Is oral lichen planus a potentially malignant disorder?: A critical appraisal; a commentary on the letter to the editor

Dear Editor,

This letter is with reference to the article titled 'Is oral lichen planus a potentially malignant disorder?: A critical appraisal' that recently appeared in JOMFP.[1] Oral lichen planus (OLP) is a common condition. Review articles have suggested a varied prevalence of OLP-0.5–2.2%, 1–2%, 0.1–4% and 1.27%.[2,3] However, all these articles are dated between 1998 and 2008. The most recent high methodological study published by González–Moles *et al.*, 2021[4] reported the overall malignant transformation of OLP as 2.28%. Other relatively recent studies by González–Moles *et al.*, 2019 and 2020, showed the worldwide prevalence of OLP as 1.01%, with the highest prevalence in Europe (1.43%) and the lowest in India (0.49%).[5] Despite the meticulous design of the studies, there remains a possibility that the population screened for determining the prevalence of OLP are essentially the patients reporting to hospitals or dental clinics and may not represent the entire general population. It is rather obvious that patients report to hospitals or dental clinics only when they are symptomatic. Therefore, it is quite likely that OLP may be underreported as the relatively asymptomatic patients may not report to clinics/hospitals to seek treatment.

Although rightly pointed out in the article by Desai *et al.*,[1,6] that it is rather improbable for the majority of OLP cases to transform into oral squamous cell carcinoma (OSCC); the status of OLP as an oral potentially malignant disorder (OPMD) cannot be entirely dismissed. One of the first studies conducted by Krutchkoff *et al.*, 1978[7] acknowledged that patients with OLP have a higher propensity to develop carcinomas but did not believe there was enough evidence to accept that OLP has the biological potential to progress into cancer. These contradictory views and the perpetual dilemma about the diagnostic criteria of OLP have led to its underdiagnosis. The exclusion of epithelial dysplasia while diagnosing OLP due to restrictive diagnostic criteria, has shown a lower malignant transformation rate, thereby making the result questionable.[8] Epithelial dysplasia being the gold standard histopathological evidence to assess the malignant transformation of OPMDs cannot be excluded from the diagnostic criteria of OLP, as the dysplasia might have been present at the initial presentation of the lesion but missed due to lack of histopathological examination. Therefore, the definitive diagnosis of OLP should be based not only on its clinical features but also on its histopathological features.

Several studies have highlighted the importance of differentiation of OLP and oral lichenoid lesion (OLL) and have designated cases with malignant transformation as OLLs, as they did not meet their diagnostic criteria of OLP.[9] This is perilous as the restrictive diagnostic criteria may often lead to significant underdiagnosis of OLP. The notion is further negated by the results of the review and meta-analysis done by González–Moles *et al.*, 2019,[8] where they did not find any significant difference between the malignant transformation rates of OLL and OLP. It is also important to note that a case of OLP, which may not show dysplastic features during initial examination but shows signs of dysplasia during subsequent follow-ups, cannot be suddenly re-diagnosed as OLL owing to the appearance of dysplasia. This further highlights the rather flawed methodology of the studies that excluded cases of OLP with dysplasia, which certainly underestimates the malignant potential of this lesion. We believe that in such cases, a more appropriate diagnostic term - 'OLP with dysplasia' or 'Dysplastic OLP' may be instated. Therefore, it can be certainly stated that all clinically appearing OLP or OLLs should be biopsied and followed up diligently for the long term as both are predisposed to transforming into OSCC.

A biopsy is especially important in atrophic/erosive OLP as they have a greater propensity to develop into oral cancer, whereas the exclusively reticular OLP does not present, in meta-analytical terms, any increased risk of malignancy.[8] It is however noteworthy, that although rare, even cases of plaque-type OLP have shown transformation into OSCC.[10] In addition, OLP produces a tumour-like microenvironment that potentiates malignant transformation.[11] The red-type OLP progresses to OSCC much faster than white-type OLP as the molecular mechanisms in those sub-types increase their malignant transformation potential significantly more than the other sub-types of OLP.[12-14]

Furthermore, studies have suggested an association between OLP and OSCC in patients with a habit of tobacco or alcohol consumption.[15] The presence of Hepatitis C Virus (HCV) infection also increases the propensity of OLP to transform into OSCC, which is quite frequently associated with OLP cases.[8] Interestingly, studies have further suggested a relationship between *Candida* infection and OLP lesions, revealing increased malignant risk in such cases due to the production of a chronic inflammation state that leads to neoplastic evolution.[15] *Candida* infection could be present at the time of initial diagnosis or develop due to injudicious use of immunosuppressive therapy to treat OLP. Hence, corticosteroids (systemic/topical) should be delivered with caution as they may do more harm than good. OLP can malignise at any age and is more predisposed when localised to the tongue.[8] Thus, long-term follow-up is imperative in patients with OLP to correctly determine their malignant risk.

Detection of malignant molecular markers is a superior identification method to assess the progression of an OPMD into OSCC. Studies have suggested the expression of p53, topo IIα and desmocollin in OLP tissues, suggesting an increased risk of malignancy.[16] A study by Chen *et al.*, 2008[17]reported the expression of matrix metalloproteinases (MMPs), transforming growth factor beta (TGF-β), and tissue inhibitors of metalloproteinases (TIMPs) in OSCC developing from OLP, and the levels were consistent with those detected in atrophic OLP, the form of OLP, which possesses the greatest risk of malignant transformation. These further assert that OLP has several molecular alterations with implications for its transformation to OSCC. Interestingly, Fitzpatrick *et al.*, 2014,[18] in their systematic review have presented a thought-provoking opinion that leaves the researchers to determine whether OLP has individual potential to develop into malignancy or early OSCC presents with a 'non-specific lichenoid appearance'!

Therefore, the literature provides sufficient evidence that suggests the predisposition of a rather naïve looking OLP lesion to transform into OSCC. Considering the aforementioned arguments, would it be wise to entirely omit OLP from the list of OPMDs? Although the consensus remains elusive, it is rather astute to keep OLP under the scanner, particularly the erosive/atrophic types for their higher possibility of developing into oral cancer. We feel that it is quite essential to inform the patient about the possible malignant risk of the lesion, even if it is minimal. However, we must abstain from over-exaggeration to avoid cancerphobia among patients. The diagnosis of OLP thus warrants careful clinico-histopathologic consideration, a long-term regular follow-up and accurate inclusion and exclusion criteria to assess its true malignant potential and thereby, its nomenclature as an OMPD.

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Conflicts of interest

There are no conflicts of interest.

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