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A Brief Overview of Oral Potentially Malignant Disorder

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Author's contribution

The sole author designed, analyzed and interpreted and prepared the manuscript.

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Review Article

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ABSTRACT

Cancer of the oral cavity is one of the most common cancers. Oral cancer is still only detectable at a late stage, and the survival rate for an oral cancer patient has essentially remained unchanged over the past three decades.
This study is concentrated on the oral precancerous lesions which are commonly seen in dental clinics and to give the general practitioners Knowledge for early detection of these lesions. A literature search was conducted using Medline, accessed via the National Library of Medicine PubMed interface, searching for articles relating to the precancerous oral lesions written in English.

Keywords: Precancerous lesion (potentially malignant disorder); oral lesion; malignant transformation.

1. INTRODUCTION

Oral cancer may develop in any part of the mouth, tongue, lips and the oropharynx (middle part of the throat). Symptoms may include red, white and/or speckled spots and patches in the mouth, swellings, lumps and rough crusts areas anywhere inside the mouth, unexplained

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bleeding, pain, tenderness or numbness in the mouth, difficulty in swallowing, speaking or chewing, hoarseness of voice, ear pain and dramatic loss in weight [1,2].

The term Potentially Malignant Disorder has been introduced in 2005 after the WHO meeting to be used instead of pre-malignant lesions and conditions, they also suggested that leukoplakia and erythroplakia have the highest malignant transformation behaviour and attention must be given to them more than the other lesions. Precancerous lesions and early oral cancers are often subtle and asymptomatic. Therefore, it is important for the clinician to have suspicion, especially if risk factors such as tobacco use or alcohol abuse is present [23]. Early detection and diagnosis is very important issue and have direct relation in the treatment and prognosis of the oral cancer.

2. RISK FACTORS

Smokers are 5 to 9 times more likely to develop oral cancer in comparison to nonsmokers, and for heavy smokers who smoke 80 or more cigarettes daily, the risk is 17 times greater [3-4]. Souto et al. [5] reported that the mean percentage of aneuploid nuclei was statistically higher in the smokers with oral squamous cell carcinoma (93.65%), as compared to non-smokers (39.3%) ($P<0.05$). Souto et al. [5] concluded in his study that tobacco use is responsible for an increased number of aneuploid nuclei in the oral epithelium. Bouquot and Meckstroth [6] reported that West Virginia is the state with the highest per capita consumption of smokeless tobacco, yet it has less oral/pharyngeal cancer than the US average Madani et al. [7] indicated that gutkha, supari - areca nut- chewing tobacco (tobacco flakes), bidi smoking and mishiri (tobacco powder, which applied as a tooth and gum cleaner) are independent risk for oral cancer. The use of smokeless tobacco appears to be associated with a much lower cancer risk than that associated with smoked tobacco [8,9]. Andre et al. [10] reported that the heavy drinkers are 30 times more likely to develop oral and oropharyngeal cancer in comparison to non-drinkers [10]. A synergistic effect of alcohol and smoking was observed by some authors. Risk of developing malignancy in patients who are both heavy smokers and drinkers is over one hundred times [10-11]. Another habit which has been strongly associated with increased risk for oral cancer is the chronic use of betel quid [12]. Betel quid chewing commonly leads to precancerous condition known as oral submucous fibrosis which has a malignant transformation rate of 7.6% 12). Prabhu and Wilson stated that Human papilloma virus (HPV) may also be associated with some oral and oropharyngeal cancers [13]. HPV-18 has been found in up to 14 percent of cases and HPV-16 has been detected in up to 22 percent of oral cancers [14-15]. The low intake of fruits and vegetables in the diet may also eventually attribute to an increased risk for cancer [16] Radoï et al. [17] reported that hot beverages tea and coffeein particular drinking may decrease the risk of oral cancer through antioxidant components which play a role in the reparations of cellular damages. Jaleel et al. [18] reported that people with the blood group A had a 10.46% likelihood to develop oral cancer compared to people of other blood groups. Plummer-Vinson or Paterson-Kelly syndrome which is an iron deficiency anemia in combination with dysphagia and esophageal web is associated with an increased risk for development of carcinoma of the oral cavity, particularly oropharynx and oesophagus [19].

3. DIAGNOSIS OF PRE MALIGNANT LESION (POTENTIALLY MALIGNANT DISORDER)

Pre-malignant lesion often presents itself as either white or red patches in oral mucosa known as leukoplakia or erythroplakia [20-23]. The patient may initially notice the presence of a non-healing ulcer when the cancer develops. Later-stage symptoms may include loosening of teeth, bleeding, dysphagia, difficulty in wearing dentures, and development of a neck mass. For visual examination and palpation, it is recommended that a tongue blade or dental mirror and a gloved hand can be used to retract the lips and extend the cheeks. To assist with retraction and examination of the lateral borders of the tongue gauze can be used for wrapping the tongue. Pre-malignant lesions are most commonly found in the lateral borders of the tongue, the floor of the mouth, the posterior aspect of the cheek, and the oropharynx. It is recommended by the American Cancer Society that an annual check-up for all individuals aged 40 and older, and every three years for those between the ages of 20 and 39 [24-25] is done.

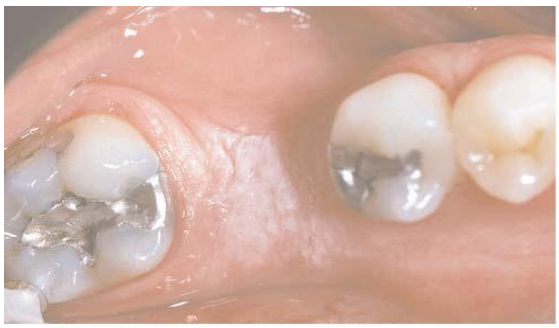
It is also recommended by the society to improve the oral cancer survival rate, by educating individuals via oral sessions and new ways of awareness (Word Choice: In most cases

advertisement or advertising usually refers to a product or services) to encourage patients to reduce (Word Choice) the risk of contracting oral cancer.

4. LEUKOPLAKIA

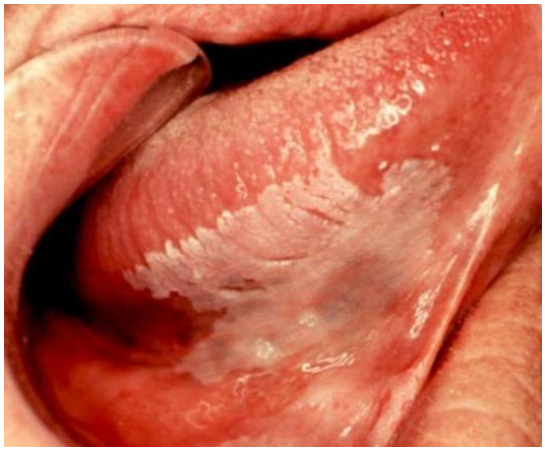
Oral leukoplakia (OL) is a white patch or plaque that cannot be rubbed off and cannot be characterized clinically or histologically as any other condition [26]. Leukoplakia has no histologic connotation and should never be used as a microscopic diagnosis.

When evaluating a patient suspected to have a leukoplakia, a rough clinical diagnosis must be done to exclude leukoplakia, for example any oral white patch can be diagnosed as a leukoplakia until it is proved that it is other condition (lichen planus, leukoedema).Oral white patches can easily develop due to local irritation. For example ,the thickened hyperkeratotic areas on the alveolar ridges of the edentulous patients, especially in patients who do not wear a dental prosthesis (Fig. 1). This hyperkeratotic area is due to the epithelium protecting the area which is preferably termed “frictional keratoses” [27]. Chronic cheek chewing (morsicatio buccarum) which leads to hyperkeratotic changes must not be termed as a leukoplakia; these lesions are not potentially malignant and can return back to normal structure if the irritant is removed. Nicotine stomatitis and tobacco pouch keratosis, are not categorized as aleukoplakias.



1. Shows hyperkeratotic on the edentulous areas of the alveolar ridges

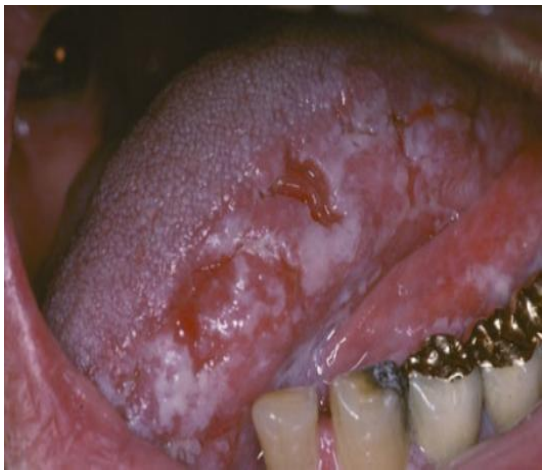
The most common sites of leukoplakia are the buccal mucosa, alveolar mucosa ,and the lower lip; however, lesions in the floor of mouth, lateral tongue, and lower lip are most likely to show dysplastic or malignant changes [28-29]. There are three clinical varieties are recognized homogeneous Fig. 2 (common; faintly white – very thick and opaque), speckled Fig. 3 (less common; non-homogenous / heterogenous leukoplakias has a high risk of malignant transformation) and verrucous [29]. Proliferative verrucous leukoplakia (Fig. 4) begins with conventional flat white patches that, over time, they tend to become much thicker and papillary in nature and may progress to verrucous carcinoma. The condition is often seen in patients without any risk factors, characterized by widespread, multifocal sites of involvement and has a high recurrence rate [30]. A study of 3,300 biopsies of oral leukoplakia by waldron and shafer showed that 19.9% of all leukoplakia showed some degree of epithelial dysplasia [31]. Dysplasia is more commonly seen in thicker leukoplakia; therefore, a verrucous leukoplakia is the most likely to show dysplastic changes compared to other forms [32]. Speckled leukoplakia or erythroplakia (leukoplakias red component) is at greatest risk for showing dysplasia or carcinoma [32].



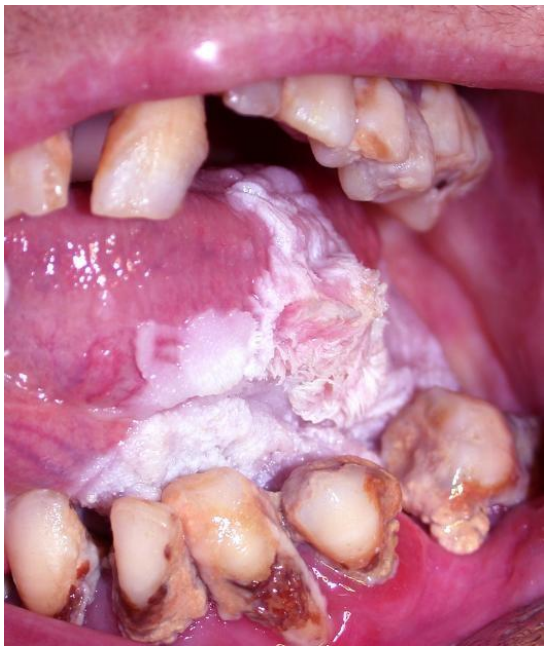
2. Shows homogeneous leukoplakia

According to Hosni et al. [32] erythroplakia and speckled leukoplakia show histopathological alterations which vary from epithelial dysplasia to invasive carcinoma and these lesions have a high potential for malignant tranformation. Recent studies have shown that these lesions have malignant transformation rates ranging from 8.9 to 17.5 percent [33-43]. Because of the smoking habits, leukoplakia is more common in men than women [44], but studies have shown that women with leukoplakia have a higher risk of developing oral carcinoma [34].

All the published data regarding the malignant transformation of oral leukoplakia in different countries have been included in Table 1.



3. Shows speckled leukoplakia



4. Shows Proliferative verrucous leukoplakia

5. ERYTHROPLAKIA

Erythroplakia is a lesion that refers to a red patch that cannot be categorized clinically or pathologically as any other condition [45]. Erythroplakia patches may be located near, or associated with, oral leukoplakias. Bouquot and Whitaker [31] suggested that erythroplakia may occur with leukoplakia in the stage called erythroleukoplakia. Erythroplakia has been considered the most severe form among all of the oral premalignant lesions because of its high malignant potential [32]. In a study done on 65 cases of erythroplakia, it was reported that 51 percent of these were invasive squamous cell carcinoma, 40 percent were carcinoma in situ or severe epithelial dysplasia, and the remaining 9 percent demonstrated mild-to-moderate dysplasia. This points to the fact that true erythroplakia has more malignant potential than leukoplakia. Villa et al. [46] indicated that Oral erythroplakia is identified as the one with the highest malignant transformation rates compared to other premalignant lesions.

6. NICOTINE STOMATITIS

Nicotine stomatitis is most common in men over 40 years of age. Pipe and cigar developed nicotine stomatitis condition, but it also occurs in cigarette smokers. Nicotine stomatitis is a lesion that develops on the palate of some smoker [47]. It appears white with raised red dots. The lesion is persistent, continuing as long as smoking persists. There are usually no symptoms associated with this lesion, even when it is long standing [48]. If the smoking is discontinued or lessened, the lesion may reverse completely. hyperkeratosis and the minor salivary gland involved shows inflammatory reaction. Nicotinic stomatitis is completely different from the palatal changes of reverse smoking clinically and histopathologically [49,50].

7. FRICTIONAL KERATOSIS

Frictional keratosis is a reactive lesion that shows white lesion in the oral mucosa commonly associated with sharp margins of a broken tooth or ill-fitting dentures, it can be diagnosed by good history taking and good examination sometimes a biopsy should be taken and it is treated by removing the cause [12].

8. PALATAL CHANGES ASSOCIATED WITH REVERSE SMOKING

Reverse smoking is a condition when putting the cigarette in reverse direction inside the mouth leads to white keratotic patches, red patches and ulceration [7].

This white keratotic patches may be due excess keratin production and small red dots may result from an inflamed opening of a minor salivary gland in the palate, ulceration occurs due to the heat which comes from the end of the cigarette which is placed inside the mouth [7].

Table 1. Shows the malignant transformation of oral leukoplakia in different countries

Authors	Country	Year	Number of patients	% of Patients with malignant transformation
Einhorn and Wersäll 2010 [44]	Sweden	1967	782	4.0
Silverman 2013 [45]	United States	1968	117	6.0
Pindborg et al. 2011 [46]	Denmark	1968	248	4.4
Kramer 2003 [47]	England	1969	187	4.8
Roed-Petersen 1971 [48]	Denmark	1971	331	3.6
Bánóczy 1996 [49]	Hungary	1977	670	6.0
Silverman et al. 2001 [50]	United States	1984	247	17.5
Lind 1987 [51]	Norway	1987	157	8.9
Bouquot and Gorlin 1986 [52]	United States	1986	463	10.3
Lan AX 2009 [53]	China	2009	409	12.7
Amsterdam 2014 [54]	Amsterdam	2014	144	2.6

9. ORAL SUB MUCOUS FIBROSIS

Oral sub mucous fibrosis is a lesion commonly found and prevalent in India, this lesion has a high rate of malignant transformation to squamous cell carcinoma, the etiology of oral sub mucous fibrosis is unknown but some of the risk factors involved are chewing of areca betel nut and eating chili peppers, deficiency of iron and B complex vitamins and folic acid and auto immune factor and genetic predisposition, symptoms of this lesion includes dryness of the mouth, dysphagia when the esophagus is involved and it can lead to hearing loss due to blockage in the Eustachian tubes, the affected areas appears smooth, atrophic and almost white and looks pallor due to the fibrosis and ischemia [12], mostly affect area are the buccal mucosa and the soft palate in the oral mucosa and these areas lose their resilience and elasticity leading to difficulty in mouth opening (trismus) and difficulty in eating, Oral sub mucous fibrosis can easily spread from the oral cavity into the pharynx and the esophagus [7].

10. CONCLUSION

Oral cavity and oro-pharnx region should be carefully inspected while examination especillay in heavy smokers and drinkers. Survival from oral cancer has very poor rates, at approximately 50% overall [21], and have not improved in recent decades despite advances in therapeutic interventions [51,52,53,45]. Detecting oral cancer at an early stage is believed to be the most effective means of reducing rates of death and morbidity [22]. Early diagnosis depends upon clinician or patient who may identify a suspicious lesion or symptom while it is still at an early stage.

A white or red patch should be carefully inspected for a change insize, color, mobility, contour, texture, or function of intraoral, extra oral or perioral tissue should arouse suspicion of the presence of malignant or premalignant lesions in these regions. All medical and dental examination should include comprehensive head and neck examinations with biopsy and further investigations when indicated. Any white lesion must be considered a potentially malignant disorder until proven otherwise. General practitioners must spend more time examining their patients thoroughly.

CONSENT

Not applicable.

ETHICAL APPROVAL

Not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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