Consensus guidelines on management of oral potentially malignant disorders

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Abstract

Oral cancer is usually preceded by oral potentially malignant disorders (OPMDs) and early detection can downstage the disease. The majority of OPMDs are asymptomatic in early stages and can be detected on routine oral examination. Though only a proportion of OPMDs may transform to oral squamous cell carcinoma (OSCC), they may serve as a surrogate clinical lesion to identify individuals at risk of developing OSCC. Currently, there is a scarcity of scientific evidence on specific interventions and management of OPMDs and there is no consensus regarding their management. A consensus meeting with a panel of experts was convened to frame guidelines for clinical practices and recommendations for management strategies for OPMDs. A review of literature from medical databases was conducted to provide the best possible evidence and provide recommendations in management of OPMDs.

Keywords:
Consensus, management, oral leukoplakia, oral lichen planus, oral potentially malignant disorders, oral submucous fibrosis

Introduction

The term oral potentially malignant disorder (OPMD) describes clinically detected oral mucosal conditions that carry an increased risk of progressing to cancer. Cancers of the lip, oral cavity, and oropharynx are among one of the most common cancers, with approximately 400,000 incident cases globally. Oral cancer has a particularly predilection in South Central Asia due to exposure to high-risk factors. In India, cancer of lip and oral cavity is rated second most among males and fifth in females. According to Globocan 2020, the incidence rate and the mortality rate was 10.3% and 5.4 per 100,000 population,
respectively. The estimated age standardized 5-year prevalence rate was 19.59%.[4]

Oral leukoplakia, erythroplakia, oral submucous fibrosis (OSMF), and oral lichen planus (OLP) among other potentially malignant disorders has risk for transition to oral squamous cell carcinoma (OSCC). Moreover, though the lesion per-se may not transform to OSCC, it may serve as a surrogate clinical lesion to identify individuals at risk of developing OSCC.[5] The majority of these disorders may be asymptomatic in the early stages of their evolution which can be detected on routine oral examination. It is therefore essential that the primary health professionals should be trained to identify OPMDs, advise further investigations and make necessary referrals to specialists for the treatment.[6]

Currently, there is a scarcity of scientific evidence on specific interventions and management of OPMDs. So far, there exists no consensus regarding their management, outcome, and follow-up. Consensus meet was held during Annual symposium, Cochin on November 8, 2019, with peer group under supervision and guidance of Dr. Moni Abraham Kuriakose. A consensus meeting with a panel of experts was convened to frame guidelines for clinical practices and recommendations for management strategies of OPMDs. The panel of experts involved members of the Oral Cancer task force, Indian Dental Association members and faculties who are experts in the field of medicine, who have carried out extensive research related to OPMDs. The brochure for CanQuer Annual symposium 2019 was circulated among the experts in head and neck oncology. All members who expressed their interest in the symposium contributed to the document. The guidelines were formulated based on an extensive literature search to avail the current shreds of evidence. All the available treatment options have been considered and the guidelines were developed based on the available clinical resources and stratified as essential, optimal, and optional based on the available resources in India.

Methodology

A systematic literature search was conducted for studies/articles in the electronic databases PubMed, Medline, Scopus, and The Cochrane Library. Current guidelines, meta-analyses, cross-sectional studies, systematic reviews, randomized controlled trials, and key cited articles were included. The articles related to the management of OPMDs namely oral leukoplakia, OSMF, and oral lichen were critically evaluated by a group of reviewers. Search terms were selected from Medical Subject Headings and included “oral leukoplakia,” “oral submucous fibrosis,” “oral lichen planus,” their synonyms, “precancerous lesion,” “and precancerous condition,” “management,” and “Malignant transformation.” The aforementioned terms were combined using the Boolean operators “AND,” “OR.” There were no restrictions with regard to the time of publication. The unpublished data and full text that are not available were excluded. Flow diagram depicted in Figure 1 shows the number of articles retrieved and selected.

The potential evidence base for the recommendations for management of OPMD suitable for Indian scenarios was developed. The consensus group meeting was held to frame the guidelines for the current practices and recommendation for management strategies for OPMDs from the existing literature. The OPMD consensus group consists of experts from oncology, oral medicine, oral pathology, head and neck surgery, and community oncology disciplines. Recommendations for each disorder and overall recommendations were discussed thoroughly and arrived at a consensus by all the participating panel members. In the case of little or no evidence, the participants discussed and proposed clinically applicable management strategies.

The Delphi technique was used to frame the guidelines, based on the discussion by the group of experts to arrive at the consensus. The initial draft was circulated to the experts for review. Experts across the country reviewed the draft remotely; they added their comments and provided their valuable input. All the comments and information were compiled and recirculated for review. This process was continued until all the experts reached a general consensus and agreed upon all the recommendations. The guidelines have been formulated based on the latest available literature till the time the guidelines...
Key Message

The consensus provides the guidelines for clinical practices in management of most common OPMDs such as oral leukoplakia, oral submucous fibrosis and oral lichen planus. The recommendation strategies aid in providing the best patient care in Indian scenarios.

were prepared. The recommendation was then resource stratified as Essential, Optimal, and Optional for clinical adaptability. Essential would be considered as those treatments that at least should be provided and may not include the standard of care. Optimal is considered as the standard of care therapy and Optional include other standards of care options, which may be considered ideal; however, they may be unaffordable to the section of the society. The evidence levels are grouped in four levels (I–IV), as shown in Table 1.[7] (Prabhash K, et al. Indian clinical practice consensus guidelines for the management of squamous cell carcinoma of head and neck).

This manuscript is a summary of the discussion and report of the guidelines in management of oral leukoplakia, OSMF, and Oral lichen planus.

Oral leukoplakia

The term leukoplakia should be used to recognize “predominantly white plaques of questionable risk having excluded other known diseases or disorders that carry increased risk for OSCC.”[8] Two main clinical types of leukoplakia are recognized, being homogeneous and nonhomogeneous leukoplakia [Figure 2a, 2b]. The distinction is based on surface color and morphological (thickness and texture) characteristics.[6] One form of leukoplakia may transform into other depending on habit cessation or continuation and natural history.

Natural history

The natural history of oral leukoplakia is broadly associated with exposure of risk factors and duration. Lifestyle risk factors include history of tobacco use (smokeless/smoking), the mixture of tobacco and areca nut use, history of alcohol use (considered as an independent or synergistic risk factor). The lesion may be asymptomatic or symptomatic with a history of burning sensation, soreness, tingling sensation, and occasional pain.[9-12]

The parameters to be observed during a clinical examination include the site, size, number, shape, surface and surrounding mucosa, extensions, texture, stretch/retract oral mucosa, scrapability, and cervical lymph node examination.[10-11] The nonhomogeneous lesion more than 2 cm size, lesion colonized with candida, presence of epithelial dysplasia, subsites of tongue, and floor of the mouth have an increased risk for malignant transformation.[8-10] Proliferative verrucous leukoplakia (PVL) has predominant white papillary projections, multifocal, more aggressive proliferation and has a high risk for malignant transformation rate (60–100%), and reports show high recurrence rate (86.7%) even after surgical removal.[11,12] A deeper tissue biopsy is required to assess the histological changes in PVL.

The overall malignant transformation rate of oral leukoplakia varies from 0.13 to 34%.[14] The clinical risk profiling for malignant transformation is depicted in Table 2.[9,10] The low-risk OPMDs are arbitrarily defined as those with less than 5% lifetime risk and high risk as those with more than 5% lifetime risk for

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<tr>
<th>Table 1: Evidence levels</th>
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<td><strong>Evidence level</strong></td>
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<tr>
<td>I</td>
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<td>III</td>
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<td>IV</td>
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<tr>
<th>Table 2: Clinical risk profiling for malignant transformation of Leukoplakia[9,14]</th>
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<tbody>
<tr>
<td><strong>Low risk</strong></td>
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<tr>
<td>Lesion size &lt;200 mm²</td>
</tr>
<tr>
<td>Homogeneous clinical appearance</td>
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<tr>
<td>Lesion size &gt;200 mm²</td>
</tr>
<tr>
<td>Individuals aged &gt;40 years</td>
</tr>
<tr>
<td>Female gender (Nonhabitual)</td>
</tr>
<tr>
<td>Family history of cancer</td>
</tr>
<tr>
<td>Presence of invasive Candida albicans</td>
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<tr>
<td>Long duration of leukoplakia</td>
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<td>Leukoplakia in nonsmokers (idiopathic leukoplakia)</td>
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malignant transformation. High-grade dysplasia was associated with a 2.78-fold (95% Confidence Interval [CI]: 1.44-5.38; \( P = 0.002 \)) increased risk of transition, as compared with low-grade dysplasia. The 5% cut off was used as a threshold at which in general active clinical intervention is considered. Studies have shown an approximate difference of 18–21% in malignant transformation between low- and high-grade dysplastic lesions.

The other suspicious features of OSCC include unhealed ulcer or erosion that lasts more than 3 weeks even after removal of the cause. The presence of palpable cervical lymph nodes increases the suspicion for OSCC. The diagnosis of leukoplakia is based on the exclusion of other white lesions. All white patches appearing in the oral cavity should not be labeled as oral leukoplakia. Leukoplakia is a nonscrapable white patch, white/red patch, often associated with tobacco, alcohol, or betel quid. Other white patches associated with any chemical or physical causative agents, history of trauma, white patches that can be Scraped off, and cases where the white color fades, on stretching the tissues, are excluded. There are several types of white lesions that are clinically distinguished from other lesions. These lesions need to be excluded in order to diagnose leukoplakia and are described in Table 3.

Indication for biopsy

Biopsy of the lesion is generally indicated for high-risk lesions as shown in Table 2. It is also mandatory to rule out other mucosal conditions masquerading oral leukoplakia and also to assess their malignant transformation risk. Biopsy is indicated in the individuals having the following features:

1. Ulcers or erosions that persists over 3 weeks duration
2. Lesion size >200 mm²
3. Nonhomogeneous appearance
4. Tongue lesions and lesions on floor of the mouth
5. Individuals aged >40 years
6. Female gender
7. Individuals with no known risk habits
8. Palpable cervical lymph nodes
9. Family history of cancer
10. Speckled appearance suggestive of candida infection
11. Leukoplakia of over 2 years duration.

Table 3: Benign disorders that need exclusion to diagnose leukoplakia

<table>
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<tr>
<th>Disorder</th>
<th>Diagnostic features</th>
<th>Recommended investigations</th>
</tr>
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<tbody>
<tr>
<td>White sponge nevus</td>
<td>Noted in early life, family history, large areas involved in oral mucosa</td>
<td>Biopsy not indicated</td>
</tr>
<tr>
<td>Frictional lesion</td>
<td>History of trauma, mostly along the occlusal plane, an etiological cause apparent, mostly reversible on removing the cause</td>
<td>Biopsy if persistent after elimination of cause, particularly in a tobacco user</td>
</tr>
<tr>
<td>Morsicatio buccarum</td>
<td>Habitual cheek - lip biting known, irregular whitish flakes with jagged out line</td>
<td>Biopsy not indicated</td>
</tr>
<tr>
<td>Tobacco pouch keratosis</td>
<td>History of chewing smokeless tobacco, wrinkles at the site of application in mild form/white or leathery lesion</td>
<td>Biopsy indicated</td>
</tr>
<tr>
<td>Chemical injury</td>
<td>Known history, site of lesion corresponds to chemical injury, painful, resolves rapidly</td>
<td>Biopsy not indicated</td>
</tr>
<tr>
<td>Acute pseudomembranous Candidiasis</td>
<td>The membrane can be wiped off leaving an erythematosum/raw surface</td>
<td>Swab for culture</td>
</tr>
<tr>
<td>Leukoedema</td>
<td>Bilateral on buccal mucosa, could be made to disappear on stretching (retracting)</td>
<td>Biopsy not indicated</td>
</tr>
<tr>
<td>Hairy leukoplakia</td>
<td>Bilateral tongue leukoplakic lesions</td>
<td>Not indicated in an identified HIV infected patient; otherwise a biopsy should be considered Specific histopathology with koilocytosis; EBV demonstrable on in situ hybridization</td>
</tr>
<tr>
<td>Smokers’ palate (“Nicotine stomatitis”)</td>
<td>Smoking history, grayish white palate</td>
<td>Biopsy not indicated</td>
</tr>
<tr>
<td>Oral lichen planus</td>
<td>Bilateral, Wickham’s striae</td>
<td>Biopsy indicated</td>
</tr>
</tbody>
</table>

EBV=Ebstein-Barr Virus
Type and site of biopsy

The purpose of a biopsy is to diagnose and characterize the lesions. Therefore, incision biopsy is generally recommended with the exceptions as noted below.

1. Incisional biopsy may be performed from the most suspicious areas of the lesion such as redness, an area of surface thickening or a symptomatic area, and need not extend to involve the healthy tissue, for the pathologist to make a correct report.
2. For multifocal or widespread leukoplakia, multiple biopsies may be required (field mapping).
3. For non-homogeneous leukoplakia, incisional biopsy may not be representative; therefore, multiple biopsies may be carried out.
4. For small leukoplakias less than 2 cm, excisional biopsy may be considered; however, the surgical team that undertakes the biopsy should have the competence to perform further surgery should it be required based on the biopsy report (high-grade dysplasia or invasive carcinoma).

Reporting of OPMD and criteria for grading of dysplasia

Characterization of the grade of dysplasia is the primary goal of histopathology [Figure 3a, b, c, d]. To lower interobserver variability as well as for clinical applicability, Kujan et al.[19] has developed a binary system to categorize epithelial dysplasia into low risk or high risk. Low risk includes lesions graded as nondysplastic or showing mild dysplasia and moderate epithelial dysplasia with three or less architectural criteria or four or less cytological criteria. On the other hand, high risk includes all lesions graded as severe dysplasia or carcinoma in situ and moderate epithelial dysplasia with four or more architectural criteria or five or more cytological criteria.[20,21] To minimize subjectivity, WHO has recommended cellular and architectural criteria for dysplasia [Table 4]. The study by Speight et al.[1] used a protocol to substantially increase the diagnostic agreement between the pathologists. The first review agreement between the two pathologists was 69.9%, with the kappa of 0.25–0.7. After the adjudication review of the third pathologist an additional 22.8% improvement was observed. In addition, the expression of S100A7, Loss of Heterozygosity (LOH), podoplanin, DNA content, Ploidy, and p16 methylation are the predictive molecular markers for malignant transformation.[22]

Management

Management strategies for patients with leukoplakia fall into three categories: close observation, surgical removal and ablation, and medical therapies.[22] The decision should be considered based on the risk assessment of malignant transformation and effectiveness of intervention.[23] Recommendation for management of low-risk leukoplakia and high-risk leukoplakia is stratified as Essential, Optional, and Optional and is provided in Tables 5 and 6 respectively. The Supplementary tables [S5(a) and S6(a)] describe the salient information and Supplementary tables [S6(b), S6(c)] discusses the summary of clinical evidence in pharmacological and nonpharmacological management of leukoplakia, respectively. Surgical treatment for oral leukoplakia has not been assessed in a Randomized controlled Trial (RCT).

Histopathologically, erythroplakia most commonly shows at least some degree of dysplasia and

![Figure 3: (a) The photomicrograph shows basal cell crowding and hyperchromatism at lower third of the epithelium suggestive of mild dysplasia. (b) Irregular epithelial stratification and loss of epithelial cell cohesion, extending up to middle third of the epithelium suggestive of moderate dysplasia. (c) Severe epithelial dysplasia involving alterations in the entire epithelial thickness. (d) The dysplastic epithelial cells extend from the basal layer to the surface of the mucosa suggestive of carcinoma in situ. (10X magnification; H&E stained)]](image)
often-even carcinoma \textit{in situ} or invasive carcinoma. Surgery, either by cold knife or by laser, is the recommended treatment modality.\cite{9,24,25} Oral cancer requires an immediate referral to a tertiary care center.

\textit{Guidelines for surveillance}$^{26-30}$

Regular follow-up is required irrespective of any treatment modalities. A general recommendation is to re-examine the OPMD and full mouth irrespective of surgical excision every 3 months for the first year. If the lesion does not relapse or change in reaction pattern, the follow-up intervals may be extended to once every 6 months. New biopsies should be taken if new clinical features emerge. Following 5 years of no relapse, education of patients for self-mouth examination is recommended. At the first time of diagnosis, the low-risk subjects would be scheduled for follow-up after 5 years.

\textbf{Oral submucous fibrosis}

OSMF is described as a chronic insidious fibrotic disorder that progresses over time and involves the entire oral mucosa. Areca nut is known to be the major risk factor among people who probably have a genetic predisposition to the disease. It is predominantly seen in South and South-East Asia. Nigam \textit{et al.}\cite{29} in 2014 noted a prevalence of 6.42%. Mello \textit{et al.}\cite{30} in a literature review noted a prevalence of 4.96% in the year 2018.

\textbf{Evaluation and Management of OSMF}

The most objective assessors of outcome include interincisal mouth opening and severity of burning sensation as rated on a Visual Analogue Scale. Measures of improvement in quality of life need to be included.\cite{31}

\textbf{Clinical criteria} – The clinical presentation [Figure 4a, b] depends on the stage of the disease. Flowchart summary of the clinical features is depicted in the Figure 5.

\textbf{Grading of OSMF}$^{31}$ – Various grading classification systems have been documented in medical literature by various authors in the past. The most suggested

\begin{table}[h]
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\begin{tabular}{|l|l|l|}
\hline
\textbf{Essential treatment} & \textbf{Optimal treatment} & \textbf{Optional treatment} \\
\hline
Betel quid/areca nut use, Tobacco, alcohol cessation Counselling & Betel quid/areca nut use, Tobacco, alcohol cessation Counselling & Betel quid/areca nut use, alcohol cessation Counselling \\
Dietary modulation – daily consumption of green leafy vegetables (75 gm daily) and seasonal fruits like mango, guava, papaya & Capsule of Curcumin extract 600 mg (3 capsules two times daily) for 6 months & Cytology \\
Topical antifungal - Clotrimazole 1% for 7 days for red and white leukoplakia & Regular surveillance & Electrocauterization \\
Topical Vitamin A application 25,000 IU twice daily for 90 days & & \\
Referral mapping - Designated referral center for patient management & & \\
Regular surveillance & & \\
\hline
\end{tabular}
\caption{Recommendations for management of low-risk leukoplakia}
\end{table}

\begin{table}[h]
\centering
\begin{tabular}{|l|l|l|}
\hline
\textbf{Essential treatment} & \textbf{Optimal treatment} & \textbf{Optional treatment} \\
\hline
Betel quid/areca nut use, tobacco, alcohol cessation counselling & Betel quid/areca nut use, tobacco, alcohol cessation counselling & Betel quid/areca nut use, tobacco, alcohol cessation counselling \\
Dietary modulation – daily consumption of green leafy vegetables (75 gm daily) and seasonal fruits like mango, guava, papaya & Dietary modulation – daily consumption of green leafy vegetables (75 gm daily) and seasonal fruits like mango, guava, papaya & \\
Biopsy & Biopsy & \\
If biopsy shows & If biopsy shows & \\
Moderate/Severe epithelial dysplasia or carcinoma \textit{in situ} & Moderate/Severe epithelial dysplasia or carcinoma \textit{in situ} & \\
Conventional surgical excision with or without grafting & Conventional surgical excision with or without grafting & \\
For larger homogeneous lesions (>4 cm) - wait and watch through rigid surveillance & For larger homogeneous lesions (>4 cm) - wait and watch through rigid surveillance & Photodynamic therapy - Aminolevulenic acid (10%, 20%) twice a week for 3 months \\
Regular surveillance & Regular surveillance & Regular surveillance \\
\hline
\end{tabular}
\caption{Recommendations for management of high-risk Leukoplakia}
\end{table}
grading system that can be routinely used in the clinical practice and help in early diagnosis and treatment:

Grade 1 – Mild: Any features of the disease triad for OSMF (burning, depapillation, blanching or leathery mucosa) with vesicles and increased salivation may be reported – and interincisal opening >35 mm

Grade 2 – Moderate: Above features of OSMF + interincisal limitation of opening 20–35 mm

Grade 3 – Severe: Above features of OSMF, decreased salivation, and sticky mucous saliva + interincisal opening <20 mm

Grade 4A – OSMF + other potentially malignant disorder on clinical examination

Grade 4B – OSMF with any grade of oral epithelial dysplasia on biopsy

Grade 5 – OSMF + oral squamous cell carcinoma.

**Indication for biopsy**

Grades 1, 2, and 3 can be diagnosed on clinical basis alone. Biopsy is indicated for Grade 4 - OSMF with any other OPMD, presence of growth superimposed on OSMF, and presence of ulcer lasting more than 3 weeks, after removal of definitive etiology (e.g., Sharp tooth). Biopsy can be combined with immunohistochemistry to evaluate expression of CD34 and CD105 to detect neoangiogenesis. [32]

**Synoptic reporting of OSMF, criteria for grades of dysplasia in OSMF**

The current reporting of dysplasia follows the WHO criteria of mild epithelial dysplasia, moderate epithelial dysplasia, and severe epithelial dysplasia. However, in view of the epithelial atrophy in OSMF, the difficulty in assessing thirds of epithelium to provide the above-mentioned grades of dysplasia has been highlighted. [33] Thus, adapting the binary classification would lend greater objectivity to grading of dysplasia in OSMF. The binary system categorizes epithelial dysplasia into low risk or high risk. [18] Epithelial dysplasia with three or less architectural criteria or four or less cytological criteria is considered as low risk. High risk involves epithelial dysplasia with four or more architectural criteria or five or more cytological criteria. [34]

The synoptic reporting of OSMF is similar to leukoplakia.

**Management**

The malignant transformation rate for OSMF has been reported to be between 7% and 30%. [35] However, oral squamous cell carcinomas associated with a OSMF are associated with good clinicopathological profile and have better prognosis and oncological outcomes. [36] Currently used treatment modalities for management of OSMF include: Nutrients and antioxidants (Vitamin A, B complex), minerals (Fe, Zn, Mg), lycopene, enzymes (collagenase, hyaluronidase, chymotrypsin), immune modulation (betamethasone, triamcinolone acetonide, dexamethasone, hydrocortisone, IFN-γ, levamisole), promotion of blood flow (pentoxifylline, nylindrin hydrochloride, buflomedil hydrochloride, isoxsuprine), anti-inflammatory (curcumin, aloe vera). The quality of these studies has been described as being “very low” with significant limitations. [31] Surgical interventions are generally reserved for more advanced cases of OSMF. Surgical excision of bands includes cold knife excision, CO₂, KTP-532, diode laser, and subsequent reconstruction with tissue flaps. Surgical techniques achieve good mouth opening, but average shrinkage of about 5 mm has been noticed in patients in the late postoperative period. [31]

The lack of reliable evidence for the effectiveness of any specific interventions for the management of OSMF is illustrated by the paucity of trials. None of these treatments have reached general acceptance and the long-term results are dubious. [12,33] Management of limitation of mouth opening is given in Tables 7 and 8, resource stratified as Essential, Optimal, and Optional. Supplementary tables [S7(a) and S8(a)]
provide the salient information of Essential, Optimal, and Optional recommended management of OSMF. The summary of current evidence in the management of OSMF is in Supplementary table S8(b).

Management of dysplasia
Low-grade dysplasia involves continued follow-up once in 3 months for the first year, and once in 6 months in case of no increase in size/change in appearance. High-grade dysplasia requires surgical excision or when the clinical signs of malignant transformation are noticed in a white/red lesion. It requires continued follow-up once in 3 months for the first year, and once in 6 months in case of no relapse. Counseling for tobacco, alcohol, and areca nut cessation and dietary modulation of using green leafy vegetables and fruits are the same as in Leukoplakia.

Surveillance
Regular follow-up is required irrespective of any treatment modalities and the final recommendation from the meeting is as per Tables 7 and 8.

Oral lichen planus
OLP is an inflammatory disorder of the skin and mucous membranes with no known cause. Malignant transformation of OLP per year ranges between 0.04 and 1.74%. The etiology of OLP is not known. The current evidence suggests the role of cell-mediated immune response with T-lymphocyte cytotoxicity directed against antigens expressed by the basal cell layer. Other factors include stress, Hepatitis C virus infection, particularly in endemic regions. Oral lichenoid reactions (OLR) are considered the variant of OLP caused by dental restorative materials and several drugs. The restorative materials such as amalgam, composite, gold, acrylic; and drugs such as nonsteroidal anti-inflammatory agents, sulfonylureas, beta-blockers, oral hypoglycaemic agents, dapsone, penicillamine have been reported to cause (OLR). Oral lichenoid lesions (OLL) are associated with tobacco chewers; the causative role of tobacco in OLP is unknown. Krutchkoff and Eisenberg reported lesions showing lichenoid features with epithelial dysplasia is a distinct histopathological entity termed as Lichenoid Dysplasia (LD) that mimics clinically and histologically OLP. They postulated that OLP cases evolve to malignancy are linked with LD. The presence of dysplasia in OLP and OLL may indicate malignant potential.

Clinical criteria
OLP may contain both red and white elements and provide, together with the different textures, the basis for the clinical classification of this disorder. The white and red components of the lesion can be a part of various clinical types. The reticular form of OLP is characterized by fine white lines or striae [Figure 6(a)]. The striae may form a network but can also show annular (circular) patterns. The striae often display a peripheral erythematous zone, which reflects a subepithelial inflammation [Figure 6(b)]. The papular type is clinically characterized by small white dots, which in most occasions intermingle with the reticular form. Plaque-type OLP shows a homogeneous well-demarcated white plaque that occurs in conjunction with striae. The bullous form is very unusual but may appear as bullous eruptions surrounded by a reticular network. Erythematous (atrophic) OLP is characterized by a homogeneous red area. This form of lesion may occur without any white papules or striae. On gingivae erythematous, OLP presents as desquamative gingivitis. In ulcerative type, fibrin-coated ulcers are surrounded by an erythematous zone with white striae in the periphery.

Diagnosis
Clinical diagnosis includes oral biopsy with histopathological evaluation. It is important that a biopsy be performed to confirm a diagnosis.

Table 7: Recommended treatment modality for management of OSMF Grade 1, 2 (mouth opening >20 mm)

<table>
<thead>
<tr>
<th>Essential</th>
<th>Optimal</th>
<th>Optional</th>
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<tr>
<td>Cessation of habit and Physiotherapy</td>
<td>Nutritional supplements</td>
<td>Clostridium collagenase</td>
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<td></td>
<td>Antioxidants</td>
<td>Imatinib</td>
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<tr>
<td></td>
<td>Temporal muscle myotomy</td>
<td>Microwave diathermy, ultrasounds</td>
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<tr>
<td></td>
<td>Intralonesion injection of hyaluronidase 1500 IU twice weekly for 5 weeks</td>
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The indication and determination of biopsy site is governed by the extensiveness OLP with erosive areas, recalcitrant lesions, and symptomatic areas. Often, the second distinct specimen obtained are subjected to direct immunofluorescent testing.

**Management**

No therapy for OLP is completely curative; the goal of treatment for symptomatic patients is palliation. Patients with OLP are carriers of a disease with systemic implications and may need the care of a multidisciplinary team. The correct diagnosis of any pathology is critical to make treatment effective and minimize iatrogenic harm. The primary goal of treatment of symptomatic OLP is the reduction, and preferably elimination of pain associated with the lesions and to reduce the frequency of symptomatic episodes. Topical corticosteroids including betamethasone, clobetasol, dexamethasone, and triamcinolone; calcineurin inhibitors such as pimecrolimus, tacrolimus, or cyclosporin; retinoids such as tretinoin; photochemotherapy and newer traditional medicine have been reported in the treatment of symptomatic OLP. Currently, there is insufficient evidence to support the effectiveness of any specific treatment as being superior.

Recommendation for management of nondysplastic OLP have been considered and resource stratified as Essential, Optimal, and Optional in Table 9. Salient information of Essential, Optimal, and Optional recommended management of oral lichen planus are given in Supplementary tables [S9(a)]. Supplementary tables [S9(b) and S9(c)] describe the summary of clinical evidences in pharmacological and nonpharmacological management of OLP, respectively.

OLP with dysplasia is treated similarly as dysplastic lesions mentioned earlier (similar to leukoplakia with dysplasia). Topical triamcinolone acetonide 0.1% or topical clobetasol propionate 0.05% in orabase (2–3 times/day/3 weeks followed by tapering during the following 9 weeks until a maintenance dose of 2 to 3 times/week) is considered as an essential treatment to reduce pain and inflammation.

**Surveillance**

Erosive and ulcerative (Symptomatic) OLP should undergo regular follow-up of up to 3 times a year. OLP with dysplasia should be examined more frequently, every 2–3 months, whereas the reticular type (asymptomatic) may be assessed annually. In case of any evidence of change in clinical appearance, increase in burning sensation/pain, the follow-up period should be shortened and biopsy should be provided.

**Conclusion**

The consensus guidelines can be a road map for clinical practitioners for managing OPMDs, and these guidelines can aid in providing the best patient care. Since no uniform practices exist in management, the expert panel drafted guidelines for their management and stratified them as Essential, Optimal, and Optional in the management of oral leukoplaikia, OSMF, and oral lichen planus. This paper presents an updated report based on the current evidences and recommendation strategies in the management of OPMDs following discussion by an expert group.

| Table 8: Recommended treatment modality for Grade 3 OSMF (mouth opening <20 mm) |
|-----------------------------|-----------------------------|-----------------------------|
| Essential | Optimal | Optional |
| Cessation of habit | Surgical treatment - Excision of fibrous bands | Reconstruction with tissue flaps |
| Physiotherapy | Temporal muscle myotomy | Coronoidectomy |

| Table 9: Recommendation for management of nondysplastic OLP |
|----------------|----------------|----------------|
| MANAGEMENT OF NONDYSPLASTIC OLP |
| Essential Treatment | Optimal Treatment | Optional Treatment |
| Psychometric evaluation and counselling | Oral swish and spit- Tab Betamethasone 0.5 mg in 10 mL water, 3 minutes, 4 times daily, 6 weeks | Topical application of cyclosporine, topical tacrolimus 0.1%, and topical retinoid acid (0.05%) in oral base |
| Topical triamcinolone acetonide 0.1% thrice daily for 2 weeks (monitor for symptoms alleviation) | Topical application of cyclosporine, topical tacrolimus 0.1%, and topical retinoid acid (0.05%) in oral base | Low-level laser therapy - 630-980 nm wavelength, power output - 20-300 mW, and duration - 10 seconds-15 minutes |
| or Clobetasol propionate 0.05% in orabase | Systemic steroids - Tab Prednisolone, 0.50-0.75 mg/kg per day for less than 10 days without tapering | Photodynamic therapy with aminolaevulinic acid (10%, 20%) once/twice a week, 2-10 minutes, 1-8 sessions |
| 2-3 times/day/3 weeks | 8 mg intralesional triamcinolone acetonide or 1.4 mg intralesional betamethasone, once a week for 2 weeks | PUYA (psoralen and ultraviolet A radiation) therapy |
| | | Oral administration of 0.6 mg/kg 8-methoxypsoralen followed by long-wave ultraviolet light irradiation |
| | The therapy is given 12 times at intervals of 2-3 days | |
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Financial support and sponsorship
Biocon Foundation.

Conflicts of interest
There are no conflicts of interest.

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