Cigar Smokers**

In some Southeast Asian and South American countries, individuals practice a habit known as reverse smoking in which the lit end of the cigarette or cigar is placed inside the mouth. This habit creates a more severe heat-related alteration of the palatal mucosa known as *reverse smoker's palate*, which has been associated with a significant risk of malignant transformation. [\[37\].](#)[\[38\]](#)

### **Actinic Keratosis**

Actinic keratosis is considered to represent a potentially malignant condition that arises in many sites including lips. It is commonly associated with exposure to sun. In Actinic keratosis, the average rate of progression to invasive cancer ranges from 0.025% to 16% per year. [\[39\]](#) Actinic cheilitis is a clinical term for an ulcerative, sometimes crust-forming lesion of the mucosa of part or entire vermilion border of the lower lip. The histopathology can vary from hyperkeratosis with or without epithelial dysplasia to early squamous cell carcinoma.

### **Tobacco Pouch Keratosis**

Another specific tobacco-related oral mucosal alteration occurs in association with smokeless tobacco use, either from snuff or chewing tobacco. Such lesions typically occur in the buccal or labial vestibule where the tobacco quid is placed, but they can also extend onto the adjacent gingiva and buccal mucosa. Overall, it is estimated that 15% of chewing tobacco users and 60% of snuff users will develop clinical lesions. Microscopically, smokeless tobacco keratoses show hyperkeratosis and acanthosis of the mucosal epithelium. True epithelial dysplasia is uncommon; when dysplasia is found, it is usually mild in degree. [\[40\]](#) Most tobacco pouch keratoses are readily reversible within 2 to 6 weeks after cessation of the tobacco habit.

### **Hereditary Disorders with Increased Risk of Malignant Transformation**

Two conditions that may have an increased risk of malignancy in the mouth are Dyskeratosis Congenital (DC) and Epidermolysis Bullosa. They are rare hereditary conditions. Most cases of DC are X-linked and affect males. Patients with DC often develop white plaques on the dorsal tongue that may be confused with leukoplakia, but the

absence of habits and their young age may point to the hereditary nature of this disorder. Malignant change within the areas of white patches is reported. In Xeroderma pigmentosum and Fanconi's anemia, there is an increased incidence of malignancies, including oral cancer.

### **1.1 AIM OF THE STUDY**

The aiming of this study was:

- 1) To report the prevalence of awareness level of “a small lesion can develop into oral cancer” in adult population (18-57) years.
- 2) To report the prevalence of awareness level of “early treatment can prevent a lesion to develop into oral cancer” in adult population (18-57) years.
- 3) To describe how the awareness levels of oral cancer are associated with the respondents' different socio-demographic and socio-economic characteristics and their last dental visit.
- 4) To study the importance of technology Integration to the conventional screening methods used in down staging the Oral Cancer.

### **1.2 THE STUDY OBJECTIVES**

1. Describe the socio-demographic factors (age, sex, marital status and ethnicity), socio-economic factors (National Statistics Socio-Economic Classification (NS-SEC), education level) and last dental visit in adult population aged 16-65.
2. Describe the awareness level of “a lesion can develop into oral cancer” of adult population aged 16-65 years.
3. Describe the awareness level of “early treatment can prevent a lesion to develop into oral cancer” of adult population aged 16-65 years.
4. Assess the relationship between socio-demographic factors (age, sex and ethnicity), socio-economic factors (National Statistics Socio-Economic Classification (NS-SEC),

education level) and last dental visit and the awareness level of “early treatment can prevent a lesion to develop into oral cancer” in adult population aged 16-65 years.

5. To integrate health and technology in conventional screening for improving public health surveillance.

6. To assess the screening efficiency of CHWs in identification of oral mucosal lesions; and to evaluate the concordance of CHWs with an onsite specialist in identification of oral mucosal lesion.

## **CONCLUSION**

Potentially malignant disorders are an important spectrum of diseases that need to be identified and followed up closely. Correct identification of their malignant potential may help in early diagnosis of cancer and down staging of the disease. Clinical examination and histopathology remain the "gold standard" for the detection of oral cancer. However, other than visual examination, no single method for screening seems to be applicable and cost effective in the general population.

A multifaceted approach that integrates health education, tobacco and alcohol control, early detection, and early treatment is needed to reduce the burden of this eminently preventable cancer. How to accomplish this is known; astonishingly, it has not been applied in most countries, and not at all in the high-burden countries. Improving awareness among the general public and primary care practitioners, investing in health services to provide screening and early diagnosis services for tobacco and alcohol users, and providing adequate treatment for those diagnosed with invasive cancer are critically important oral cancer control measures. Imaging, histopathology, cancer surgery and radiotherapy infrastructure and services, trained professionals, and the availability of chemotherapeutic agents are inadequate in many Low and middle income countries, seriously compromising early detection and optimum treatment.

The aims of this study were to report the prevalence of awareness level of “a small lesion can develop into oral cancer” and the awareness level of “early treatment can prevent a lesion to develop into oral cancer” of adult population (16-65) years, living in a deprived

area in Karnataka state of India. Also to relate these awareness levels with the respondents' characteristics and their dental attendance.

## **7.1 FUTURE SCOPE OF RESEARCH**

Primary prevention, especially smoking cessation, and secondary prevention, focused on high risk individuals, is likely to be both cost-effective and affordable in Low and middle income countries. Additional studies are required to assess the cost-effectiveness and budget implications of visual screening for oral cancers in Low and middle income countries. mHealth concept can be an cost effective solution for screening methods. These studies should focus on the screening delivery structure to identify the most cost-effective approach to provide oral cancer screening to high-risk individuals. When cancer screening policies are implemented, the success of the program will depend on participation by the target population. Even when screening and follow-up care is free of charge, patients may not be able to afford to lose a day's wage to attend screening clinics or travel to health centers to receive follow-up diagnostic testing or treatments. The indirect costs borne by the patients may be particularly challenging among those in the lower socioeconomic strata. These are the very individuals likely to be at higher risk for developing oral cancers; it is, therefore, vital that identifying approaches to encourage and sustain participation among this potentially hard-to-reach high-risk population be given high priority.

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