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CASE REVIEW

FINDING LEUKOPLAKIA: THE DENTIST'S WINDOW OF OPPORTUNITY

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ABSTRACT

India has the dubious distinction in accounting for almost half of all oral cancer cases in the world . Ironically, out of all cancers, Oral Squamous cell carcinoma (OSCC) is one of the most preventable cancers that occur in people where the patient simply has to make a definite life style choice (to use or not to use tobacco) to reduce the risk of its occurrence. General Dentist can play an important role in prevention and in early recognition of signs and prompt referral of patients. This review will focus particularly on early identification of Leukoplakia in dental practice and is an update about the influence of internal and external environmental factors associated with pre cancer stage, recognizing the clinical spectrum of Leukoplakia for identifying individuals at greater risk and provide suggestions for instituting a realistic plan for clinical follow up and performing opportunistic screening.

KEY WORDS: Oral Potentially malignant disorders, Leukoplakia, Pre-Cancer screening, opportunistic screening.

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INTRODUCTION:

The current challenge with regards to Oral Squamous cell carcinoma (OSCC) in India is not only its increasing incidence or the dismal long term survival after treatment, but the fact that people continue to put themselves at risk through smoking, chewing tobacco and drinking alcohol. And all of this continues to happen despite the public being educated in various platforms, health care workers creating awareness in rallies and campaigns and the government placing regulations and ban of sale of chewable tobacco products in few states in India.
India is the third largest tobacco producer and second largest consumer of tobacco worldwide.[1] The epidemiological burden and demographic disaster caused by OSCC in India is well known to dentists and even other health care providers. The five year survival for oral Squamous cell carcinoma from the time of diagnosis has not improved remarkably, primarily because majority of patients are diagnosed at higher clinical stages of the disease that jeopardizes the outcome and survival [2].

This situation suggests that both the dentists and/or patients are failing to recognize early mucosal changes that indicate oral cancer development and are evading timely clinical evaluation of such changes [3]. Interestingly, with regards to OSCC, in 90% of cases, there is always a preceding stage or precursor stage of disease that exists for a variable and extended period of time before transforming in to OSCC [4].
Practically not all cases of pre-malignancy transform to malignancy. Usage of the prefix "Pre" implies that there is a definitive consequence of the disorder to transform in to malignancy. So, Oral Potentially Malignant Disorders (OPMD) is an umbrella term used to predict risk of cancer in the lesion/condition at the time of diagnosis or in the future. And this is depicted as a percentage [5]. Given the ready anatomic access of oral cavity to visual and tactile examination, detecting OPMD's before they become early carcinoma should not be very difficult for the General Dentist [6].

OBJECTIVES:

This review will focus particularly on early identification of Leukoplakia in dental practice and is an update about the following aspects of OPMD's

- Influence of internal and external environmental factors associated with pre cancer stage.
- Recognizing the clinical spectrum of Leukoplakia and to identify individuals at greater risk.
- Instituting a realistic plan for clinical follow up and perform Opportunistic screening.

INTERNAL & EXTERNAL FACTORS FOR OPMD'S:

Cancer is a genetic disease where the genetic mutations may be spontaneous or acquired. Acquired mutations are associated with etiological factors that cause DNA damage. These factors are traditionally classified as initiators (inaugurating the genetic event) and promoters (propels the genetic event forward) [7].

Tobacco (Smoking and Smokeless):

Tobacco use is the single most important preventable risk factor for cancer[8].
Smoking tobacco includes products like bidi, manufactured cigarette, hand-rolled cigarette, pipe, cigar, hukkah, water-pipe, chutta, dhumti and chillum. Studies consistently show a dose response relationship with increased incidence of OSCC related to frequency and duration of smoking. Smokeless tobacco is available courtesy products like betel quid with tobacco, khaini, gutka and these are consumed by chewing. Other smokeless tobacco products, such as mishri, gul, bajjar and gudakhu, are applied to teeth and gums while snuff is inhaled. In India, prevalence of the use of smokeless tobacco is much higher (21.4%) than that of tobacco smoking (10.7%) [1].

Most smokeless tobacco products consumed in Indian sub continent are unregulated such as Paan (mixture of betel leaf, lime, tobacco, catechu, areca nut); Zarda (powdered tobacco and slaked lime that is rubbed on gums) seems to account for the predominance of buccal and gingival carcinoma in India [9].

Smokeless tobacco exhibits different risk for different brands and preparations. This is attributable to presence/absence of additives, flavoring agents, modifiers, etc that enhance the carcinogenic

potential[3].

Even non tobacco containing chewable products like Pan masala containing areca is considered a risk as, recently, Areca has been upgraded to a **Group 1 carcinogen.** There is sufficient evidence in humans for the carcinogenicity of betel quid without added tobacco as it can cause cancers of the oral cavity [10].

Any history of tobacco or areca use, past/ present must be viewed as a potential risk for OPMD and OSCC[8].

Alcohol:

Alcohol is a well recognized promoter of carcinogenesis in OSCC. Ethanol potentiates the effect of tobacco. The effect is addictive and multiplicative in heavy drinkers. Dehydration effect of alcohol renders mucosa vulnerable to carcinogens in tobacco[11].

Ethanol is oxidized to acetaldehyde. Acetaldehyde associated with the consumption of alcoholic beverages is carcinogenic to humans (Group 1 carcinogen) [12].

Human Papilloma Virus (HPV):

HPV is a epitheliotropic DNA virus with two varieties: High risk (HPV type 16 and 18) and Low risk. High risk HPV is associated with oro-pharyngeal and base of tongue OSCC especially in non-smokers and nondrinkers and young individuals[13].

Few population studies are suggesting that possible change in sexual practices, multiple oral sex partners may predispose to HPV associated OSCC [13, 14].

WHO (2017) Head and Neck Tumor book has reclassified OSCC based on HPV etiology adding HPV associated OSCC and Oro pharyngeal squamous cell carcinoma[15].

Genetic Susceptibility:

It is well known that only a fraction of smokers and drinkers develop OSCC. Incidence of OSCC in patients below 40 years with no tobacco/ alcohol use has been increasing in recent years and may be attributed to genetic susceptibility. Individuals with underlying defects in key genes/ molecules that maintain homeostasis are predisposed to develop OSCC when exposed to initiating and promoting agents. Inherently deficient functions in DNA repair; Cell cycle regulation; Apoptosis; Immune surveillance may predispose to OSCC [16].

Also, mitochondrial DNA appears to be a source of maternal genetic susceptibility for Tongue OSCC [17].

Chronic Mechanical Irritation:

The usual example of sharp tooth as a risk factor appears to have come back to prominence as a factor that predisposes to OSCC due to persistent chronic inflammation[18].

OPMD- CLINICAL SPECTRUM:

Clinically visible pre cancerous mucosal changes are frequently observed at sites of future tumor presentation. Similar appearing lesions are found surrounding the periphery of actual tumor for a few millimeters. So, clinically visible pre cancerous lesions demonstrate a risk for cancer development. These recognized mucosal lesions are usually described as Leukoplakia, Erythroplakia, or erythro-leukoplakia. Whether any of the above mentioned lesions harbor potential for progression to OSCC is indicated only by histopathology which is the gold standard for diagnosis [4].

Leukoplakia

The old dictum, all Leukoplakic lesions are white, but all white lesions are NOT Leukoplakia is a useful guide in recognizing Leukoplakia. Leukoplakia is white non-scrapable mucosal patch or plaque that cannot be attributed clinically to any other diagnosable condition".

Lesion which is diagnostically ambiguous strictly on clinical grounds can be designated as Leukoplakia. If a dentist is able to recognize a white lesion as specific definable white lesions, such as Linea Alba, Frictional keratosis, Morsicatio

buccorum, Leukoedema, Lichen planus, etc then the term Leukoplakia *cannot* be used.

A white non scrapable lesion on cancer prone sites where there is no obvious or identifiable source of friction is classic example of Leukoplakia. In patients with known history of exposure to carcinogen, a clinically indeterminate white lesion irrespective of location may be regarded as Leukoplakia[5].

Thus the designation Leukoplakia is reserved for use as an exclusively provisional diagnosis than a definitive diagnosis.

Leukoplakia- Clinical types:

Leukoplakia is clinically classified as Homogenous and Non- homogenous (Ulcerated, Nodular, Verrucous variants) that commonly occur in the site of buccal mucosa, alveolar mucosa, floor of mouth, tongue, lips and palate [5].

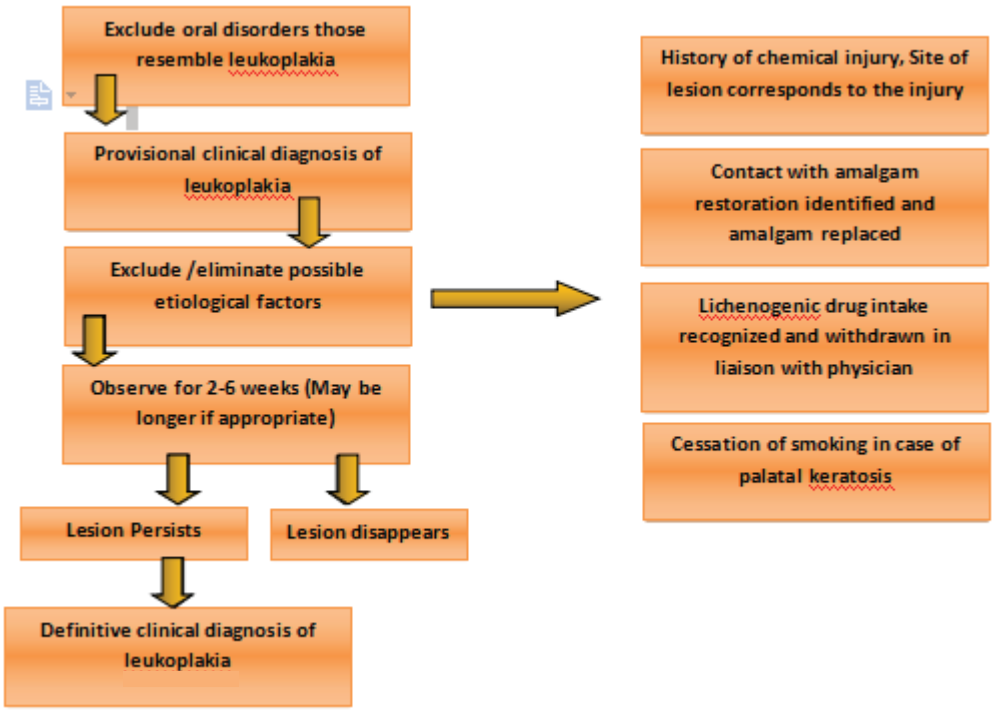
High Risk Group [19]

- All non-homogenous leukoplakias.
- Homogenous leukoplakia more than $2cm^2$ in size.
- Homogeneous leukoplakia on the floor of the mouth, the soft palate or the tongue regardless of size.
- Homogeneous leukoplakia regardless of size in a patient without any known risk factors ("idiopathic" leukoplakia).
- Homogeneous leukoplakia involving multiple sites.
- Leukoplakia of any size in immuno-compromised patient.

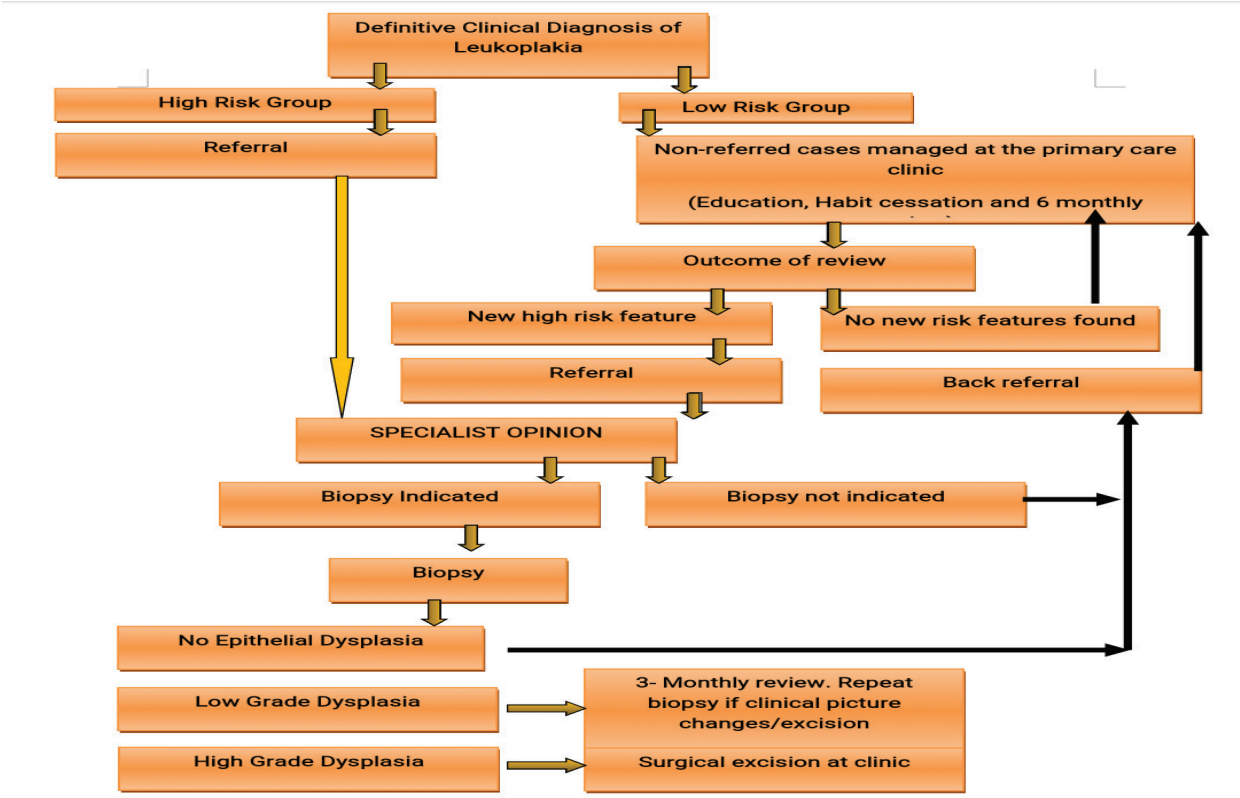
Low Risk Group [19] **:**

Homogeneous leukoplakia less than $2cm^2$ in size on the buccal mucosa, commisure and lips in a patient with known risk factors.

Flow chart for the clinical diagnosis of leukoplakia [19]



Flow chart for the management of leukoplakia [19]



After representative biopsy and histopathological examination, the clinical diagnosis of Leukoplakia MUST be replaced with a definitive histopathological diagnosis. There can never be an h/p diagnosis of Leukoplakia. The following h/p diagnosis is possible [3]:

- Benign hyperkeratosis (most common)
- Epithelial dysplasia
- Squamous cell carcinoma.

Recently it was recommended that a two tiered binary system for classifying dysplasia can be followed (LOW GRADE and HIGH GRADE) in the place of mild, moderate, severe dysplasia. Such a classification is useful for the dentist to draw a more meaningful, patient centric, treatment plan as well as follow up plan [20].

Irrespective of grade of dysplasia, the h/p diagnosis should alert the dentist there is a recognised risk and so clinical vigilance and follow up is mandatory. Even a low grade dysplasia can transform to malignancy over a period of time [3].

OPPORTUNISTIC SCREENING:

In OPMD, the epithelial tissue acquires ***genotypic alteration long before it is visible clinically*** as a mucosal abnormality. So the mucosa appears ***deceptively clinically normal***. This is a great limitation of standard oral examination. The biology of this process itself likely attributes to the dentist's failure to identify suspicious lesions as early as possible[3].

This need for earlier detection has fuelled the demand for Oppurtunistic screening. The dentist must grab every opportunity to evaluate the oral cavity for OPMD's when patient comes for any of the dental needs [21]. It is cost effective, and does not require special time, place, event planning or preparation of the patient. It can be done in a regular dental practice setting solely by one provider itself, irrespective of the speciality. There is implied consent by the patient and hence less apprehension in screening process [22]. It is useful in all three levels of prevention.

Primary Prevention: Oppurtunistic screening can be done for every patient irrespective of presence of habits. If relevant, the dentist must identify the

patient with habit of tobacco and alcohol usage. It is essential to educate about life style modifications and counsel on good hygiene and nutrition. For those patients needing help in quitting the habits the dentist can refer them to tobacco cessation centers.

Secondary Prevention: It is not always easy for patients to change habits or lifestyle. For those patients with habits, screening should be done at defined intervals for pre symptomatic disease. The assessment for risk is based on life style information and the follow up frequency can be decided accordingly[23]. Also the defined high risk population should be screened for HPV[24].

Tertiary Prevention: Patients treated for OSCC will still have dental needs (caries prevention, xerostomia, mucositis, prosthodontic rehabilitation). During every visit, the patient can be evaluated for any suspicious mucosal changes for recurrence of OSCC[23].

CONCLUSION:

It is vital that general dentists who serve as the gatekeepers of the oral cavity understand the disease and recognize the clinical features of OPMD's and OSCC[3]. More importantly, there is a need to acknowledge and seek professional opinion from Oral Physicians and Oral Pathologists in case of ambiguity in diagnosis of mucosal lesions.

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CONFLICTS OF INTEREST:

There are no conflicts of interest.

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